THE
2020-21

Medical-Dental-Legal UPDATE

Medical Malpractice • Risk Management • Practice Management
Healthcare Law • Selected Clinical Topics

American Educational Institute, Inc.

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David R. Victor, JD
President

Dear Registrant:

You practice in a dynamic and challenging environment. While keeping clinically current is imperative, it isn't enough. You must also acquire the skills necessary to navigate a professional liability minefield, manage a more effective and efficient practice, and master a maze of healthcare laws and regulations. ***The 2020-21 Medical-Dental-Legal Update*** is designed to assist you in that endeavor.

In one course you will receive 20 hours of vital instruction from national experts in the fields of law, medicine, pharmacology, asset protection, revenue cycle management and practice management. And their presentations include topics ranging from dermatologic disorders, professional burnout, and prescription drug seekers, to sleep disorders, asset protection and lipids management.

To help you assess your level of comprehension we offer brief self-evaluations that may be taken either before or after the presentations concerned. These tests are included in this syllabus and are identified by the black edges of the pages on which they are featured.

As always, I am very interested in your reaction to this year's presentation. Please do me the favor of taking the time to complete the evaluation questions presented on screen for each presentation. In addition, I encourage you to contact any of our faculty members directly with questions or comments.

Finally, I urge you to take advantage of the diversity of professionals enrolled this week. Chances are your classmates include physicians, dentists, and attorneys. What better way to gain another perspective on these multi-faceted issues than to discuss them with a colleague from a different discipline.

Thank you for your participation and please accept my best wishes for a safe, enjoyable and enlightening visit.

Cordially,
American Educational Institute, Inc

David R. Victor, Esq
President

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COURSE OBJECTIVES

After completing ***The 2020-21 Medical-Dental-Legal Update*** you should have acquired the knowledge that will better enable you to better:

- Recognize and treat common **dermatologic disorders**.
- Manage patients with **heart failure** with reduced ejection fraction.
- Assess **cardiovascular risk** and identify cardioprotective medical and lifestyle approaches.
- Identify the symptoms of and avoid **professional burnout**.
- Identify and manage **sleep disorders**.
- **Define, diagnose and treat heart failure**.
- Safeguard your office against prescription **drug seekers**.
- Understand and utilize protocols for **lipids management**.
- Enhance the **patient experience**.
- Utilize techniques for building and protecting your **professional reputation**.
- Understand and manage **practice regulatory risk**.
- Screen for, diagnose and treat **depression**.
- **Protect personal and professional assets** from practice liabilities.
- Successfully treat **highly non-compliant patients**.
- Increase **patient collections**.
- Identify and manage **patient and business practice risks**.
- Glean valuable prognostic information from conventional **exercise stress tests**.
- Diagnose and treat **common hand problems and injuries**.
- Manage **hypertensive patients**.
- Select the most beneficial **practice corporate structure**.

All learning objectives above address IOM/ACGME core competencies.

THE 2020-21

Medical-Dental-Legal UPDATE

FACULTY DISCLOSURES

The individuals listed below have control over the content of ***The 2020-21 Medical-Dental-Legal Update***. None of them have a financial relationship with a commercial interest whose products or services are discussed in the presentation(s) over which they have control:

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Louis Kuritzky, MD, of Gainesville, Florida, is a board-certified, family practitioner and a certified Specialist in Hypertension with the American Society of Hypertension. He is clinical faculty at the Family Medicine Residency Program of North Florida Regional Medical Center in Gainesville and a clinical assistant professor emeritus at the University of Florida.

Dr. Kuritzky has given over 1,000 presentations to national and international medical audiences on dozens of clinical topics and has authored over 150 articles in journals including *New England Journal of Medicine, JAMA, Comprehensive Therapy, Hospital Practice, Consultant, Postgraduate Medicine, Journal of Pain and Palliative Care,* and *Patient Care.*

You may contact Dr. Kuritzky with any questions or comments at (352) 377–3193 or by email at lkuritzky@aol.com.

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Dermatology Potpourri

Pronounced facial flushing and persistent erythema of rosacea effectively treated by carvedilol, a nonselective β-adrenergic blocker

Chia-Chi Hsu, MD, Julia Yu-Yun Lee, MD

Journal of the American Academy of Dermatology
Volume 67, Issue 3, Pages 491-493 (September 2012)
DOI: 10.1016/j.jaad.2012.04.017

ELSEVIER

Erythematotelangiectatic Rosacea Endorsed Treatments

Severe Erthyematotelangiectatic Rosacea

- B-Blockers
- Clonidine
- Naloxone
- Ondansetron
- Endoscopic Thoracic Sympathectomy

HSU CC, Lee JYY J Am Acad Dermatol 2012;67(3):491-492

ETR: Carvedilol Case Series

- Study: ETR Case series (n= 11)
- Based upon initial success in 1 case
- Previous Failed Rx with ≥1 of
  - Doxycycline
  - Corticosteroids
  - Propranolol
  - Clonidine
  - Metronidazole
  - Ondansetron
  - Tacrolimus/pimecrolimus
  - Thoracic sympathectomy
  - Stellate ganglion block
  - Pulsed dye laser

HSU CC, Lee JYY J Am Acad Dermatol 2012;67(3):491-492

ETR: Carvedilol Case Series

- Rx: carvedilol 3.125 mg/d → 31.25 mg/d divided b.i.d.-t.i.d. added to existing Rx x 1 yr
- Metrics:
  - Photo-based facial erythema
  - Cheek temperature
  - VAS 0-10 (pt assessment)

HSU CC, Lee JYY J Am Acad Dermatol 2012;67(3):491-492

ETR: Carvedilol Case Series Results

"All patients experienced significant clinical improvement within 3 weeks (range 3-21 days, mean 10.5 days)."

HSU CC, Lee JYY J Am Acad Dermatol 2012;67(3):491-492

ETR: Carvedilol Case Series Results

	Carvedilol
Cheek Temperature	↓2.2^0 C
VAS: Baseline	8.4/10
VAS End of Rx	2.1/10
	*all results are MEAN

HSU CC, Lee JYY J Am Acad Dermatol 2012;67(3):491-492

ETR: Carvedilol Case Series Discussion

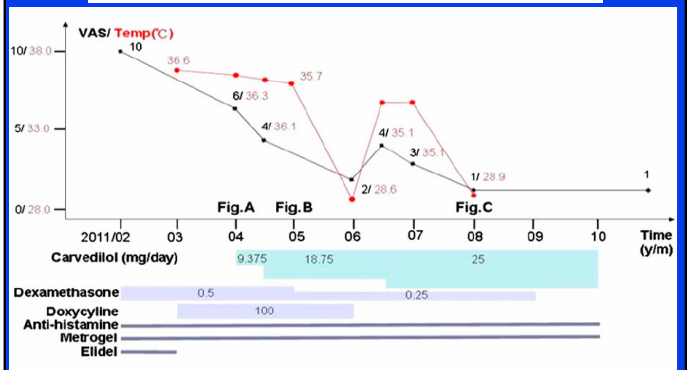
"Carvedilol appears special among β-blockers in its significant antioxidant and anti-inflammatory properties, which may explain its efficacy in treating ETR in the current study."

HSU CC, Lee JYY J Am Acad Dermatol 2012;67(3):491-492

Carvedilol for ETR

HSU CC, Lee JYY
J Am Acad Dermatol 2012;67(3):491-492

Carvedilol: Rosacea



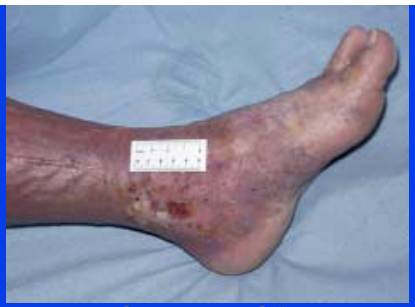
HSU CC, Lee JYY J Am Acad Dermatol 2012;67(3):491-492

Venous Ulcers: Simvastatin?

"Simvastatin has shown potential wound-healing properties; however, no studies have investigated its use in venous ulcers."

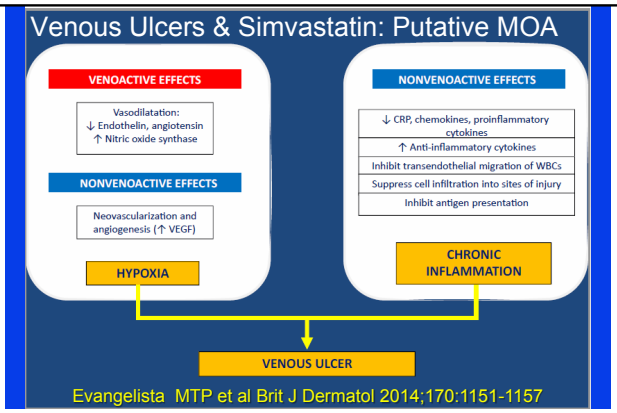
Evangelista MTP et al Brit J Dermatol 2014;170:1151-1157

Venous Insufficiency Ulcer



Grey JE, Enoch S, Harding KG "Venous and arterial leg ulcers" BMJ 2006;332:Feb 11:347-350

Venous Ulcers & Simvastatin: Putative MOA



Evangelista MTP et al Brit J Dermatol 2014;170:1151-1157

Venous Ulcers: Simvastatin?

- Study: RDBPCT venous insufficiency ulcers (n=66)
- Rx: ≤10 wks simvastatin 40 mg/d vs pbo
  - All pts: elevation, compression, etc.
- Outcome: Ulcer healing

Evangelista MTP et al Brit J Dermatol 2014;170:1151-1157

Venous Ulcers & Simvastatin: Outcomes

	Placebo	Simvastatin	p
All Ulcers			
Healed	34%	90%	*
Time to Heal	8.55 weeks	7.53 weeks	
Ulcer ≤ 5 cm			
% Healed	50%	100%	*
Time to Heal	6.89 weeks	8.40 weeks	*
Ulcer > 5 cm			
% Healed	0%	67%	*
Time to heal		9.17 weeks	

Evangelista MTP et al Brit J Dermatol 2014;170:1151-1157

Venous Ulcers & Simvastatin: Outcomes

"…simvastatin 40 mg daily, in addition to standard wound care and compression, is associated with a significant improvement in healing rate and time, as well as improved patient quality of life when compared with placebo…."

Evangelista MTP et al Brit J Dermatol 2014;170:1151-1157

Venous Insufficiency Ulcers: Physical Therapy

"Leg elevation…is also considered standard of care. Leg elevation requires raising lower extremities above the level of the heart…"

Collins L, Seraj S "Dx and Rx of Venous Ulcers" Amer Fam Phys 2010;81(8):989-996

Schamberg's Disease

- AKA: Progressive pigmented purpuric dermatosis, Purpura Simplex
- Males > Females
- Cause Unknown
- Characteristic feature: "orange-brown, pinhead-sized 'cayenne pepper' spots."
- "Lesions persist, but 67% eventually clear."

Habif T Clinical Dermatology 6th Edition Elsevier 2016

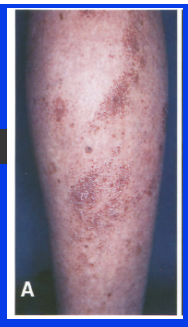
Schamberg's Disease: Pentoxifylline

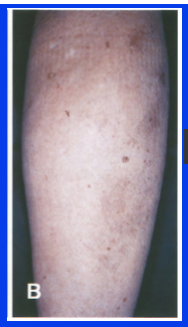
- Study: Schamberg's disease patients (n=3)
- Rx: pentoxifylline 300 mg t.i.d. x 8 weeks
- Site: Tokyo, Japan
- Outcome: all 3 improved; 1 recurrence responded to re-Rx

Kano Y, et al J Am Acad Dermatol 1997;36:827-830

Schamberg's: Pentoxifylline Rx x 8 weeks

Before





After

Kano Y, et al J Am Acad Dermatol 1997;36:827-830

Schamberg's Disease: Pentoxifylline

- Study: Schambergs Disease patients (n=30)
- Rx: pentoxifylline 400 mg t.i.d. X 9 weeks

	Mild	Moderate	Marked
Improvement	4 (13.3%)	5 (16.6%)	17 (56.6%)

"Improvement was seen in 26 (86.6%) of patients."

- "We conclude that pentoxifylline should be considered as 1st line therapy in all patients with Schamberg's disease."

Majid RM J Pakistan Assoc Dermatologists 2008;18:97-99

Pharmacology & Pharmacy, 2013, 4, 266-273
http://dx.doi.org/10.4236/pp.2013.42038 Published Online April 2013 (http://www.scirp.org/journal/pp)

Scientific Research

Evaluation of the Efficacy and Safety of 1% Sodium Chloride (LiceFreee Spray) against 1% Permethrin Crème Rinse on Head Lice Infested Individuals

Lidia Serrano[1], Lorraine S. Decesar[1], Loan Pham[2*]

Pediculosis capitis
1% NACL vs 1% Permethrin Creme

PREMISES

- Various Rx methods: physical removal, combs, topicals, systemic agents
- Typical topical: day 0 and day 7-10
  - Dose #1 kills nymphs/adults but not ovae
  - Dose #2: allows hatched ovae kill
- Resistance problems: permethrin sensitivity 97-99% (1998)→ 10-72% > 1999

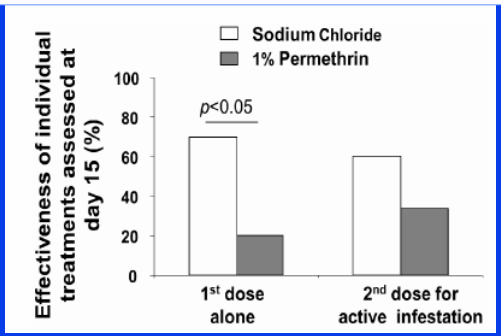
Serrano L, et al Pharmacology & Pharmacy 2013;4:266-273

Pediculosis capitis
1% NACL vs 1% Permethrin Creme

- Study: patients (age 6-43) with at least 10 live head lice identified (n = 42)
- Family screened: enrolled if +
- Outcome: Presence of live lice day 8, 15

Serrano L, et al Pharmacology & Pharmacy 2013;4:266-273

Lice-Free at Day 15



Serrano L, et al Pharmacology & Pharmacy 2013;4:266-273

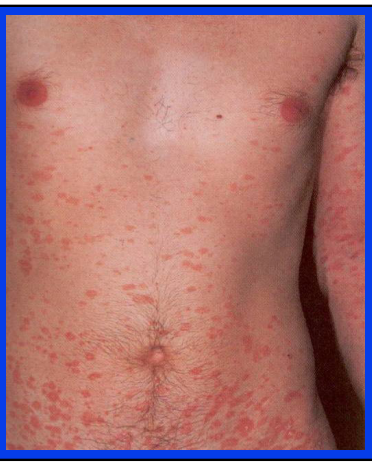
How Come NaCl Works At all?

"…in vitro data have shown that the ovicidal activity of gelled 1% NaCl formulation is > that of permethrin…..the in vivo ovicidal efficacy of NaCl Spray has yet to be determined…."

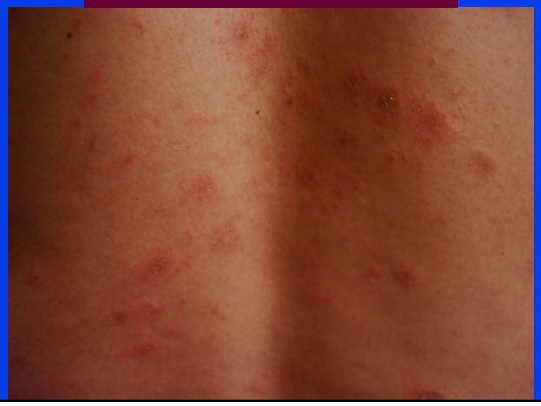
Serrano L, et al Pharmacology & Pharmacy 2013;4:266-273

Hx

- A 23 y.o. grad student complains of rash for one week. Rash is 'all over', and mild-moderately pruritic
- SH/FH/ROS: nothing contributory
- No meds
- No known new contacts



His Back



Pityriasis Rosea: Definition

- pityriasis ion [Greek: *pityron* bran + iasis]
  - "a name originally applied to a group of skin diseases characterized by the formation of fine branny scales, but now used only with a modifier"

Dorland's Illustrated Medical Dictionary 26th Edition
1981 WB Saunders (Philadelphia)

Pityriasis Rosea

- Common, benign, self-limiting, usually aSx
- Etiology? "there is some evidence that it is viral in origin" (Frat house and military base outbreaks)
- >75% between age 10-35 (mean = 25)
- Antecedent URI: 68.8%
- DDx: secondary syphilis, guttate psoriasis, viral exanthems, drug eruption

Habif T *Clinical Dermatology* 2004 Mosby (Philadelphia)

Pityriasis Rosea: Clinical

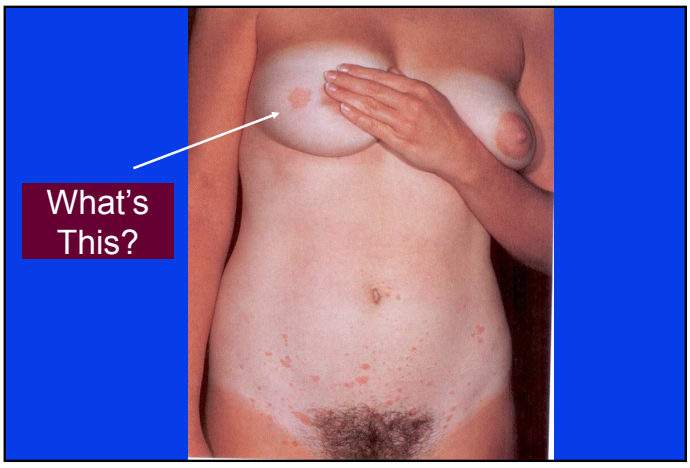
- Herald Patch: 2-10 cm round-oval lesion appears abruptly (17%)
  - Site: anyplace (trunk or proximal extremities most common)
  - May be mistaken for tinea
- Eruptive phase (mean 7-14 days post HP)
  - Max lesions within 2 weeks
  - Truncal mostly (6% extremity dominant)

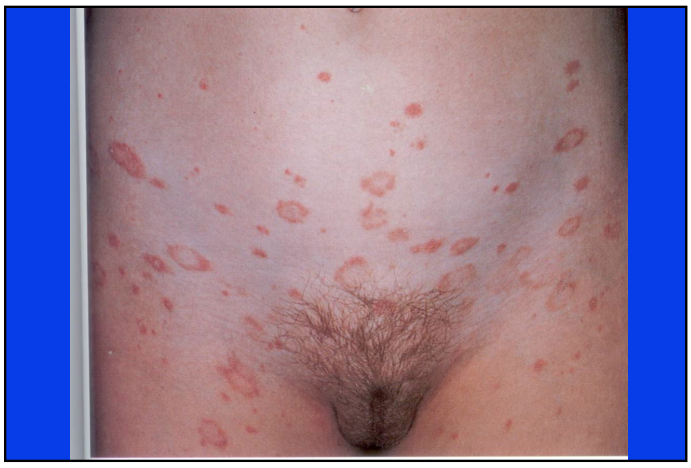
Habif T *Clinical Dermatology* 2004 Mosby (Philadelphia)

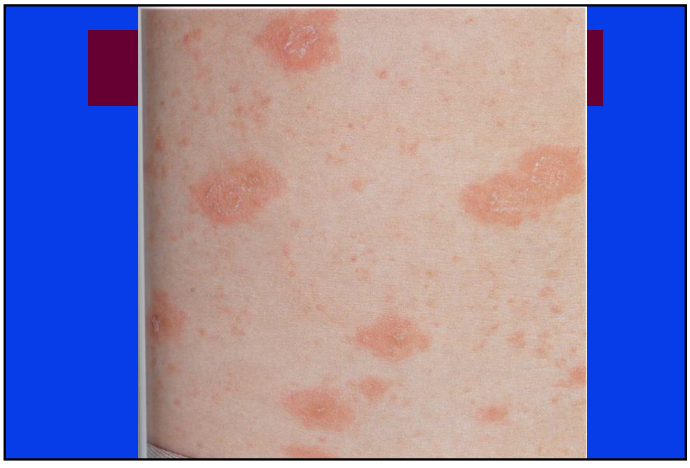
Pityriasis Rosea: Clinical Lesions

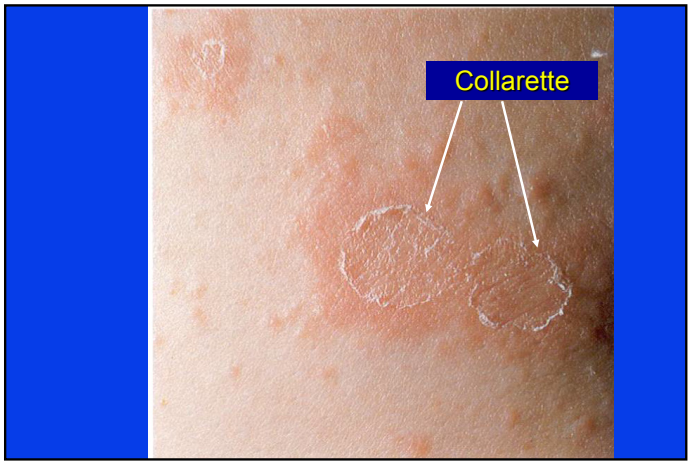
- Adults: oval plaques
- Children, PG women, sometimes blacks: more commonly papular
- Lesion coloration
  - Caucasians: pink
  - Blacks: hyperpigmented
- Lesion orientation: skin lines ('Xmas tree')
- Fine wrinkled scale (collarette)

Habif T *Clinical Dermatology* 2004 Mosby (Philadelphia)









Pityriasis Rosea: Acyclovir

- PREMISE: HHV-6/HHV-7 associated
- STUDY: consecutive PR patients (n=87) Department of Dermatology
- Rx: 7 d acyclovir 800mg 5 x/d vs placebo
- LAB (serology):
  - HHV-6, HHV-7
  - EBV, V-Z, CMV, Rubella, Parvo 19
  - Borrelia, Toxo

Drago F, Vecchio F, Rebora A "Use of high-dose acyclovir in pitryriasis rosea" J Am Acad Dermatol 2006;54-82

Pityriasis & Acyclovir: Demographics

	Acyclovir	Placebo
Age	28.4 (18-40)	26.5 (18-37)
Men	24	25
Women	18	20
Herald Patch	95%	84%
Systemic Sx	45.2%	35.6%
IgM HHV-6	2/24	2/19
IgM HHV-7	5/24	2/19

Drago F, Vecchio F, Rebora A "Use of high-dose acyclovir in pitryriasis rosea" J Am Acad Dermatol 2006;54-82

Pityriasis: Acyclovir Rx Success

Treatment	Partial Regression at Day 7	Partial Regression at Day 14	Complete Regression at Day 7	Complete Regression at Day 14
Placebo	22.2%	40%	4.5%	4.4%
Acyclovir	61.9%	11.9%	28.6%	78.6%

Drago F, Vecchio F, Rebora A "Use of high-dose acyclovir in pitryriasis rosea" J Am Acad Dermatol 2006;54-82

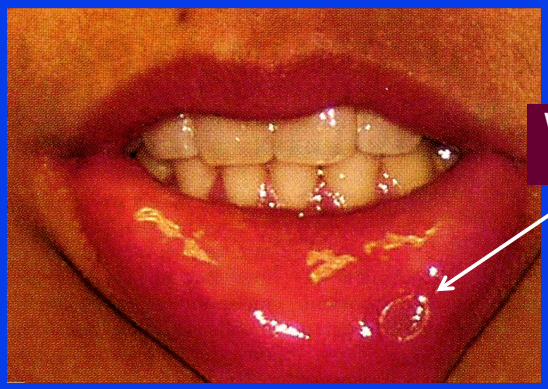
Pityriasis: Acyclovir Rx Success

Treatment	Onset of New Lesions at Day 7	Onset of New Lesions at Day 14	Reduction of Systemic Sx at Day 7	Reduction of Systemic Sx at Day 14
Placebo	100%	55.6%	0%	2.2%
Acyclovir	40.5%	9.5%	36.8%	33.3%

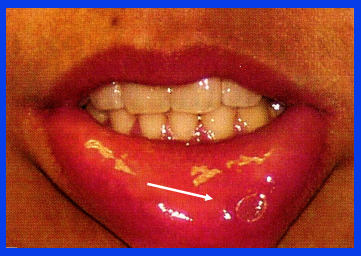
Drago F, Vecchio F, Rebora A "Use of high-dose acyclovir in pitryriasis rosea" J Am Acad Dermatol 2006;54-82

Those Clever 1950's TV Ads

"_____ has been shown to be an effective decay-preventive dentifrice that can be of significant value when used as directed in a conscientiously applied program of oral hygiene and regular professional care."



Recurrent Apthous Ulcers: What to Do?



Sodium lauryl sulfate (SLS) & Recurrent Aphthous Ulcers

- PREMISE: 1989 study compared SLS-free TP with SLS-TP in allergic stomatitis patients
- STUDY: compare frequency of multiple minor recurrent aphthous ulcers: SLS TP vs SLS-free TP
- SUBJECTS: 10 healthy volunteers (lab screen WNL) with Hx multiple recurrent aphthous ulcers

Herlofson B, Barkvoll P. "Sodium lauryl sulfate and recurrent aphthous ulcers" Acta Odontol Scand 1994;52:257-259

Sodium Lauryl Sulfate and Recurrent Aphthous Ulcers

- METHOD: 3 month run-in with regular TP (all contained SLS) Rx : SLS-TP vs SLS-free TP X 3 months, then crossover
- RESULTS: mean ulcers = 17.8 → ↓ 5.1

Herlofson B, Barkvoll P. "Sodium lauryl sulfate and recurrent aphthous ulcers" Acta Odontol Scand 1994;52:257-259

Sodium lauryl sulfate and Recurrent Aphthous Ulcers

"…. it appears likely that SLS may denature the mucosal mucin layers. Mucins are principal organic constituents of mucus, the visco-elastic material that covers all mucosal surfaces."

Herlofson B, Barkvoll P. "Sodium lauryl sulfate and recurrent aphthous ulcers" Acta Odontol Scand 1994;52:257-259

Some SLS-Free Toothpastes

- Hello
- Verve
- Tom's of Maine
- Himalaya Neem and Pomegranate
- Red Seal

Amazon.com Accessed Sept 16, 2018

Recurrent Apthous Ulcers

- Premise: incidental observation β-blocker (for another indication) → improvement in aphthous ulcers
- Study: (n=95) propranolol 30 mg/d X 7d, 20 mg/d X 7 d, 10 mg/d X 65d
- Inclusion: 2-7 ulcers at baseline, recurrences Q6-8 weeks
- Exclusion: herpes, Behcets

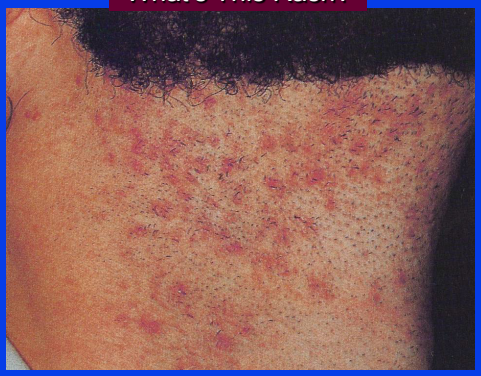
Goldman EK "β-Blocker Effective in Clearing Recurrent Aphthous Ulcers" Family Practice News 2002 (Nov 1):24

Recurrent Apthous Ulcers: Results

- Complete resolution: 72/95 (68%) v 6/84 (7.7%) placebo
- Partial improvement: 23/95 (32%)
- Some patients remain disease free X 3 years
- No adverse effects
- Subtherapeutic level of Rx for BP impact

Goldman EK "β-Blocker Effective in Clearing Recurrent Aphthous Ulcers" Family Practice News 2002 (Nov 1):24

What's This Rash?



Pseudofolliculitis Barbae (Razor Bumps)
AKA Acne Keloidalis Nuchae

- Ex: Curving hair growing back into skin
- 10-30 X more common in African Americans
- Standard Rxs:
  - D-C shaving
  - Dislodge hair with needle
  - Depilatories (Ba Sulfide, Ca Thioglycolate): 3-10 min application → ↓ hair shaft sulfide bonds → soft fluffy hair tip on breakage

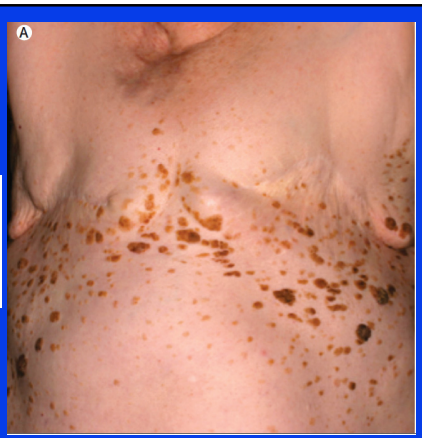
Habif T P. Clinical Dermatology 3rd Edition 1996 Mosby (St Louis)

Eflornithine (Vaniqa) for Pseudofolliculitis

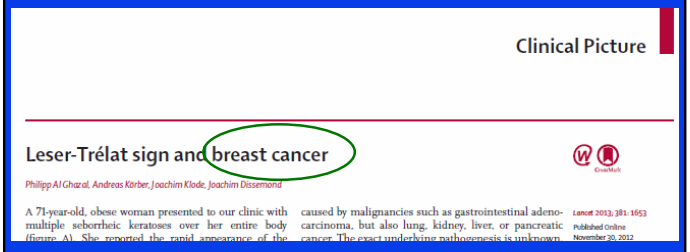
- Study: AA men (n = 10) ≥ grade 3 Pseudofolliculitis, present at least 2 years
- Rx : eflornithine 13.9% cream b.i.d. X 16 wks
- Results: ≥1 point ↓ PB severity scale in 8/10

Tucker ME "Eflornithine Cream Helps Eliminate 'Razor Bumps in Black Men" Family Practice News 2001; October 15: page 9

Leser-Trelat Sign
Sudden Eruption and Rapid Increase in Size and # of seborrhoeic keratoses



Ghazal PA et al Lancet 2013;381(May 11): p 1653



Clinical Picture

Leser-Trélat sign and breast cancer

Philipp Al Ghazal, Andreas Körber, Joachim Klode, Joachim Dissemond

A 71-year-old, obese woman presented to our clinic with multiple seborrheic keratoses over her entire body (figure A). She reported the rapid appearance of the caused by malignancies such as gastrointestinal adenocarcinoma, but also lung, kidney, liver, or pancreatic cancer. The exact underlying pathogenesis is unknown

Lancet 2013; 381: 1653
Published Online November 30, 2012

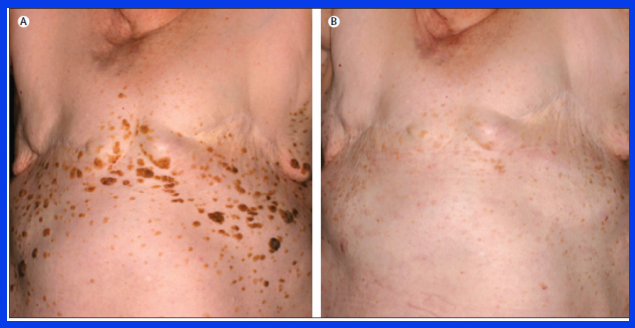
Ghazal PA et al Lancet 2013;381(May 11): p 1653

Leser-Trelat Sign

"It is usually caused by malignancies such as GI adenocarcinoma, but also lung, kidney, liver, or pancreatic cancer. The exact underlying pathogenesis is unknown."

Ghazal PA et al Lancet 2013;381(May 11): p 1653

Success with Seborrheic Keratoses



Ghazal PA et al Lancet 2013;381(May 11): p 1653

The impact of chocolate consumption on acne vulgaris in college students: A randomized crossover study

Delost GR, Delost ME, Lloyd J
J Am Acad Dermatol 2016;75(1):220-222

Acne Lesions: Chocolate vs Jelly Beans

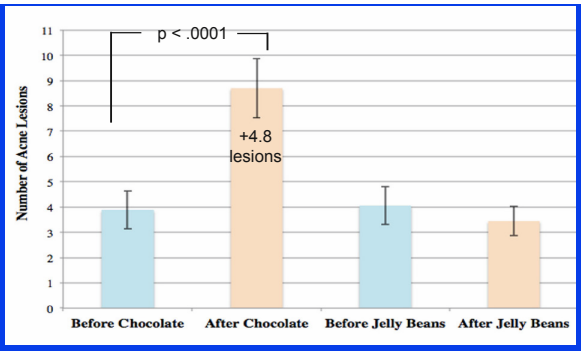
- Study: Single-blind randomized XO study Youngstown State Univ students (n=60)
- Rx: One Hershey's milk chocolate bar (= 1.55 oz) vs 15 jelly beans (equivalent glycemic load) then cross-over
- Outcome: Acne lesions at 48 hrs post 'dose'

Delost GR, Delost ME, Lloyd J *J Am Acad Dermatol* 2016;75(1):220-222

Acne Lesions: Chocolate vs Jelly Beans

Delost GR, Delost ME, Lloyd J *J Am Acad Dermatol* 2016;75(1):220-222

Acne Lesions: Chocolate vs Jelly Beans



Delost GR, Delost ME, Lloyd J *J Am Acad Dermatol* 2016;75(1):220-222

Acne Chocolate vs Jelly Beans Conclusions

"…the chocolate consumption group had a statistically significant increase in acne lesions…present across gender, age, frequency, and severity classifications."

Delost GR, Delost ME, Lloyd J *J Am Acad Dermatol* 2016;75(1):220-222

Acne & Chocolate: Why?

"Netea et al demonstrated that chocolate consumption primed human blood mononuclear cells to release more proinflammatory cytokines, interleukin1β, and TNFα upon stimulation with *Propionibacterium acnes*."

Delost GR, Delost ME, Lloyd J *J Am Acad Dermatol* 2016;75(1):220-222

Chocolate & Cognitive Function

"A subclass of flavonoids called flavanols, which are widely present in cocoa, green tea, red wine, and some fruits, seems to be effective in slowing down or even reversing the reductions in cognitive performance that occur with aging."

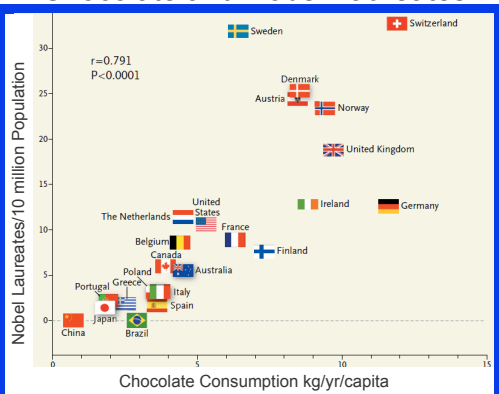
Messerli RH Chocolate Consumption, Cognitive Function, and Nobel Laureates" NEJM 2012;367(16):1562-1564

Chocolate & Cognitive Function

"Dietary flavanols have also been shown to improve endothelial function and to lower BP by causing vasodilation in the peripheral vasculature and in the brain."

Messerli RH Chocolate Consumption, Cognitive Function, and Nobel Laureates" NEJM 2012;367(16):1562-1564

Chocolate and Nobel Laureates



Messerli FH NEJM 2012;367:16:11562-1564

How Much Chocolate, Then?

"The minimally effective chocolate dose seems to hover around 2 kg/year, and the dose-response curve reveals no apparent ceiling…"

Messerli RH Chocolate Consumption, Cognitive Function, and Nobel Laureates" NEJM 2012;367(16):1562-1564

Relation of Diagonal Ear Lobe Crease to the Presence, Extent, and Severity of Coronary Artery Disease Determined by Coronary Computed Tomography Angiography

Haim Shmilovich, MD[a,*], Victor Y. Cheng, MD[b], Ronak Rajani, MD[a], Damini Dey, PhD[b], Balaji K. Tamarappoo, MD, PhD[a], Ryo Nakazato, MD, PhD[a], Thomas W. Smith, MD[a], Yuka Otaki, MD, PhD[a], Rine Nakanishi, MD, PhD[a], Heidi Gransar, MS[a], William Paz, RT[a], Raymond T. Pimentel, RT[a], Sean W. Hayes, MD[b], John D. Friedman, MD[b], Louise E.J. Thomson, MBChB[b], and Daniel S. Berman, MD[b]

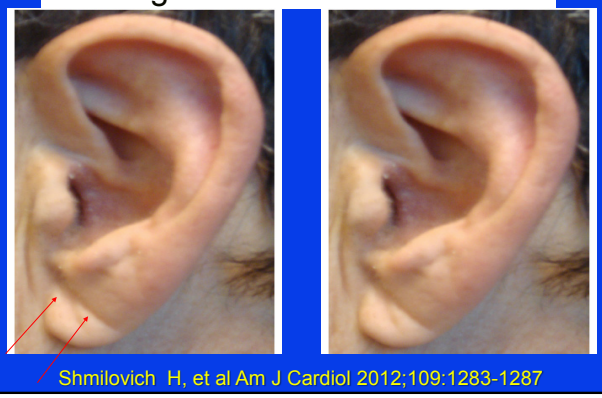
Am J Cardiol 2012;109:1283-1287

Frank's Sign

"Diagonal ear lobe crease (DELC)…is a wrinkle-like line extending diagonally from the tragus across the lobule to the rear edge of the auricle of the ear….first associated with CAD…by Frank published in 1973."

Shmilovich H, et al Am J Cardiol 2012;109:1283-1287

Diagonal Ear Lobe Crease



Shmilovich H, et al Am J Cardiol 2012;109:1283-1287

Frank's Sign: Valid?

"Controversy exists concerning the relation between diagonal ear lobe crease and CAD"

Shmilovich H, et al Am J Cardiol 2012;109:1283-1287

Frank's Sign: Valid?

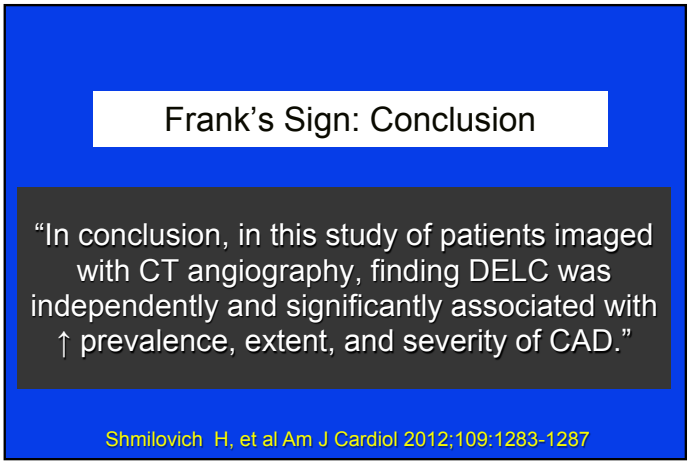
- Study: aSx Adults with no Hx CAD (n=430)
- Metric: Coronary CT Angiography
- Endpoints:
  - Any CAD
  - Significant CAD (≥50% stenosis)
  - Multivessel disease
  - # segments with plaque

Shmilovich H, et al Am J Cardiol 2012;109:1283-1287

Frank's Sign: Outcome

"After adjusting for confounders, DELC remained a significant predictor of all 4 measurements of CAD (Odds Ratio 1.8-3.3, p 0.002-0.017)."

Shmilovich H, et al Am J Cardiol 2012;109:1283-1287



SELF EVALUATION

Dermatology Potpourri

1. A 36 y.o. has failed multiple treatments to reduce facial flushing attributed to rosacea. She is frustrated that people keep inquiring about excessive alcohol intake, since she does not drink. She has failed multiple 'traditional' treatments. What might help?

a. Niacin (as nicotinic acid) 2 g daily p.o.
b. Nifedipine 60 mg po
c. She should stop lying about being a non-drinker & sober-up
d. Carvedilol

2. Marcus A is a 62 y.o. man with a venous insufficiency ulcer that has failed elevation, compression, pentoxifylline, and aspirin. What else might help?

a. Simvastatin
b. Ramipril
c. Doxycycline
d. Carbamazepine

3. Ellen is a 68 y.o. woman with a recalcitrant venous insufficiency ulcer. She has tried elevation for 30 minutes 4 times daily by sitting in her recliner. Are there additional physical therapy maneuvers she might employ?

a. No; elevation is elevation and it has failed
b. No: 30 minutes is twice as much as she needs
c. Yes, but they do not employ elevation
d. Yes, but technique of elevation must be clarified

4. A 48 y.o. man seeks advice about asymptomatic spots on both lower legs, gradually progressive for at least 5 years. No other health problems or medications. This is

a. Uniformly fatal guttate melanosis.
b. Schamberg's Disease
c. Lamivudine toxicity from adulterated cocaine
d. Venous insufficiency

5. "But Doc, I am embarrassed to wear shorts, people think I have some weird contagious disease. Isn't there anything I can do to get rid of it?" You might try

a. Pentoxifylline (Trental)
b. Cryotherapy
c. Imiquimod (Aldara)
d. Venous insufficiency

6. A 6 y.o. child was sent home from school because of head lice. Which of the following topical agents has demonstrated the greatest treatment efficacy?

a. 1% Permethrin Cream Rinse(Elimite, NIX)
b. 1% NaCl (LiceFreee Spray)
c. Mupirocin Cream (Bactroban)
d. Fluticasone Spray (Flonase)

7. Pityriasis Rosea: How could you treat this?

a. Acyclovir
b. Fluconazole
c. Selenium Sulfide Shampoo
d. No treatment is required

8. A 42 y.o. otherwise healthy male physician complains of recurrent multiple aphthous ulcers since he was an adolescent. Non-smoker, no chewing tobacco, no illicit substances or medications. What is causing this?

a. Recurrent herpes virus infections
b. Bechet's syndrome
c. Recurrent adenovirus infections
d. Sodium Laurel Sulfate (SLS) in toothpaste

9. A 24 y.o. AA man joined the Army 6 months ago. He has shaved his hair to conform to regulations, but now has irritating bumps on his neck. The bumps represent

a. Pseudofolliculitis barbae
b. Condyloma acuminata
c. Diffuse papilloma infection
d. Allergy to his shave cream

10. A college student asks your opinion about acne. Which of the following might actually worsen acne

a. Facial cleansing soap < t.i.d.
b. Chocolate
c. Jelly Beans
d. Masturbation

Answer Key: 1. D, 2. A, 3. D, 4. D, 5. A, 6. B, 7. A, 8. D, 9. A, 10. B

Carole C. Foos, CPA

Carole C. Foos, CPA of Cincinnatti, Ohio is a partner in OJM Group, a physician focused financial planning and asset management firm, and a Certified Public Accountant (CPA) offering tax analysis and tax planning services to the firm's clients. Carole has over 25 years of experience in accounting, tax planning and financial consulting. She is a co-author of numerous books for physicians, including Wealth Management Made Simple and newly published Wealth Planning for the Modern Physician: Residency to Retirement. Carole has authored numerous articles and presented many lectures, webcasts, and podcasts on tax planning and wealth management.

You may contact Ms. Foos with your questions and comments at 513-309-3946, or by email at Carole@OJMGroup.com.

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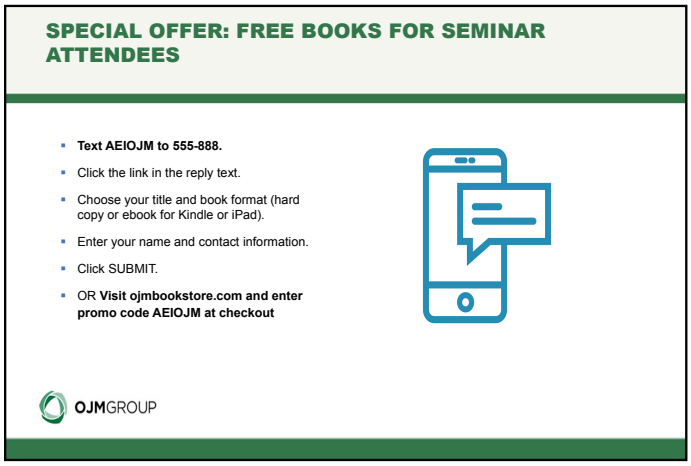
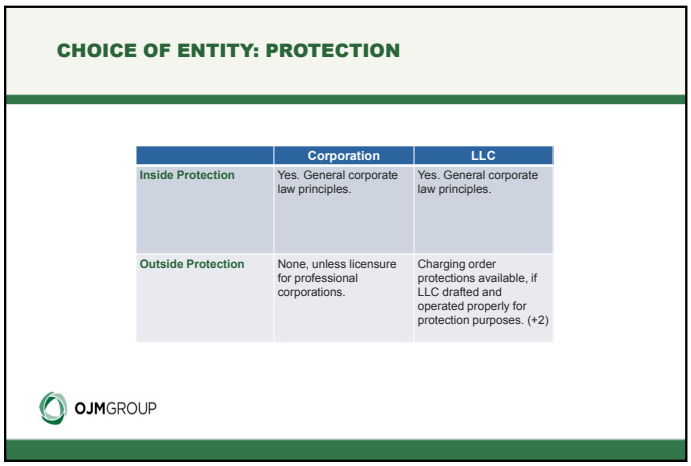
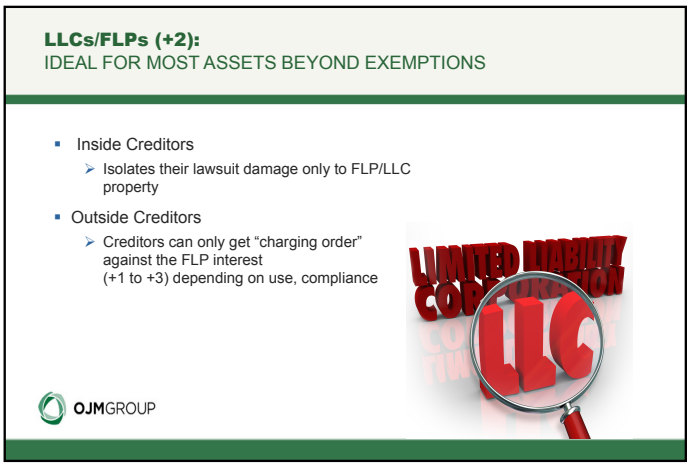
Choosing the Optimum Practice Corporate Structure - Parts 1 & 2

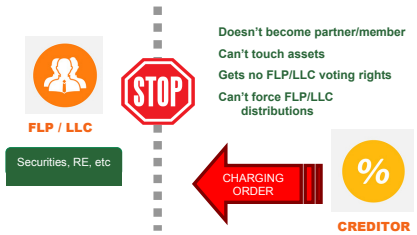
Carole C. Foos, CPA







WHAT A *CHARGING ORDER* MEANS



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KEYS TO PROTECTION: LLCs/FLPs

- Proper partnership/operating agreement
- Compliance with annual formalities
- Key: experienced attorney who has annual monitoring/gifting plan
- Without the elements above, the LLC/FLP may not protect

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PROS AND CONS

- Sole Proprietorship / Single Member LLC
  - Sole proprietorship lacks asset protection and exit planning
    - Complete managerial control for owner
    - Personal liability
  - Single member LLC can choose to be taxed as a corporation
  - Single member LLC disregarded entity taxed like a sole proprietor
  - Form 1040 with Schedule C / self employment/ individual tax rates

- Multiple Member LLC
  - Legal entity provides good asset protection
  - Choose how you are taxed

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SOLE PROPRIETORSHIP

Revenue $1.8 million

Net Taxable Income $900,000

Tax Liability *

Income Tax	$270,149
Self Employ & addl med	$ 46,408
Total Tax	$316,557

* assumes married filing jointly, 2020 with $900,000 of taxable income and self employment income of $900,000

- First $250k income subject to 2.9% Medicare tax; rest subject to 3.8% Medicare tax
- All income reported on individual Form 1040
- Long term care premiums subject to age based limitations

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PROS AND CONS

Partnership

- Files Form 1065
- Income flows to individual tax returns of partners and taxed at individual rates and generally subject to SE tax
- May be taxed on undistributed income
  - General Partnership
    - All partners liable for company debt and liabilities
    - Ability to specially allocate expenses and make disproportionate distributions
    - General partners can make binding decisions/ borrow money
    - Allocated recourse debt = basis
  - Limited Partnership
    - General partners liable for debt and liabilities
    - Limited partners don't have management responsibilities or liability
    - Not usually feasible for medical practice

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PARTNERSHIP

Revenue $1.8 million

Net Taxable Income $900,000

Tax Liability *

Income Tax	$270,149
Self Employ& addl med	$ 46,408
Total Tax	$316,557

* assumes married filing jointly, 2020 with $900,000 of taxable income and self employment income of $900,000

- First $250k income subject to 2.9% Medicare tax; rest subject to 3.8% Medicare tax
- All income reported on individual Form 1040
- Long term care premiums subject to age based limitations

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PROS AND CONS

Corporation

- Files entity tax return (1120 or 1120S)
- C Corporation
  - Net income subject to corporate tax rates (21% flat rate)
  - Distributions of profits to shareholders taxed as dividend income to shareholders personally
  - Can reduce corporate profit and corporate level tax with reasonable compensation to shareholders
  - Can deduct shareholder health insurance, group term life and long-term care insurance
  - Can utilize medical reimbursement plans and flexible spending plans
  - May have double level of tax upon sale

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C CORPORATION WITH OWNER COMP

Revenue $1.8 million
Other operating expenses
$900,000

Bonus and Salary to Owner $800,000

Net Corporate Profit $100,000

Tax Liability *	
Salary from C corporation	$800,000
Income Taxable to Owner	$800,000
Individual Income Tax	$233,149
FICA & Medicare tax – ER share	$ 20,137
FICA & Medicare tax – EE share	$ 25,087
Corporate Tax	$ 21,000
Total Tax	$299,373

- $800,000 subject to Medicare tax
- Separate corporate return filed
- Income not zeroed out in corporation subject to corporate tax (double taxation possibility)
- Long term care premiums not subject to age based limitations, fully deductible

* assumes married filing jointly, 2020 with $800,000 of taxable income and compensation income of $800,000
* assumes other corporate deductible expenses of $900,000

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PROS AND CONS

Corporation

- S Corporation
  - Generally no tax at corporate level
  - Income and loss flow to individual shareholder returns and taxed at individual rates
    - May be taxed on undistributed income
  - Reasonable compensation to shareholders providing services via W2 wages
  - Distributions of profits not subject to Medicare tax or double taxation
    - Distributions must be pro-rata based on ownership
  - No corporate deduction for health insurance for >2% shareholders (may be able to take SE Health Insurance deduction on 1040)
  - No flexible spending et al for >2% shareholders
  - Gain on sale flows to shareholder level

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S CORPORATION

Revenue $1.8 million

Salary to Owner $450,000

S Corporation Distribution $450,000

Net Taxable Income to Owner $900,000**

Tax Liability *	
Income Tax	$270,149
FICA Tax (employer and employee)	$ 31,925
Total Tax	$302,074

- $450,000 subject to 2.9% / 3.8% Medicare tax
- Separate S Corporation return filed
- All net S corp income flows to individual return, regardless of amount distributed to owner
- Long term care premiums subject to age based limitations

* assumes married filing jointly, 2020 with $900,000 of taxable income and compensation income of $450,000

** $450k of salary plus $450k of net S corp income which is distributed

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PROS AND CONS

Multiple Entity Structure

- Can you bifurcate business divisions?
- Separate assets to protect them?
- Take advantage of various structures' tax benefits?

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MEDICAL PRACTICE: MULTIPLE ENTITIES

Traditional Benefits: Profit-Sharing, 401(k)

(Affiliated service rules apply)

PRACTICE ENTITY *(PC)*

EMPLOYEES OWNERS

SERVICES AGREEMENT

C Corp Sponsored Traditional Benefits

LTCI, Non-qualified *(Affiliated service rules apply)*

MANAGEMENT / BILLING / MARKETING ENTITY

C CORP OR LLC TAXED AS C

OWNERS ***EMPLOYEES POSSIBLE***

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PROS AND CONS

- Asset Protection
  - Claims of admin. entity / employees separated from medical practice and *vice versa*
- Tax
  - Doctors can access benefits of S and C Corporations. Can be significant tax savings.
- Exit Strategy
  - Benefits can tie to long-term Exit Strategy

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TWO-ENTITY STRUCTURE

- Separate corporate return filed
- $450,000 subject to 2.9% / 3.8% Medicare tax
- Income not zeroed out in corporation subject to corporate tax (double taxation possibility)
- Long term care premiums not subject to age based limitations, fully deductible

S Corp Medical Practice

Revenue $1.5 million
Expenses $900,000 Owner Salary $200,000
S distribution $400,000

C Corp Marketing Corp

Revenue $300,000
Salary to Owner $250,000
C corp profit $50,000

Tax Liability *	
S Corporation Income	$ 400,000
Salary from C corporation	$ 250,000
Salary from S Corp	$ 200,000
Taxable Income	$ 850,000
Income Tax	$ 251,649
FICA tax – employer share	$ 15,062
FICA tax – employee share	$ 16,862
Corporate Tax	$ 10,500
Total Tax	$294,073

* assumes married filing jointly, 2020 with $850,000 of taxable income and compensation income of $450,000

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SUMMARY

- Highest tax resulted from sole proprietorship / partnership
  - All income subject to FICA / Medicare
- Two-Entity structure had lowest current tax
  - Owner got $850,000 vs $900,000
  - $50k left in corp will be subject to dividend tax when distributed – likely $10,000 plus $1,900 NII ($305,973)
- C corporation had second lowest current tax
  - Owner got $800,000 vs. $900,000
  - $100k left in corp will be subject to dividend tax when distributed – likely $20,000 plus $3,800 NII ($323,173)

- **Must consider potential additional C Corp deductions you would take advantage of as well as exit strategy, debt structure and distributions**

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CONTACT ME

- Schedule a free no-obligation consultation
- Contact the presenter:
  - Carole C. Foos, CPA
  - 877.656.4362
  - carole@ojmgroup.com

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DISCLOSURE

The information, analysis, and opinions expressed herein are for general and educational purposes only. Nothing contained in this commentary is intended to constitute personalized legal, tax, accounting, securities, or investment advice, nor an opinion regarding the appropriateness of any investment, nor a solicitation of any type. All investments carry a certain risk, and there is no assurance that an investment will provide positive performance over any period of time. An investor may experience loss of principal. Investment decisions should always be made based on the investor's specific financial needs and objectives, goals, time horizon, and risk tolerance. The asset classes and/or investment strategies described may not be suitable for all investors and investors should consult with an investment advisor to determine the appropriate investment strategy. Past performance is not indicative of future results. Indices are unmanaged and their returns assume reinvestment of dividends and do not reflect any fees or expenses. It is not possible to invest directly in an index. Information obtained from third party sources are believed to be reliable but not guaranteed. All opinions and views constitute our judgments as of the date of writing and are subject to change at any time without notice.

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SELF EVALUATION

Choosing the Optimum Practice Corporate Structure - Parts 1 & 2

1. A single member LLC cannot be taxed as

a. A corporation
b. A partnership
c. An S corporation
d. A sole proprietorship

2. T/F - A C corporation can deduct shareholder health insurance, group term life insurance and long term care insurance.

3. T/F - Distributions of S corporation profits are subject to Medicare tax.

4. T/F - A corporation provides superior asset protection from outside creditors over an LLC.

5. A single member LLC choosing to be taxed as a sole proprietor

a. Reports income and expenses on Schedule C of Form 1040
b. Files a separate business entity tax return
c. Doesn't have to pay federal income tax
d. Is not subject to any Social Security or Medicare tax

Answer Key: 1. B, 2. T, 3. F, 4. F, 5. A

Bradford E. Adatto, Esq.

Bradford E. Adatto Esq., of Dallas, Texas, is partner at ByrdAdatto, a business and health care boutique law firm with offices in Dallas and Chicago. His background is in regulatory, transactional, and securities law with deep expertise in healthcare law born originally of his family's longtime involvement in the healing professions. Mr. Adatto regularly counsels clients with respect to federal and state health care regulations that impact investments, transactions, and contract terms, including Medicare fraud and abuse, anti-trust, anti-kickback, anti-referral, and private securities laws. He has been recognized as Top Rated Lawyer by the *Dallas Morning News* (2016), a Best Lawyer in Dallas in health care by *D Magazine* (2016 & 2018-2019), selected as a Best Lawyer in America in health care (2017-2019), and recently named as a Best Lawyer in Texas (2019) and Texas Super Lawyer (2019).

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Practice Risk Assessment - Part 1: The Government

The Regulations of Health Care

- Patient Protection & Affordable Care Act
- Affordable Care Act Implementation
- Out-of-network Referrals
- Medicare-Medicaid Anti-Fraud & Abuse Amendments
- Anti-Kickback Statute
- Management Service Organizations
- Anti-Referral Regulations (Stark II)
- The False Claims Act (FCA)
- Increased Joint Venture Activity and Market Consolidation
- Occupational Safety and Health Administration Regulations (OSHA)
- Physician Payment Sunshine Act (Sunshine Act)
- Health Insurance Portability Accountability Act (HIPAA)
- Telemedicine
- Health Information Technology for Economic Clinical Health Act (HITECH)
- Anti-Markup Rule
- Overpayments and Self-disclosure
- Provider Reimbursement and Emphasis on Quality Care
- State Licensure Laws
- Corporate Practice of Medicine
- Anti-Trust Laws
- The Health Care Quality Improvement Act
- Joint Commission on Accreditation of Healthcare Organizations (JCAHO)

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Top Liability Risk

- Government Enforcement
- Patients
- Partners
- Employees

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Government Enforcement

- Anti-Referral Laws
- Anti-Kickback Laws
- Board Jurisdiction

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Top Liability Risk – Part I

- Government Enforcement
  - Anti-Referral Laws
  - Anti-Kickback Laws
  - Board Jurisdiction

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Ancillary Compensation

- Imaging Centers
- ASCs
- Labs
- Pain Management Centers
- Medical Office Buildings
- Stem Cell Therapy
- Physical Therapy
- Neuromonitoring
- Anesthesia Services
- Device Companies

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Regulators

- **Federal Level**
  - Office of Inspector General (OIG)
  - Department of Justice (DOJ)
  - Federal Bureau of Investigations (FBI),
  - Centers for Medicare and Medicaid (CMS)
  - Office of Civil Rights (OCR)
  - Health and Human Services (HHS)
  - Federal Trade Commission (FTC)

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Who is Complaining?

- Patients
- Former or current employee
- Competitor
- Ex-Spouse

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What do angry people do?

- Post Negative Reviews
- File Complaints with Medical and Dental Boards
- File Complaints with State or Federal Agency

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Pandora's Box

- Investigators Powers
  - Interview witnesses
  - Demand medical, personnel, and business records
  - Conduct site visits

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How to Spot Potential Red Flags

- Anti-Referral Laws
- Anti-Kickback Laws
- Board Jurisdiction

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How to Spot Potential Red Flags

- **Anti-Referral Laws**
- Anti-Kickback Laws
- Board Jurisdiction

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Anti-Referral Laws – a.k.a. Stark Law

- Governs physician self-referrals
- Stark prohibits a physician from the following:

1. Referring Medicare, Medicaid, or other federally-funded government programs ("**Program Patients**")
2. For the furnishing of designated health services ("**DHS**")
3. To an entity with whom the physician (or an immediate family member)
4. Has a financial relationship.

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Physician

- Only includes doctors of medicine or osteopathy, dental surgery or dental medicine, podiatric medicine, optometry, and chiropractors.
- Stark does not apply to nurse practitioners, physician assistants, registered nurses, any other licensed professional, or unlicensed individuals.

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DHS

- Clinical laboratory services
- Physical therapy services, occupational therapy services, outpatient speech-language pathology services
- Radiology and certain other imaging services
- Radiation therapy services and supplies
- Durable medical equipment and supplies
- Parenteral and enteral nutrients, equipment and supplies
- Prosthetics, orthotics, and prosthetic devices and supplies
- Home health services
- Outpatient prescription drugs
- Inpatient and outpatient hospital services

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Immediate Family Member

- Broadly define to include:
  - Spouse; birth parent, stepparent and adoptive parent; child, grandchild and stepchild; sibling and step-sibling; all-in-laws; grandparent and spouse of a grandparent

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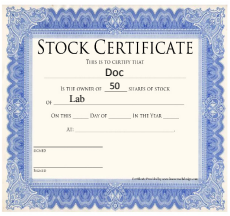
Stark In Action

1. Referring Program Patient
2. DHS - Lab
3. Physician has a financial relations
4. **Must Meet a Stark Exception**



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Stark Exceptions

- Must meet every element of a Stark Exception
- Failure to meet one element, will violate the exception
- Over a dozen Stark Exceptions

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Violation Example

- 1,000 claims between August of 2019 and March of 2020 and collected $500,000

- Return Funds $500,000.00 (***Must return funds***)
- Penalty $23,863,000.00 (***1,000 claims X $23,863 per claim***)
- **Total amount owed** **$24,363,000.00**

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Baby Stark

- State self-referral laws are implemented on the premises that the referral of a patient by provider to another provider of service in which the referring provider has a financial interest represents a potential conflict of interest.
- Payor sources (i.e. state programs, or commercial)
- Payor indifferent (doesn't matter who makes payment, even cash)

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How to Spot Potential Red Flags

- Anti-Referral Laws
- **Anti-Kickback Laws**
- Board Jurisdiction

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Federal Anti-Kickback

- Prohibits knowingly and willfully soliciting, receiving any remuneration, directly or indirectly overtly or covertly, in cash or in kind,
- In return for referring a patient to a person, or
- Furnishing or arranging for the furnishing of any item or service
- Payable by Medicare, Medicaid, TRICARE or other Federal health care programs
- or, in return for
  - purchasing,
  - leasing,
  - ordering, or
- arranging for or recommending
  - purchasing,
  - leasing, or
  - ordering any good,
  - facility, service, or item
  - payable by Medicare or Medicaid.

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Anti-Kickback In Action

1. Referring Program Patients
2. For the furnishing of services
3. **To an entity with whom the physician is receiving remuneration**

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Safe Harbors

- *Not* be treated as criminal offenses
- Over 20 different types
- Failure to meet every element of a Safe Harbor does **not** make it ***per se* illegal**

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Violation

- Criminal
  - Felony, $25,000, and
  - five years in jail
- Civil
  - $50,000 per violation and
  - exclusion from the federal health care programs.
- Subject to False Claims Act since claims submitted pursuant to a violation of law may be deemed to be false

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FMV / Form & Substance

Fair Market Value (FMV)

- Value of the property for general commercial purposes or
- The value of the equipment when obtained from a manufacturer or professional distributor

Form & Substance

- The terms and conditions described in the documents must match the actual services being rendered in the arrangement

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The Other Guys

- **Federal Level**
  - Office of Inspector General (OIG)
  - Department of Justice (DOJ)
  - Federal Bureau of Investigations (FBI),
  - Centers for Medicare and Medicaid (CMS)
  - Office of Civil Rights (OCR)
  - Health and Human Services (HHS)
  - Federal Trade Commission (FTC)
- **State Level**
  - Attorney General (AG)
  - District Attorney (DA)
  - Medical or Dental Board

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State Anti-Kickback Laws

- Prohibiting payments for referrals, securing or soliciting patients
- Payor sources (i.e. state or commercial programs)
- Payor indifferent (doesn't matter who makes payment, even cash)

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Texas Laws

Anti-Kickback Law

- A person commits an offense if agrees to accept, directly or indirectly remuneration for securing or soliciting a patient
- Statue is **payor indifferent**.

Commercial Bribery

- If fiduciary, without the consent of his beneficiary, solicit, accept, or agree to accept any benefit from another person.
- The term "fiduciary" specifically includes a physician

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Florida Anti-Kickback Laws

- Patient Brokering Prohibition Act
  - Prevents Health Care Provider or Facility
  - Payor Indifferent
  - Paying or receiving any form of remuneration for referral

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Patient Referrals

- Providing patients any kind of reward in exchange for them referring additional patients
  - Cash
  - Treatments
  - Discounts
  - Gift Cards
  - Anything of value

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Refer a Friend

1. Referring Patients
2. For the furnishing of services
3. **Physician pays for the referral**

Anti-Kickback In Action



Go See My Doc!

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How to Spot Potential Red Flags

- Anti-Referral Laws
- Anti-Kickback Laws
- **Board Jurisdiction**

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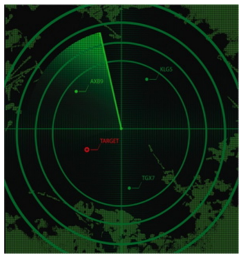
Board Jurisdiction

- What complaints are within Board jurisdiction?
  - Any behavior exposing a patient to unnecessary risk of harm;
  - Failure of care, including follow-up care;
  - Failure to meet the standard of care;
  - Impairment by dependency or mental illness;
  - Unprofessional or unethical behavior



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Informal Investigation

1. Board notifies via mail of complaint.
2. You will have a set timeframe (15 days to 45 days*) to submit appropriate response and documents.
3. Based on the information you send, the Board may dismiss or proceed.

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Top Liability Risk – Part I

- Government Enforcement
  - Anti-Referral Laws
  - Anti-Kickback Laws
  - Board Jurisdiction


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Takeaways

1. Identify Your Risk
2. Conduct Your Due Diligence
3. Build Your Team of Advisors (Financial/Legal/Accounting)

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Supplemental Material

To receive a copy of our supplemental material, visit our website:

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SELF EVALUATION

Practice Risk Assessment - Part 1: The Government

True or False

1.___ If I do not refer Medicare, and Medicaid patients to an entity that I have a financial arrangement, the federal Anti-Referral Law, a.k.a. Stark, does not apply.

2.___ If I do not meet every element of a federal Anti-Kickback safe harbor, the arrangement is automatically illegal.

3.___ If no Medicare, Medicaid, or other federally-funded government programs ("Program Patients") are involved, I am not subject to any federal health care laws.

4.___ The Federal Anti-Kickback prohibits only applies if a physician is paid in cash.

5.___ If I do not bill Medicare, Medicaid, other federally-funded government programs, or commercial payors, meaning I only take cash paying patients, I am not subject to any state health care Anti-Kickback laws.

6.___ HIPAA only applies to physicians, and other health care providers who electronically submit claims to health insurance.

7.___ If I do not bill Medicare, Medicaid, other federally-funded government programs, or commercial payors, meaning I only take cash paying patients, I am not subject to any state HIPAA laws.

Answer Key: 1. T, 2. F, 3. F, 4. F, 5. F, 6. T, 7. F

C. Wayne Weart, PharmD, FASHP, BCPS

C. Wayne Weart, PharmD, of Charleston, South Carolina, is professor of the Department of Clinical Pharmacy and Outcome Sciences at Medical University of South Carolina (MUSC) College of Pharmacy, as well as professor of Family Medicine in the College of Medicine, MUSC. Prior to MUSC he instructed at West Virginia University.

Dr. Weart has authored more than 100 publications and he has presented hundreds of hours of lectures to numerous professional groups and societies, medical and house staffs at both West Virginia University and MUSC, and national pharmacy and medical seminars across the country. He has received numerous awards and honors in his field including: "Outstanding Teacher" awards at both West Virginia University and MUSC; "Hospital Pharmacist of the Year" in both South Carolina and West Virginia; and designation as a Fellow of the American Society of Health Systems Pharmacists. In 1991 Dr. Weart was among the first pharmacists to become a board-certified pharmacotherapy specialist.

You may contact Dr. Weart with any questions or comments at (843) 792-3606 or by email at weartcw@musc.edu.

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Evidence-Based Management of Heart Failure with Reduced Ejection Fraction

Prevalence of Heart Failure

• On the basis of data from **NHANES 2011 to 2014, an estimated 6.5 million Americans ≥ 20 years of age had HF. This represents an increase from an estimated 5.7 million US adults with HF based on NHANES 2009 to 2012** (NHLBI)

• **Projections show that the prevalence of HF will increase 46% from 2012 to 2030, resulting in >8 million people ≥ 18 years of age with HF.**

• On the basis of data from the 2005 to 2014 community surveillance component of the ARIC study of the NHLBI: There are **1,000,000 new HF cases annually (495,000 males and 505,000 females) Black males have the highest incidence of HF across all age groups. This higher risk reflected differences in the prevalence of hypertension, DM, and low SES.** African Americans had the highest proportion of incident HF not preceded by clinical MI (75%).

- Circulation 2018; 137: e67-e492

Heart Failure Mortality

- **Among Medicare beneficiaries, the overall 1-year HF mortality rate declined slightly from 1998 to 2008 but remained high at 29.6%**, and rates of decline were uneven across states.
- In the NHLBI's ARIC study, the **30-day, 1-year, and 5-year case fatality rates after hospitalization for HF were 10.4%, 22%, and 42.3%, respectively, and blacks had a greater 5-year case fatality rate than whites** (P<0.05).
- Observed **mortality declines have been primarily attributed to evidence-based approaches to treat HF risk factors and the implementation of ACEIs, β-blockers, coronary revascularization, implantable cardioverter-defibrillators, and cardiac resynchronization therapies.**
  - Circulation 2018; 137: e67-e492

Heart Failure Mortality

- Using data from a national HF registry, researchers studied nearly **40,000 Medicare beneficiaries who were hospitalized with HF between 2005 and 2009. Some 46% had reduced ejection fractions (≤40%), 8% had borderline ejection fractions (41%–49%), and 46% had preserved ejection fractions (≥50%).**
- **The overall 5-year mortality rate was 75%, with no significant differences across ejection fraction groups. The majority of deaths occurred in the first 2 years after admission**.
- Editorialists conclude: **"Ejection fraction does not appear to be an accurate biomarker for risk stratification after a patient has crossed the threshold to an HF admission.** These data should serve as another wake-up call to all providers to recognize the risk associated with HF."
  - Journal of the American College of Cardiology November 2017 DOI: 10.1016/j.jacc.2017.08.074

Costs for Heart Failure

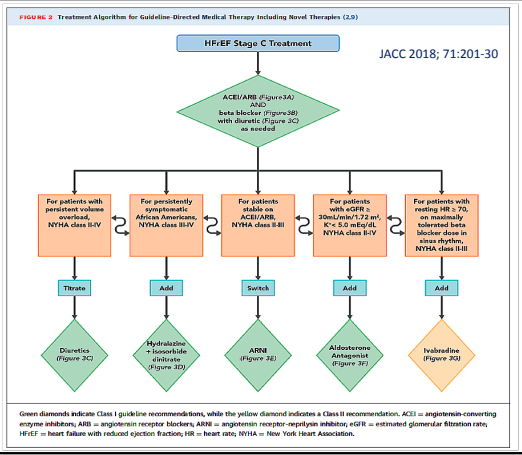
- **In 2012, total cost for HF was estimated to be $30.7 billion (2010$), of which 68% was attributable to direct medical costs.** Circulation 2018; 137: e67-e492
- Projections suggest that **by 2030, the total cost of HF will increase almost 127%, to $69.7 billion**, from 2012, amounting to ≈$244 for every US adult.
- Data from 63,678 Medicare patients (**2005-11**) with a mean age of 81.8 years were included in the analysis. The **mean per-patient cost of an HF-related hospitalization was $14,631**. The mean per-patient cost of a cardiovascular (CV)-related or all-cause hospitalization was $16,000 and $15,924, respectively. (Risk Manag Healthc Policy. 2017; 10: 63–70)
- The cumulative rate of all-cause hospitalization was 218.8 admissions per 100 person-years, and the **median length of stay for HF-related, CV-related, and all-cause hospitalizations was 5 days.** Also, **22.3% of patients were readmitted within 30 days, 33.3% were readmitted within 60 days, and 40.2% were readmitted within 90 days.**

What would you recommend?

- **70y/o, 80 Kg male patient who has HFrEF (EF 28%); NYHA Class III; elevated BNP 523 pg/ml; s/p MI with CABG (in the last month); history of hypertension (BP 150/94, HR 78); Type 2 diabetes (A1c 8.0); proteinuria 400 mg/24 hrs; serum creatinine 1.4mg/dl; EGFR ~51 mL/min/1.73m2; serum potassium 4.5 mEq/L.**
- Current meds: lisinopril 10 mg QD; metoprolol tartrate 50 mg QAM; clopidogrel 75 mg QAM; ASA 81 mg QAM; metformin 500 mg ER BID; pioglitazone 30 mg QAM; simvastatin 20 mg QHS.

What is good and what should we consider changing?

- Discussion?
  - What if any Meds would increase his risk of HFrEF?
  - Are any of his HFrEF, Diabetes, Lipid/ASCVD or BP meds optimized?
  - What would you want to see him on?
  - BP goal <130/80 with HFrEF, DM and proteinuria?
  - S/P MI and CABG high intensity statin plus lipid profile to know if to add ezetimibe/PCSK-9 inhibitor?

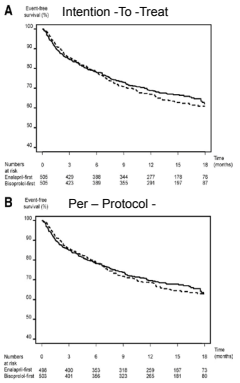


Initial Medication Choice BB or ACEI/ARB?

- In a patient with new-onset HFrEF, a common question is whether to initiate a beta blocker or ACEI/ARB first. Data from the randomized CIBIS (Cardiac Insufficiency Bisoprolol) III trial suggest that either is safe.
- **Initiation of ACEI or ARB is often better tolerated when the patient is still congested ("wet"; when renin-angiotensin-aldosterone system activation is less), whereas beta blockers are better tolerated when the patient is less congested ("dry") with adequate resting heart rate.**
  - JACC 2018; 71:201-30

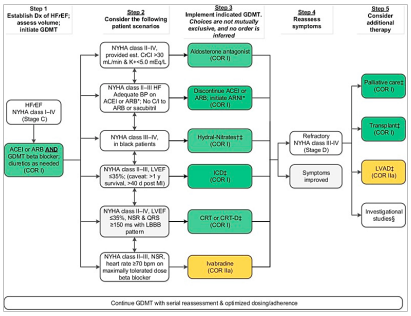
Effect on Survival and Hospitalization of Initiating Treatment for Chronic Heart Failure With Bisoprolol Followed by Enalapril, as Compared With the Opposite Sequence
(Cardiac Insufficiency Bisoprolol Study (CIBIS) III. Circulation. 2005; 112:2426–35)

Randomized 1010 patients with mild to moderate CHF and left ventricular ejection fraction ≤35%, who were not receiving ACE inhibitor, β-blocker, or angiotensin receptor blocker therapy, to open-label monotherapy with either bisoprolol (target dose 10 mg QD; n=505) or enalapril (target dose 10 mg BID; n=505) for 6 months, followed by their combination for 6 to 24 months. The 2 strategies were blindly compared with regard to the combined primary end point of all-cause mortality or hospitalization and with regard to each of these end point components individually. **Bisoprolol-first treatment was noninferior to enalapril-first treatment**



Effect on Survival and Hospitalization of Initiating Treatment for Chronic Heart Failure With Bisoprolol Followed by Enalapril, as Compared With the Opposite Sequence, Volume: 112, Issue: 16, Pages: 2426-2435, DOI: (10.1161/CIRCULATIONAHA.105.582320)

GMDT = Guideline-Directed Management and Therapy



2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure – J Cardiac Failure 2017; 23:628-651

2017 ACC/AHA/HFSA Focused Update-Guideline for the Management of Heart Failure with Preserved EF

7.3.3. Pharmacological Treatment for Stage C HFpEF: Recommendations

Recommendations for Stage C HFpEF

COR	LOE	Recommendations	Comment/Rationale
I	B	Systolic and diastolic blood pressure should be controlled in patients with HFpEF in accordance with published clinical practice guidelines to prevent morbidity (164, 165).	2013 recommendation remains current.
I	C	Diuretics should be used for relief of symptoms due to volume overload in patients with HFpEF.	2013 recommendation remains current.
IIa	C	Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HFpEF despite GDMT.	2013 recommendation remains current.
IIa	C	Management of AF according to published clinical practice guidelines in patients with HFpEF is reasonable to improve symptomatic HF.	2013 recommendation remains current (Section 9.1 in the 2013 HF guideline).
IIa	C	The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HFpEF.	2013 recommendation remains current.
IIb	B-R	In appropriately selected patients with HFpEF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate >30 mL/min, creatinine <2.5 mg/dL, potassium <5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations (83, 166, 167).	NEW: Current recommendation reflects new RCT data.
See Online Data Supplement C.			

Starting and Target Doses of Select Guideline-Directed Medical Therapy for Heart Failure

	Starting dose	Target dose	Cost
Beta Blockers			
Bisoprolol	1.25 mg once daily	10 mg once daily	~$20-36.00/10 mg tabs x 30
Carvedilol	3.125 mg twice daily	25 mg twice daily for weight <85 kg and 50 mg twice daily for weight ≥85 kg	~$10-28.00/25 mg tabs x 60
Metoprolol succinate	12.5–25 mg/d	200 mg daily	~$31-37.00/200mg tabs x 30
ARNI			
Sacubitril/valsartan	24/26 mg–49/51 mg twice daily	97/103 mg twice daily	~$482-503.00/97/103 mg tabs x 60
ACEI			
Captopril	6.25 mg 3× daily	50 mg 3x daily	~$84-232.00/50 mg tabs x 90 tabs
Enalapril	2.5 mg twice daily	10–20 mg twice daily	~$25-35.00/20 mg x 60 tabs
Lisinopril	2.5–5 mg daily	20–40 mg daily	Free-$10.00/40 mg x 30 tabs
Ramipril	1.25 mg daily	10 mg daily	~$8-26.00/10mg x 30 caps
ARB			
Candesartan	4–8 mg daily	32 mg daily	~$46-106.00/32 mg tabs x 30
Losartan	25–50 mg daily	150 mg daily	~$8-27.00/50 mg tabs x 90
Valsartan	40 mg twice daily	160 mg twice daily	~$22-100.00/160mg tabs x 60

ACC 2017 Pathways for Optimization of Heart Failure Treatment JACC 2018, 71: 201-230

Starting and Target Doses of Select Guideline-Directed Medical Therapy for Heart Failure

			Cost
Aldosterone antagonists			
Eplerenone	25 mg daily	50 mg daily	~$48-116.00/50 mg tabs x 30
Spironolactone	12.5-25 mg daily	25-50 mg daily	~$8-15.00/50 mg tabs x 30
Vasodilators			
Hydralazine	25 mg 3× daily	75 mg 3× daily	~$25-52.00/25 mg tabs x 270 tabs
Isosorbide dinitrate*	20 mg 3× daily	40 mg 3× daily	~$78-200.00/40 mg tabs x 90 tabs
Fixed-dose combination isosorbide dinitrate/ hydralazine†	20 mg/37.5 mg (one tab) 3× daily	2 tabs 3× daily	~$625.00/20/37.5 mg Bidil tabs x 180 tabs
Ivabradine			
Ivabradine	2.5-5 mg twice daily	Titrate to heart rate 50-60 bpm. Maximum dose 7.5 mg twice daily	~$460.00/7.5mg Corlanor tabs x 60 tabs

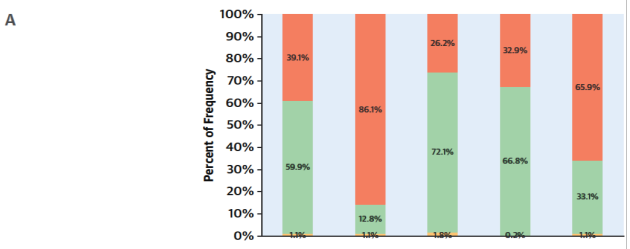
*The AHA/ACC/HFSA Guidelines do not recommend use of isosorbide mononitrate

ACC 2017 Pathways for Optimization of Heart Failure Treatment JACC 2018, 71: 201-230

How many patients with HFrEF are receiving Guideline Directed Medical Therapy?

- **The CHAMP-HF (Change the Management of Patients with Heart Failure) registry** included outpatients in the United States with chronic HFrEF receiving at least 1 oral medication for management of HF.
- **3,518 patients from 150 primary care and cardiology practices were incl**uded. Mean age was 66 +/- 13 years, 29% were female, and mean EF was 29 +/- 8%.
- Among eligible patients, **27%, 33%, and 67% were not prescribed ACEI/ARB/ARNI, beta-blocker, and MRA therapy, respectively.**
- **When medications were prescribed, few patients were receiving target doses of ACEI/ARB (17%), ARNI (14%), and beta-blocker (28%), whereas most patients were receiving target doses of MRA therapy (77%).**
- **Among patients eligible for all classes of medication, 1% were simultaneously receiving target doses of ACE/ARB/ARNI, beta-blocker, and MRA.**
  - In adjusted models, older age, lower blood pressure, more severe functional class, renal insufficiency, and recent HF hospitalization generally favored lower medication utilization or dose.
  - (J Am Coll Cardiol 2018;72:351–66)

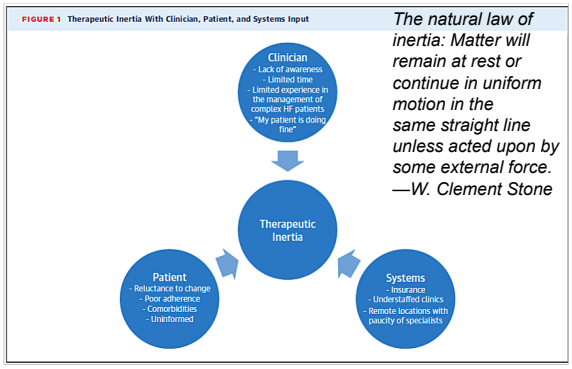
CENTRAL ILLUSTRATION Use and Dosing of Guideline-Directed Medical Therapy Among Patients With Chronic HFrEF in Contemporary U.S. Outpatient Practice



	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta-Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38

J Am Coll Cardiol 2018;72:351–66

Therapeutic Inertia



The natural law of inertia: Matter will remain at rest or continue in uniform motion in the same straight line unless acted upon by some external force. —W. Clement Stone

J Am Coll Cardiol 2018;72:367–69

ATLAS STUDY DESIGN

Circulation 1999;100:2312-2318

- **3,164 patients with moderate to severe congestive heart failure**
- randomized 5 year double-blind trial
- **lisinopril**
  2.5 - 5 mg/day vs. 32.5 - 35 mg/day
  - **Lisinopril 40 mg ~ $0-10.00/30**

ATLAS RESULTS

Circulation 1999;100:2312-2318

Outcomes at 3 yrs	Hazard ratio (95% CI)	Number Needed to Treat (NNT)
Mortality plus hospitalization	0.88 (0.82-0.96)	26
Mortality plus HF hospitalization	0.85 (0.78- 0.93)	17
CV mortality plus CV hospitalization	0.91 (0.84-0.99)	30
Mortality plus CV hospitalization	0.92 (0.84-0.99)	34

ATLAS RESULTS

Circulation 1999;100:2312-2318

- **Cough - the major reason for drug discontinuation - occurred more often in the low-dose group, probably because their CHF was not as well controlled**
- **90% of patients randomized to high-dose therapy achieved target dose**
- **Resulted in an estimated 250,000 fewer hospitalizations / yr at an annual savings of $2 billion**

ARB's in Heart Failure

- **Elite II no benefit in morbidity and mortality with losartan 50mg QD over captopril 50mg TID, but when dosed at 150 mg QD in the HEAAL Trial reduced CV hospitalization for HF (100 mg ~ $10-25.00/30)**
- **Val-Heft IV valsartan 160mg BID was not better than ACEI plus BB unless the patient was not on an ACEI (IE ACEI intolerant patients) (160 mg ~ $100.00/60)**
- **CHARM candasartan 32mg QD was better than ACEI plus BB alone in the CHARM Added Trial and especially in ACEI intolerant patients including patients with angioedema (90% of this group was able to tolerate the ARB) The CHARM Alternative Trial (32 mg ~ $50.00/30)**

Doses of Beta-blockers in HF

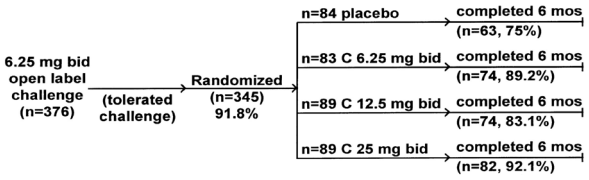
- **Bisoprolol - initial dose 1.25mg QD titrated as tolerated to a target dose of 10mg QD (10 mg ~ $20.00/30)**
  - **CIBIS II trial - NYHA Class III and IV, 15 months, 34% reduction in all cause mortality NNT=20**
- **Extended release metoprolol – initial dose 12.5 -25 mg QD titrated to a target dose of 200mg QD (200 mg ~ $30.00/30)**
  - **MERIT-HF trial – NYHA Class II and III, 21 months, 34% reduction in total mortality NNT=27**

Doses of Beta-Blockers in HF

- **Carvedilol – initial dose 3.125 mg BID titrated to a target dose of 25 mg BID (50 mg BID for patients >85 Kg) (25 mg ~ $10-25.00/60)**
  - **COPERNICUS trial – NYHA Class III and IV, 10.4 months, 35% reduction in total mortality NNT=14**
  - **COMET trial – NYHA Class II and III, 58 months, 17% reduction in total mortality NNT=18 (trial compared BID carvedilol to 50mg BID generic metoprolol at less than recommended doses)**

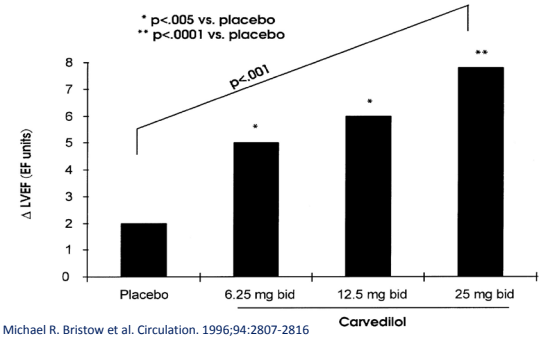
Study design and overall outcome of the MOCHA trial

(dose response of carvedilol in chronic heart failure, protocol 220).



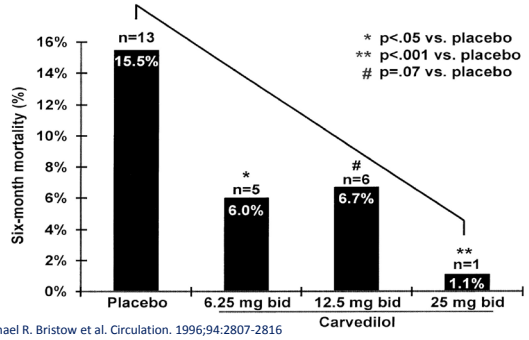
Michael R. Bristow et al. Circulation. 1996;94:2807-2816

Carvedilol protocol 220 (MOCHA): LVEF data at end of 6-month maintenance period as change (Δ) from baseline values.



Michael R. Bristow et al. Circulation. 1996;94:2807-2816

Carvedilol protocol 220 (MOCHA): six-month crude mortality as deaths per randomized patients×100.



Michael R. Bristow et al. Circulation. 1996;94:2807-2816

How would you select an evidence-based beta blocker in these patients?

- All patients have HFrEF with reduced EF and are NYHA Class III (include specific beta blocker and target dose)
  - Patient with hard to control BP?
  - Patient who is a smoker with moderate COPD (FEV1 <70 but >50) and he is on Anoro Ellipta QD and Combivent Respimat PRN

Which beta blocker would you prescribe?

- Patient with HFrEF and mixed COPD/asthma?
  - A. Carvedilol BID
  - B. Metoprolol succinate QD
  - C. Bisoprolol QD
  - D. Atenolol QD
  - E. No beta blocker

Beta-blockers in Patients with COPD/Asthma?

- **Bisoprolol** has data for use in heart failure and coronary artery disease and **has a beta-1/2 receptor selectivity ratio of 14:1, which is higher than either atenolol (5:1) or metoprolol (2:1)** [Br J Pharmacol 2005; 144: 317–322].
- **In a cross-over study of 51 patients with COPD and heart failure, directly comparing 6 weeks of bisoprolol, metoprolol and carvedilol** [J Am Coll Cardiol 2010; 55: 1780–1787], **FEV1 was lowest with carvedilol and highest with bisoprolol with metoprolol in between.**

Beta-blockers in Patients with COPD/Asthma?

- **In a randomised controlled trial comparing bisoprolol (mean dose 6.4 mg) and carvedilol (mean dose 47 mg) in patients with heart failure and COPD, FEV1 significantly improved by 137 mL with bisoprolol, but not with carvedilol (30 mL improvement)** [Respir Med 2011; 105: Suppl. 1, S44–S49].
  - Excellent review - Beta-blockers in COPD: time for reappraisal Eur Respir J 2016; In press | DOI: 10.1183/13993003.01847-2015

Beta Blockers in Patients with COPD

- Retrospective cohort study using a disease specific database of 5977 patients aged >50 years with a diagnosis of COPD in Scotland.
- Main outcome measures Hazard ratios for all cause mortality, emergency oral corticosteroid use, and respiratory related hospital admissions.
- **Mean follow-up was 4.35 years, mean age at diagnosis was 69.1 years, and 88% of β blockers used were cardio-selective. There was a 22% overall reduction in all cause mortality with β blocker use.** Furthermore, there were additive benefits of β blockers on all cause mortality at all treatment steps for COPD.
  - BMJ 2011;342:d2549

Beta Blockers in Patients with COPD

- **There were similar trends showing additive benefits of β blockers in reducing oral corticosteroid use and hospital admissions due to respiratory disease. β blockers had no deleterious impact on lung function at all treatment steps when given in conjunction with either a long acting β agonist or anti-muscarinic agent.**
- **One possibility is that up-regulation of β2 adrenoceptors by chronic β blockade may improve the effectiveness of β2 agonists.**
  - BMJ 2011;342:d2549

β-Blocker Therapy and Risk of Chronic Obstructive Pulmonary Disease – A Danish Nationwide Study of 1·3 Million Individuals

- A total of 301,542 new users of β-blockers and 1,000,633 new users of any other antihypertensive drugs aged 30–90 years without any history of COPD hospitalizations were included in the present study and followed in the Danish National Patient Registry for incident admissions for COPD and COPD death between 1995 and 2015.
- **People treated with β-blockers continuously for more than 6 months had a 19.7% lower risk of COPD hospitalization during follow-up compared to people treated with any other antihypertensive drugs** (adjusted hazard ratio 0·80, 95% CI 0·79–0·82). Risk of COPD hospitalization was lowered in the groups treated with β-blockers among patients with ischemic heart disease (0·72, 0·69–0·75), cardiac arrhythmias (0·76, 0·72–0·80), asthma (0·69, 0·61–0·79), hypertension (0·91, 0·86–0·96), and diseases of the pulmonary circulation (pulmonary embolism and cor pulmonale) (0·72, 0·59–0·87). **All-cause mortality as well as risk of COPD death during follow-up was 44% lower in the group treated with β-blockers compared to the group treated with any other antihypertensive drugs** (0·56, 0·53–0·59). https://doi.org/10.1016/j.eclinm.2019.01.007

ARNI (Angiotensin Receptor Neprilysin Inhibitor) - Valsartan/Sacubitril - Entresto

- **FDA approved 7-8-2015 indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction.**
- It is usually administered in conjunction with other heart failure therapies including an evidence based beta blocker and when appropriate an aldosterone antagonist, and replaces the ACE inhibitor or other ARB.

Film-coated tablets (sacubitril/valsartan): **24/26 mg; 49/51 mg; 97/103 mg for BID dosing**
Cost: $16.00 per day or $485.00/mo GoodRx.com

Valsartan/Sacubitril - Entresto

- **If switching from an ACE inhibitor to (sacubitril/valsartan) allow a washout period of 36 hours between administration of the two drugs**
- **The recommended starting dose is 49/51 mg (sacubitril/valsartan) twice-daily.**
- **Double the dose of after 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) twice-daily, as tolerated by the patient.**
- **Reduce the starting dose to 24/26 mg (sacubitril/valsartan) twice-daily for:**
  - **patients not currently taking an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) or previously taking a low dose of these agents**
  - **patients with severe renal impairment**
  - **patients with moderate hepatic impairment**

Valsartan/Sacubitril - Entresto

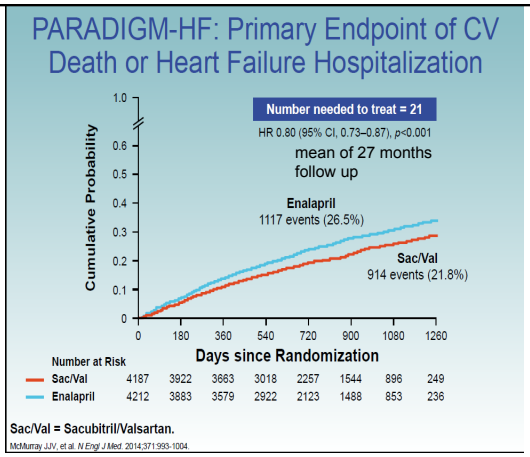
- In the **double-blind period of PARADIGM-HF, 0.5% of patients treated with (valsartan/sacubitril) and 0.2% of patients treated with enalapril had angioedema.**
  - associated with a higher rate of angioedema in Black than in non-Black patients

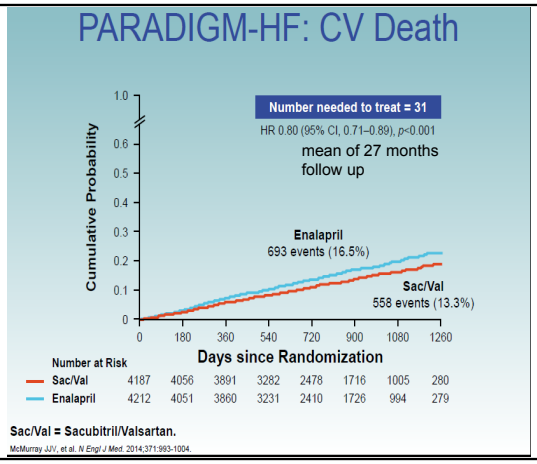
PARADIGM-HF Trial

- **Compared the angiotensin-neprilysin inhibitor LCZ696 (200 mg BID) with the angiotensin converting enzyme inhibitor enalapril (10 mg BID) in 8399 patients with heart failure and reduced ejection fraction (<35%, NYHA Class II-IV)** able to tolerate ACEI or ARB and also on stable doses of beta blocker/mineralocorticoid antagonist unless not tolerated, in a double-blind trial. (NOTE **only 5% of pts were black and <10% from North America)**
- **200 mg of LCZ696 delivers the equivalent of 160 mg of valsartan** (evidence-based dose of valsartan in HF and post MI)
  - DOI: 10.1161/CIRCULATIONAHA.114.013748

PARADIGM-HF Trial

- After a **mean of 27 months follow up** the LCZ696-treated patients as compared to the enalapril treated patients required:
  - Less intensification of medical treatment for heart failure (520 versus 604; hazard ratio, 0.84; 95% confidence interval, 0.74–0.94; P=0.003)
  - Fewer emergency department visit for worsening heart failure (hazard ratio, 0.66; 95% confidence interval, 0.52–0.85; P=0.001).
  - Fewer hospitalizations for worsening heart failure (851 versus 1079; 23% reduction P<0.001)
  - **Less hospitalization for any cause; annualized rates of 30.3% and 26.3% respectively. These differences reflected a 12.6% RRR; ARR 4.0%; NNT 25** with LCZ696 instead of enalapril (hazard ratio, 0.87; 95% CI, 0.82–0.93; P<0.0001).
  - Less likely to require intensive care (768 versus 879; 18% reduction, P=0.005).
  - **All cause mortality: 835 patients in the enalapril group and 711 in the LCZ696 group, corresponding to annualized rates of 7.5% and 6.0%, respectively. HR 0.84 (95% CI 0.76-0.93 p=0.0009); RRR 16%; ARR 1.5%; NNT 67**
    - DOI: 10.1161/CIRCULATIONAHA.114.013748





Valsartan/Sacubitril – Entresto in PARADIGM - HF

- **Mean daily doses achieved were LCZ696 375 mg and enalapril 18.9 mg**; 76% and 75% of LCZ696 and enalapril patients, respectively, maintained the target dose through the end of the study.
- **Incidence of symptomatic hypotension was 14% with LCZ696 and 9.2% with enalapril (P < 0.001); number needed to harm (NNH) with LCZ696 was 20.8**.
- **Incidence of serum creatinine elevated to at least 2.5 mg/dL was 3.3% with LCZ696 and 4.5% with enalapril (P = 0.007); NNH with enalapril was 83.3**.
- **Incidence of serum potassium greater than 6 mmol/L was 4.3% with LCZ696 and 5.6% with enalapril (P = 0.007); NNH with enalapril was 76.9.**
- **Incidence of cough was 11.3% with LCZ696 and 14.3% with enalapril (P < 0.001); NNH with enalapril was 33.3.**

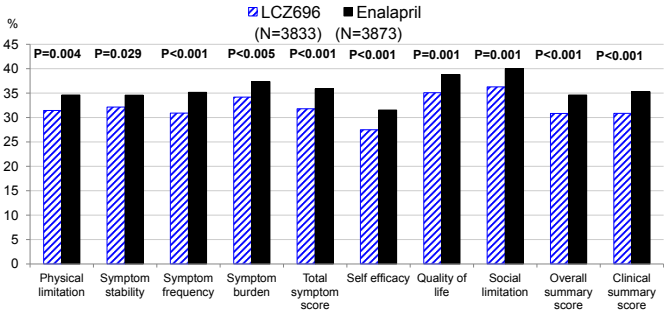
Valsartan/Sacubitril – Entresto in PARADIGM - HF

- **Estimating the Long-Term Treatment Benefits of Sacubitril–Valsartan** (N Engl J Med 2015; 373:2289-2290)
- Using actuarial estimates from the PARADIGM-HF trial, and assuming that the protective effects of sacubitril–valsartan remain consistent with long-term use, we extrapolated from the available short-term follow-up data to **estimate that treatment with sacubitril–valsartan would result in a projected benefit of 1 to 2 years of increased life expectancy and survival free from heart failure for patients (45 to 75 years of age) such as those in the PARADIGM-HF trial.**

Valsartan/Sacubitril – Entresto

- **A recent analysis on JAMA Cardiology reports that 84% of heart failure patients with reduced ejection fraction**--the population Entresto is approved to treat--**would be eligible for therapy** with Entresto. That's **almost 2.3 million patients**. Using the drug properly in these patients **could prevent 28,484 deaths every year**, the study concluded, or a range of 18,230 to 41,017 per year.
  - JAMA Cardiol. doi:10.1001/jamacardio.2016.1724 Published online June 22, 2016.

PARADIGM-HF: Percentage of patients with at least 5 points deterioration in KCCQ (Kansas City Cardiomyopathy Questionnaire) scores at month 8



Clinical summary score based on the physical limitation and total symptom score domains. Death imputed as zero. The analysis included all patients with at least one KCCQ data point

Valsartan/Sacubitril – Entresto and Alzheimers?

- **Neprilysyn degrades multiple peptides including angiotensin, endothelin 1, adrenomedullin, opioids, bradykinin, and amyloid-β peptide (Aβ).**
  - In animal models, neprilysin plays a critical role in maintaining the homeostasis of Aβ in the brain and an **accumulation of Aβ in the brain is associated with the pathogenesis of Alzheimer disease.**
    - Disruption of the neprilysin gene elevated oligomeric Aβ levels in the brain and accelerated the development of cognitive dysfunction in a genetic mouse model of Alzheimer disease
  - Studies in the eye suggest that a similar pathogenic mechanism **may contribute to the development of age-related macular degeneration?**
    - JAMA (January 5), 2016; 315: 25-26

Valsartan/Sacubitril – Entresto and Alzheimers?

- The theoretical risks associated with valsartan/sacubitril moved the **FDA to require the sponsor to conduct a "multicenter, randomized, double-blind, active-controlled trial to evaluate the effects of Entresto compared to valsartan on cognitive function** as assessed by a comprehensive neurocognitive battery and [positron emission tomography] imaging in patients with chronic heart failure with preserved ejection fraction. The timetable for the final report is March 2022.
  - JAMA (January 5), 2016; 315: 25-26

Valsartan/Sacubitril – Entresto Safety Concern

- The **November 1, 2017 edition of ISMP QuarterWatch, a publication from the Institute for Safe Medication Practices, reports that a so-called "drug safety signal"** has been detected recently **for valsartan/sacubitril (Entresto) as regards hypotension** being a serious side effect which warrants more attention — and, perhaps, and an increased warning.
- Relying upon "New data from 2017 Q1" of the U.S. Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS), this leading drug safety publication ends its recent report on valsartan/sacubitril (Entresto) with these statements in the final Conclusions section:

Valsartan/Sacubitril – Entresto Safety Concern

- **ISMP identified 1,684 adverse event reports indicating a hypotension-related event (ranging from dizziness to blackouts with some requiring hospitalization)**, more than for any other cardiovascular drug we monitored over the 12 months ending in 2017 Q1. **They occurred in older patients (median age 70 years), and although there were 69 reported deaths, in two-thirds of the cases, the health consequences were not severe.**
- **The FDA has not yet made any label changes.**
- **CAUTION PATIENTS!!!**

New Focused Update on New Pharmacologic Therapy for Heart Failure

- **Recommendation for ARNI (angiotensin receptor – neprilysin inhibitor) i.e.. valsartan/sacubitril - Entresto**
  - **"The clinical strategy of inhibition of the renin angiotensin system with ACE inhibitors (COR 1/LOE A) or ARB (COR 1/LOE A) or ARNI (COR 1/LO#E B-Randomized) in conjunction with evidence-based beta blockers and aldosterone antagonists in selected patients is recommended for patients with chronic HFrEF to reduce morbidity and mortality"**
    - Journal of the American College of Cardiology (2016), doi: 10.1016/j.jacc.2016.05.011.

New Focused Update on New Pharmacologic Therapy for Heart Failure

- **"In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.' (COR 1/LOE B-R)**
- "**ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor."** (COR III Harm/LOE B-R)
- **"ARNI should not be administered to patients with a history of angioedema"** (COR III harm/LOE EO)
  - Journal of the American College of Cardiology (2016), doi: 10.1016/j.jacc.2016.05.011.

Ivabradine – Corlanor

by Amgen

- **April 15, 2015 The FDA approved ivabradine (Corlanor, Amgen) for reducing the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction of 35% or less, who are in sinus rhythm with resting heart rate of 70 bpm or more, and either are on maximally tolerated doses of beta blockers or have a contraindication to beta-blocker use.** The drug acts by blocking the hyperpolarization-activated cyclic nucleotide–gated channel responsible for the cardiac pacemaker.
- FDA granted Ivabradine expedited approval and did not hold an FDA Cardiovascular Advisory Committee Meeting.
- The drug has been available for several years in Europe, where it is sold by Servier under the brand names of Corlentor and Procoralan

Ivabradine – Corlanor

- **Ivabradine causes a dose-dependent reduction in heart rate.** The size of the effect is dependent on the baseline heart rate (i.e., greater heart rate reduction occurs in subjects with higher baseline heart rate). At recommended doses, heart rate reduction is approximately 10 bpm at rest and during exercise. Analysis of heart rate reduction vs. dose indicates a plateau effect at doses > 20 mg twice daily.
- **Ivabradine does not have negative inotropic effects.**

Ivabradine – Corlanor

SHIFT Trial

- The Systolic Heart failure treatment with the *If* inhibitor ivabradine Trial (**SHIFT) was a randomized, double-blind trial comparing Ivabradine and placebo in 6558 adult patients with stable NYHA class II to IV (primarily II and III) heart failure, left ventricular ejection fraction ≤ 35%, and resting heart rate ≥ 70 bpm**. Patients had to have been clinically **stable for at least 4 weeks on an optimized and stable clinical regimen, which included maximally tolerated doses of beta-blockers and, in most cases, ACE inhibitors or ARBs, spironolactone, and diuretics,** with fluid retention and symptoms of congestion minimized. Patients had to have been hospitalized for heart failure within 12 months prior to study entry.
  - Lancet. 2010;376:875–885

Ivabradine – Corlanor

- All subjects were initiated on ivabradine 5 mg (or matching placebo) twice daily and the dose was increased to 7.5 mg twice daily or decreased to 2.5 mg twice daily to maintain the resting heart rate between 50 and 60 bpm, as tolerated.
- The primary endpoint was a composite of the first occurrence of either hospitalization for worsening heart failure or cardiovascular death.
  - **89% of patients were taking beta-blockers, with 26% on guideline-defined target daily doses**. The main reasons for not receiving the target beta-blocker doses at baseline were hypotension (45% of patients not at target), fatigue (32%), dyspnea (14%), dizziness (12%), history of cardiac decompensation (9%), and bradycardia (6%).
  - **91% of patients were taking either an ACEI or ARB**
  - **83% of patients were taking diuretics and 60% aldosterone antagonists**
    - Lancet. 2010;376:875–885

Ivabradine – Corlanor

	Ivabradine		Placebo				
Endpoint	N=3241 N	%	N=3264 N	%	HR 95% CI	P-value	ARR/NNT
Primary composite of time to first hospitalization for HF and CV death	**793**	**24.5%**	**937**	**28.7%**	**0.82 (0.75-0.90)**	**<0.0001**	**4.2%/24**
Hospitalization for worsening HF	**505**	**15.6%**	**660**	**20.2%**	**0.74 (0.66-0.83)**	**<0.0001**	**4.6%/24**
CV death as first event	**288**	**8.9%**	**277**	**8.5%**			

Mean follow-up 23 months. Ivabradine's benefit on the primary endpoint in SHIFT appeared to decrease as the dose of beta-blockers increased, with little if any benefit demonstrated in patients taking guideline-defined target doses of beta-blockers.
Lancet. 2010;376:875–885

Ivabradine – Corlanor

Adverse Effects from SHIFT Trial:

Bradycardia	10%	2.2%
Hypertension	8.9%	7.8%
Atrial Fibrillation	8.3%	6.6%
Phosphenes, visual brightness*	2.8%	0.5%

*Phosphenes are phenomena described as a transiently enhanced brightness in a limited area of the visual field, halos, image decomposition (stroboscopic or kaleidoscopic effects), colored bright lights, or multiple images (retinal persistency).

Postmarketing reports: syncope, hypotension, angioedema, erythema, rash, pruritus, urticaria, vertigo, diplopia, and visual impairment. Lancet. 2010;376:875–885

Ivabradine – Corlanor

Dosage Adjustment Table

Heart Rate	Dose Adjustment
> 60 BPM	**Increase dose by 2.5 mg BID up to a maximum dose of 7.5 mg BID**
50-60 BPM	**Maintain the dose**
< 50 BPM	**Decrease the dose by 2.5 mg BID, if current dose is 2.5 mg BID discontinue therapy**

Available as a scored 5 mg tablet and 7.5 mg unscored tablet
Cost is reported to be ~$465.00 per month wholesale

Pharmacologic Therapy: Aldosterone Antagonists

- **An aldosterone antagonist is recommended for patients on standard therapy, including diuretics, who have:**
  - **NYHA class II - IV HF from reduced LVEF (≤ 35%)**
- **One should be considered in patients post-MI with clinical HF or diabetes and an LVEF < 40% who are on standard therapy, including an ACE inhibitor (or ARB) and a beta blocker.**
  - **–Spironolactone 25 mg ~ $ 10.00/30)**
  - **–Eplerenone 25 mg ~ $25.00/30)**

Strength of Evidence = A

Table 2. Aldosterone Antagonists in Heart Failure: Evidence From Randomized Controlled Trials

Trial	n	Population	Primary Endpoint	Mean Length of Follow-up (Months)	ACE inhibitor or ARB, %	β-blocker, n (%)	All-cause Mortality, n (%) RR (95% CI)	Death or HF Hospitalization, n (%) RR (95% CI)	Serious Hyperkalemia, n (%)
RALES[7]	822 S 841 P	NYHA Class III/IV (IV within 6 months prior) (SCr >2.5 mg/dL or serum potassium >5 mmol/L excluded)	All-cause mortality	24	95% S 94% P	11% S 10% P	284 (35) S 386 (46) P 0.7 (0.60–0.82), *P* < .001 NNT=9	CV death or CV hospitalization 0.68 (0.59–0.78), *P* < .001	≥6 mmol/L 14 (2) S 10 (1) P, *P* = .42
EPHESUS[8]	3319 E 3313 P	AMI, LVEF ≤40, and HF symptoms (SCr >2.5 mg/dL or serum potassium >5 mmol/L excluded)	Co-primary: Time to death from any cause Time to CV death or first CV hospitalization	16	86% E 87% P	75% E 75% P	478 (14.4) E 554 (16.7) P 0.85 (0.75–0.96), *P* = .008 NNT=44	CV death or CV hospitalization 885 (26.7%) E 993 (30%) P 0.87 (0.79–0.95), *P* = .002 NNT=25	≥6 mmol/L 180 (5.5) E 126 (3.9) P *P* = .002
EMPHASIS-HF[31]	1364 E 1373 P	NYHA Class II (NYHA III/IV, eGFR <30 mL/min, serum potassium >5 mmol/L excluded)	CV death or first HF hospitalization	21 (median)	94% E 93% P	87% E 87% P	171 (12.5) E 213 (15.5) P 0.76 (0.62–0.93), *P* = .008 NNT=33	CV death or HF hospitalization (primary endpoint) 249 (18.3) E 356 (25.9) P HR 0.63 (0.54–0.74), *P* < .001 NNT=14	>6 mmol/L 33 (2.5) E 25 (1.9) P, *P* = .29 >5.5 mmol/L 158 (11.8) E 96 (7.2) P, *P* < .001

ACE, angiotensin-converting enzyme; AMI, acute MI; CV, cardiovascular; E, eplerenone; eGFR, estimated glomerular filtration rate; HF, heart failure; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; S, spironolactone; P, placebo; RALES, Randomized Aldactone Evaluation study; SCr, serum creatinine.

Aldosterone Antagonists and Renal Function

- **Aldosterone antagonists are not recommended when:**
  - **Creatinine > 2.5mg/dL (or clearance < 30 mL/min)**
  - **Serum potassium> 5.0 mmol/L**
  - **Therapy includes other potassium-sparing diuretics**

Strength of Evidence = A

- **It is recommended that potassium be measured at baseline, then 1 week, 1 month, and every 3 months**

Strength of Evidence = A

- Supplemental potassium is not recommended unless potassium is < 4.0 mmol/L

Strength of Evidence = A

–2017 ACC/AHA/HFSA Heart Failure Focused Update

Spironolactone in Patients with HFpEF

- **New: patients with HFpEF (preserved EF)(>/=45%), elevated BNP levels or hospitalization in last year and eGFR > 30ml/min, Cr < 2.5 mg/dl, potassium <5.0 mmol/L might be added to reduce hospitalizations.**
  - 2017 ACC/AHA/HFSA Heart Failure Focused Update

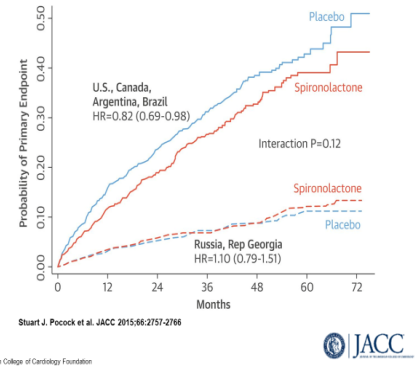
Treatment Of Preserved Cardiac Function Heart Failure with an Aldosterone anTagonist (TOPCAT)

TOPCAT - HF*p*EF EF >45%

- Randomized, double-blind trial, N=3,445
  - Mean duration: 3.3 years
  - Sponsor: NHLBI
- Treatment
  - Spironolactone
    - 15mg QD; increased to max of 45mg/day by month 4
  - Placebo
- Outcome
  - Primary: death from CV causes, aborted cardiac arrest, or hospitalization for HF
  - Endpoints adjudicated

N Engl J Med 2014;370:1383-92.

TOPCAT Trial



Stuart J. Pocock et al. JACC 2015;66:2757-2766

JACC

2015 American College of Cardiology Foundation

A-Heft Trial

1,050 African-American patients with advanced heart failure
New York Heart Association (NYHA) class 3-4 for ≥ 3 months
LV function ≤ 35% (≤ 40% if LV dilated per echo)
90% receiving diuretics, 69% ACE-inhibitor, 17% angiotensin receptor blocker, 74% beta-blocker

Isosorbide dinitrate (ISDN) plus hydralazine
Tablet containing 20 mg ISDN and 37.5 mg hydralazine (BiDil®, NitroMed) 3X daily. Dosage could be doubled by enrolling physician.
n=518
44.2% female
44.8% diabetic

Placebo
n=532
36.1% female
37.0% diabetic

Bidil 37.5/20mg ~ $600.00/180
Generic hydralazine 25 mg ~$25.00/270 and isosorbide dinitrate 40 mg ~$75-100.00/90

Primary Endpoint:
Weighted composite of all-cause death, first hospitalization for heart failure, and change in quality of life at a mean follow-up of 10 months

www.Clinical trial results.org

Presented at AHA 2004

A-HeFT Outcomes

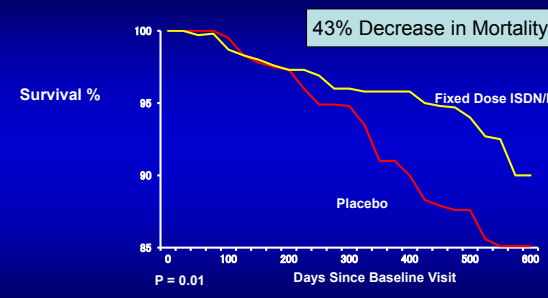
End point	ISDN-HDZN (n=518)	Placebo (n=532)	P	NNT
Primary end point composite score	-0.1	-0.5	0.01	
All-cause mortality (%)	6.2	10.2	0.02	25
1st HF hospitalization (%)	16.4	24.4	0.001	13
Change in quality-of-life score at 6 months**	-5.5	-2.7	0.02	

Taylor AL et al. N Engl J Med 2004; 351;2049-57

Heart Failure Society of America

A-HeFT All-Cause Mortality

43% Decrease in Mortality NNT 25



Taylor AL et al. N Engl J Med 2004;351:2049-57

Heart Failure Society of America

Question?

- How many of us still use digoxin in our patients with HFrEF?
- What are the potential benefits/risks?
- Do we have any concerns with digoxin levels?

Should We Recommend Digoxin?

- **AHA/ACC 2013 "Digoxin can be beneficial in patients with HFrEF, unless contraindicated, to decrease hospitalizations for HF." In the new 2017 AHA/ACC/HFSA guidelines it is not on the algorithm?**
- **UpToDate 12/2018 "For most patients with heart failure with reduced ejection fraction (HFrEF), we suggest not routinely using digoxin. We reserve use of digoxin for patients with HFrEF on optimal evidence-based therapy with NYHA functional class III or IV; some experts also require a left ventricular ejection fraction (LVEF) <25 percent). "**
- **"We suggest maintaining digoxin levels between 0.5 and 0.8 ng/mL in both men and women (Grade 2B). Higher serum levels should be avoided since they are associated with an increased risk of toxicity, without clear evidence of enhanced efficacy."**

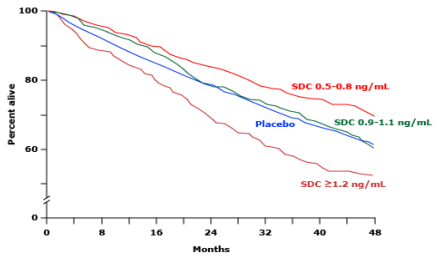
Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure

Outcome	Digoxin (n = 3397)	Placebo (n = 3403)	Risk Ratio (95% CI)	*P*-value
All-cause mortality	1181 (34.8%)	1194 (35.1%)	0.99 (0.91-1.07)	0.8
Due to worsening HF	394 (11.6%)	449 (13.2%)	0.88 (0.77-1.01)	0.06
Due to CV causes	1016 (29.9%)	1004 (29.5%)	1.01 (0.93-1.10)	0.78
Hospitalization	2184 (64.3%)	2282 (67.1%)	0.92 (0.87-0.98)	0.006
For worsening HF	910 (26.8%)	1180 (34.7%)	0.72 (0.66-0.79)	< 0.001
For CV reasons	1694 (49.9%)	1850 (54.4%)	0.87 (0.81-0.93)	< 0.001
Toxicity suspected	67 (2%)	31 (0.9%)	2.17 (1.42-3.32)	< 0.001

HF = heart failure; CV = cardiovascular

N Engl J Med. 1997 Feb 20;336(8):525-33.

Serum digoxin in HF is correlated with survival



Among 3782 patients with heart failure (HF) receiving digoxin or placebo in the DIG trial, there was a significant association between serum digoxin concentration (SDC) and all-cause mortality. Compared with placebo, survival was significantly better for patients with SDC 0.5 to 0.8 ng/mL, and significantly worse for patients with SDC ≥1.2 ng/mL.

Data from Rathore SS, Curtis JP, Wang Y, et al. JAMA 2003; 289:871.

Digoxin and Outcomes?

- **Kaiser Northern Calif** examined new digoxin use and risks of death and HF hospitalization, controlling for medical history, laboratory results, medications, HF disease severity, and the propensity for digoxin use. We also conducted analyses stratified by sex and concurrent β-blocker use. **Among 2891 newly diagnosed patients with systolic HF, 529 (18%) received digoxin**.
- **During a median 2.5 years of follow-up, incident digoxin use was associated with higher rates of death (14.2 versus 11.3 per 100 person-years) and HF hospitalization (28.2 versus 24.4 per 100 person-years)**. In multivariable analysis,
- **incident digoxin use was associated with higher mortality (hazard ratio, 1.72; 95% confidence interval, 1.25–2.36) but no significant difference in the risk of HF hospitalization (hazard ratio, 1.05; 95% confidence interval, 0.82–1.34).**
  - Results were similar in analyses stratified by sex and β-blocker use.
    - Circ Cardiovasc Qual Outcomes. 2013;6:525-533

Digoxin After 230 years?

- The **Editorial by Dr. Opie entitled "Digitalis, Yesterday and Today, But Not Forever" concludes:** "This conclusion is the opposite of what the earlier studies favoring digoxin use in the bygone era of imperfect therapy for HF had found, with the **new conclusion that therapy for HF that includes β-blockade and full angiotensin-II modulation dispenses with the need for taking the risks of adding digoxin therapy**. The data at our disposal, taking into account the current study, allow us to seriously question the advice on digoxin given by both the current and influential guidelines, European and American."
  - Circ Cardiovasc Qual Outcomes. 2013;6:511-513

SELF EVALUATION

Evidence-Based Management of Heart Failure with Reduced Ejection Fraction

1. According to the CHAMP-HF (Change the Management of Patients with Heart Failure) registry, what % of heart failure patients were receiving Guideline Directed Therapy at recommended doses?

a. ~75%
b. ~50%
c. ~25%
d. ~10%
e. ~1%

2. Which dose of angiotensin receptor blocker (ARB) is not a target dose for patients with heart failure with reduced ejection fraction (HFrEF)?

a. Losartan 150 mg/day
b. Valsartan 160 mg BID
c. Candesartan 32 mg/day
d. None of the above, all are recommended

3. Which beta blocker/dose is **not** recommended in the guidelines for treating patients with reduced ejection fraction heart failure (HFrEF)?

a. Bisoprolol 10 mg once a day
b. Carvedilol 25 o 50 mg BID based upon body weight
c. Metoprolol succinate 200 mg once a day
d. Metoprolol tartrate 100 mg BID

4. Which beta-blocker would you recommend for a patient with heart failure with reduced ejection fraction and mixed asthma/COPD?

a. Carvedilol BID
b. Metoprolol succinate QD
c. Bisoprolol QD
d. Atenolol QD
e. No beta blocker

5. Which statement about the Angiotensin Receptor Neprilysin Inhibitor (ARNI) - Valsartan/Sacubitril - Entresto is **not** correct?

a. ACE inhibitors must be discontinued for 36 hours before starting valsartan/sacubitril to reduce the risk of angioedema.
b. The new guidelines for treatment of patients with reduced ejection fraction heart failure recommends “In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality”.
c. The one potential adverse effect that was significantly greater in the PARADIGM HF Trial with enalapril than with valsartan/sacubitril was hypotension.
d. In the PARADIGM HF Trial the valsartan/sacubitril arm reduced CV mortality and heart failure hospitalization significantly greater than the ACEI enalapril.

Answer Key: 1. E, 2. D, 3. D, 4. C, 5. C

Barry A. Franklin, PhD

Barry A. Franklin, PhD, of Royal Oak, Michigan, is director of Preventive Cardiology and Cardiac Rehabilitation at William Beaumont Hospital which, during his tenure, has achieved national recognition in the diagnosis and treatment of coronary artery disease. He served as president of the American Association of Cardiovascular and Pulmonary Rehabilitation (1989–1990) and of the American College of Sports Medicine (1999–2000).

Dr. Franklin is a past editor in chief of the *Journal of Cardiopulmonary Rehabilitation* and currently holds formal editorial board appointments with 15 other scientific and clinical journals. He has written or edited nearly 600 scientific and clinical publications, including 27 books and, since 1976, he has given over 1000 invited presentations to state, national and international audiences. In 2015 Dr. Franklin was listed by Thomson Reuters among *The World's Most Influential Scientific Minds (Clinical Medicine)*, something quite rare for a non-physician.

You may contact Dr. Franklin at Barry.Franklin@beaumont.org.

Beaumont Health
Health Center
4949 Coolidge Highway
Royal Oak, MI 48073

Barry A. Franklin, PhD
Director of Preventive Cardiology and Cardiac Rehabilitation

Preventive Cardiology and Lifestyle Medicine Update

Critical Question: Do You Have Coronary Artery Disease?

"Cleveland Clinic studies (using IVUS) suggest that ~85% of individuals in the U.S. over 50 have atherosclerotic CAD. So for me, the question isn't whether middle-aged and older adults have heart disease – they probably do. It's how to prevent acute catastrophic cardiac events."

Ira M. Grais, MD

Tuzcu EM, et al. Circulation 2001; 103: 2705-2710.

The Devastation & Incidence of Sudden Cardiac Death*

Tim Russert
(Age 58)

James Gandolfini
(Age 51)

Members of the population cohort among whom sudden cardiac death is most common:

Men aged 60 ± 5 years

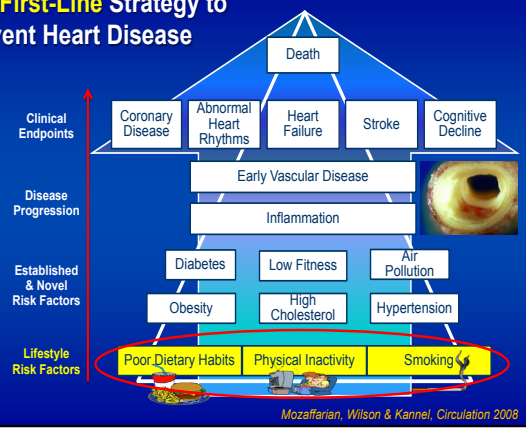
** ~310,000 sudden cardiac deaths/year (850 Americans/day)*

Cardiovascular Disease: Our #1 Killer

About 803,000 people die as a result of atherosclerotic cardiovascular disease each year in the United States, and 17.3 million worldwide, making it one of the biggest societal killers.

Critical Question: What can we do to 'help clients/patients help themselves/families' to avoid being among the fatalities every year?

The First-Line Strategy to Prevent Heart Disease



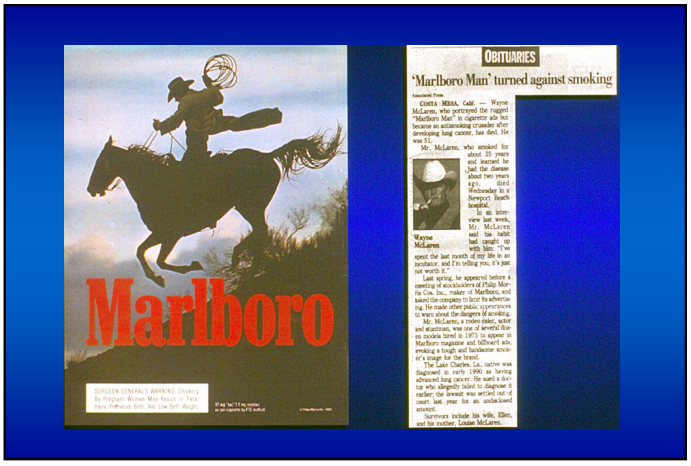
Mozaffarian, Wilson & Kannel, Circulation 2008

Outline (5 Topics)

Topic 1

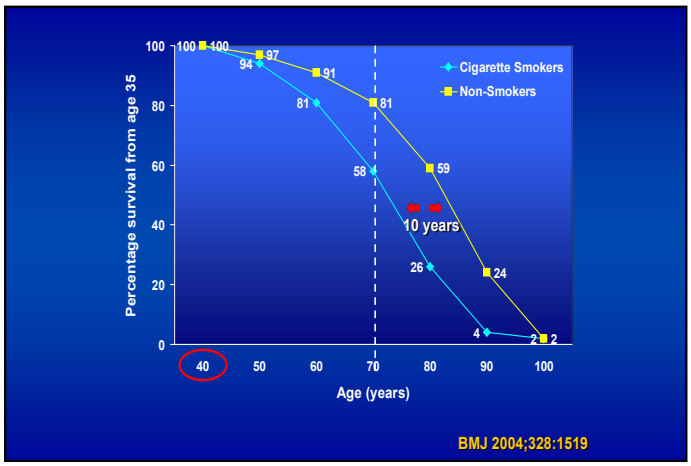
- Hazards of Cigarette Smoking and Secondhand Smoke
- Cardioprotective Medications
- Evidence-based Dietary Strategies
- Walking Distance/Speed, Physical Activity, Fitness, Mortality, Atrial Fibrillation, Coronary Calcium, Heart Failure, HIIT, Medical Marvels
- Genetics versus Lifestyle/ Healthy Lifestyle Factors and Life Expectancy

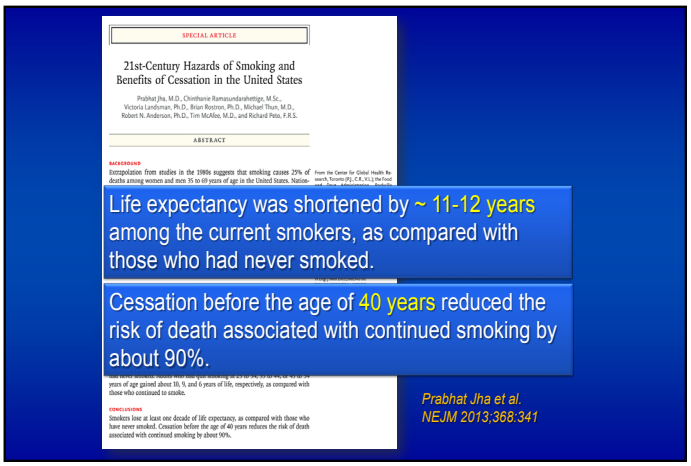

RESTAURANT
COMMON PRECIPITATING FACTORS IN ANGINA PECTORIS: HEAVY MEAL, EXERTION, COLD, SMOKING
CHARACTERISTIC DISTRIBUTION OF PAIN IN ANGINA PECTORIS


Marlboro
SURGEON GENERAL'S WARNING: Smoking By Pregnant Women May Result in Fetal Injury, Premature Birth, And Low Birth Weight
OBITUARIES
'Marlboro Man' turned against smoking
Associated Press
COSTA MESA, Calif. — Wayne McLaren, who portrayed the rugged "Marlboro Man" in cigarette ads but became an antismoking crusader after developing lung cancer, has died. He was 51.
Mr. McLaren, who smoked for about 25 years and learned he had the disease about two years ago, died Wednesday in a Newport Beach hospital.
In an interview last week, Mr. McLaren said he hadn't caught up with him: "I've spent the last month of my life in an incubator, and I'm telling you, it's just not worth it."
Last spring, he appeared before a meeting of stockholders of Philip Morris Cos. Inc., maker of Marlboro, and asked the company to limit its advertising. He made other public appearances to warn about the dangers of smoking.
Mr. McLaren, a rodeo rider, actor and stuntman, was one of several Texas models hired in 1975 to appear in Marlboro magazine and billboard ads, evoking a tough and handsome smoker's image for the brand.
The Lake Charles, La., native was diagnosed in early 1990 as having advanced lung cancer. He sued a doctor who allegedly failed to diagnose it earlier; the lawsuit was settled out of court last year for an undisclosed amount.
Survivors include his wife, Ellen, and his mother, Louise McLaren.
Wayne McLaren


MR. BOFFO By Joe Martin
PSYCHIC READINGS
(Discounts for Smokers)
We give discounts to smokers because there's less to tell . . .
Fortune Teller
JOE MARTIN


Papers
Mortality in relation to smoking: 50 years' observations on male British doctors
Richard Doll, Richard Peto, Jillian Boreham, Isabelle Sutherland
Abstract
Introduction
1951 prospective study
BMJ 2004;328:1519


Percentage survival from age 35
Age (years)
Cigarette Smokers
Non-Smokers
10 years
BMJ 2004;328:1519


SPECIAL ARTICLE
21st-Century Hazards of Smoking and Benefits of Cessation in the United States
ABSTRACT
Life expectancy was shortened by ~ 11-12 years among the current smokers, as compared with those who had never smoked.
Cessation before the age of 40 years reduced the risk of death associated with continued smoking by about 90%.
Prabhat Jha et al.
NEJM 2013;368:341

Special Report

Cardiovascular Effects of Secondhand Smoke

Secondhand smoke increases the risk of coronary heart disease and cardiac events by ~ 30%.

Circulation 2005;111:2684-2698

THE NEW ENGLAND JOURNAL of MEDICINE

Since the end of March 2006, smoking has been prohibited by law in all enclosed public places throughout Scotland.

ABSTRACT

BACKGROUND

Previous studies have suggested a reduction in the total number of hospital admissions for acute coronary syndrome after the enactment of legislation banning smoke-

Overall, the number of admissions for acute coronary syndrome decreased from 3235 to 2684 – a 17% reduction (95% CI, 16 to 18)* – as compared with a 4% reduction in England (which has no such legislation) during the same period and a mean annual decrease of 3% (maximum decrease, 9%) in Scotland during the decade preceding the study.

CONCLUSIONS

The number of admissions for acute coronary syndrome decreased after the implementation of smoke-free legislation. A total of 67% of the decrease involved non-smokers. However, fewer admissi

all reduction.

Pell JP et al. NEJM 2008;359:482

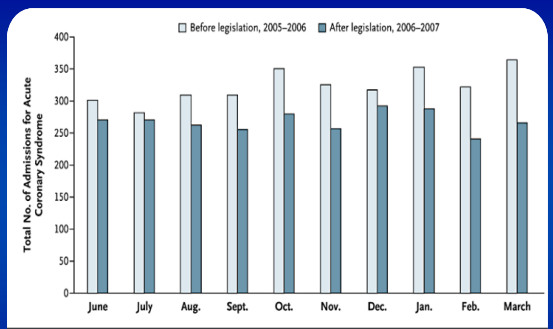


Figure 1. Admissions for Acute Coronary Syndrome According to Month before and after Smoke-free Legislation.

Pell JP et al. NEJM 2008;359:482

Influence of Secondhand Smoke on the Triggering of Acute Cardiac Events

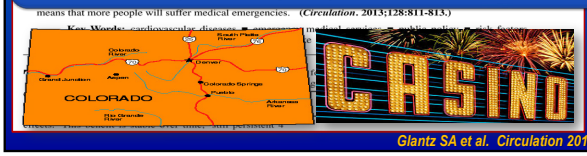
Changes in Ambulance Calls After Implementation of a Smoke-Free Law and Its Extension to Casinos

Stanton A. Glantz, PhD; Erin Gibbs, BS

Background—Casinos are often exempted from legislation mandating smoke-free environments, potentially putting

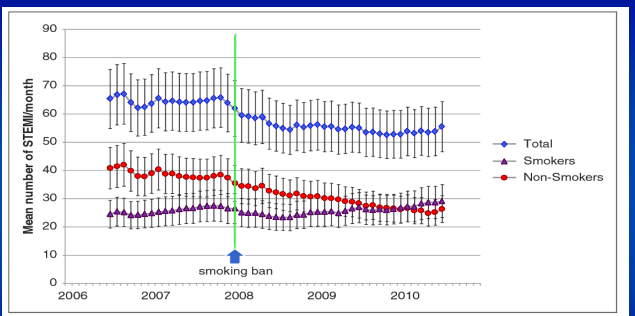
Initial implementation of the smoke-free law (which exempted casinos) was followed by a significant 22.8% drop in ambulance calls from locations other than casinos, but no significant change in calls from casinos. The law requiring smoke-free casinos taking effect was followed by a 19.1% drop in ambulance calls from casinos, but no change in calls originating outside casinos.

means that more people will suffer medical emergencies. (*Circulation*. 2013;128:811-813.)



Glantz SA et al. Circulation 2013;128:811-813

Smoking Ban in Public Areas: Bremen Germany



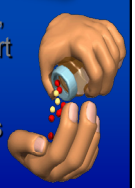
These results may be explained by the protection of non-smokers from passive smoking and the absence of such an effect in smokers by the dominant effect of active smoking.

Schmucker J et al. Eur J Prev Cardiol 2014;21:1180-1186

Outline

Topic 2

- Hazards of Cigarette Smoking and Secondhand Smoke
- Cardioprotective Medications
- Evidence-based Dietary Strategies
- Walking Distance/Speed: Physical Activity, Fitness, Mortality, Atrial Fibrillation, Coronary Calcium, Heart Failure, HIIT, Medical Marvels
- Genetics versus Lifestyle/ Healthy Lifestyle Factors and Life Expectancy



Cardioprotective Medications

Aspirin

Statin (Cholesterol Lowering)

Beta- blockers (Post MI, LV dysfunction)

ACE-I or ARB (EF ≤ 40%, DM, HTN)

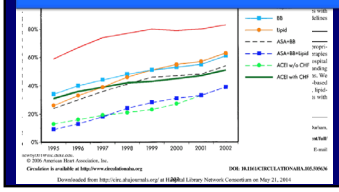
18 - 44% Risk Reduction (Median, 23%)

Health Services and Outcomes Research

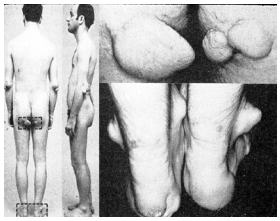
Long-Term Adherence to Evidence-Based Secondary Prevention Therapies in Coronary Artery Disease

Nearly 30% of patients were not consistently using aspirin, and fewer than half reported consistent long-term use of ß blockers, lipid-lowering therapy, or combinations of these life-saving drugs.

In multivariate analysis, nonadherence remained significantly associated with increased all-cause mortality risk for ß blockers (hazard ratio [HR] 1.50, 95% CI 1.33 – 1.71), ACE inhibitors (HR 1.74, 95% CI 1.52 – 1.98), and statins (HR 1.85, 95% CI 1.63 – 2.09). Ho PM et al. Am Heart J 2008



FROM THE EDITOR



Extreme Hypercholesterolemia = Malignant Atherosclerosis

In adults with plasma total cholesterol (TC) levels < 150 mg/dl, atherosclerotic plaques large enough to narrow arterial lumens rarely develop and symptomatic or fatal organ ischemia rarely occurs. Most such adults live in underdeveloped countries or in the Eastern world or both.

hypertension and cigarette smoking is high but the level of plasma TC is low, i.e., < 150 mg/dl, the occurrence of symptomatic or fatal coronary heart disease is virtually nonexistent. About 15 years ago, I visited Kampala, Uganda, and examined many aortas, coronary arteries and

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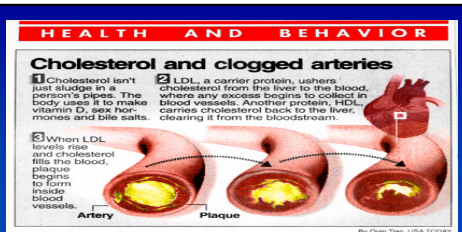
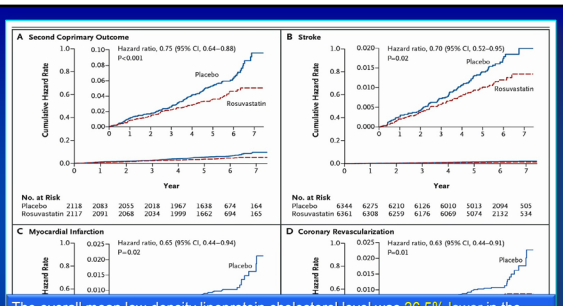


Cholesterol-lowering drugs to play larger role in heart health

TC ↓	LDL↓	HDL↑
22% - 47%	27% - 60%	7%

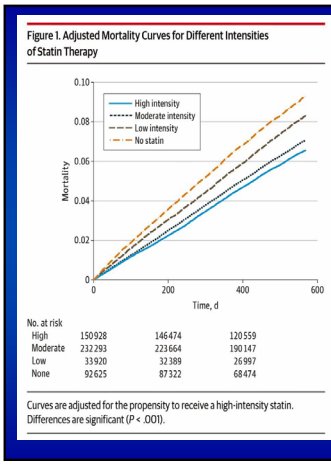
**Roberts WC. AJC 2006;78:1550*



The overall mean low-density lipoprotein cholesterol level was 26.5% lower in the rosuvastatin group than in the placebo group.

Treatment with rosuvastatin at a dose of 10 mg/day resulted in a significantly lower risk of cardiovascular events (25%-37%) than placebo in an intermediate-risk, ethnically diverse population without cardiovascular disease .

Heart Outcomes Prevention Evaluation (HOPE)-3 Trial NEJM April 2016



- **High-Intensity Statins Increase Survival**
  - rosuvastatin 20 or 40 mg or atorvastatin 40 or 80 mg

Rodriguez F et al. JAMA Cardiol 11/09/2016

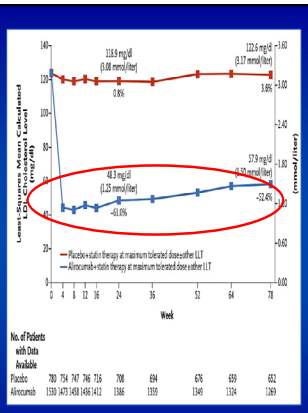
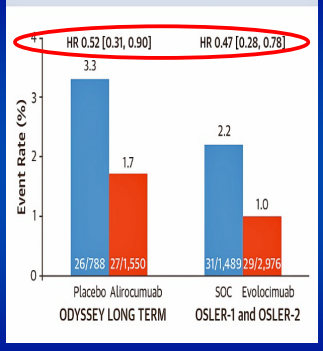


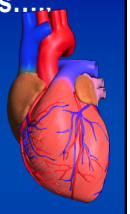
FIGURE 1 Cardiovascular Events in Long-Term PCSK9 Trials



This article was published on March 15, 2015 at NEJM.org

Giugliano RP et al. JACC 2015;65:2638-51

Resting Heart Rate and Blood Pressure ?
Lower #'s Associated with Longer Lives…..



In conclusion, in post-MI pts, this meta-regression of randomized clinical trials robustly suggests that the benefit of drugs modifying HR is strongly related to the magnitude of reduction in resting HR.

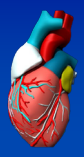
Each 10 bpm reduction in resting HR is estimated to reduce the relative risk of cardiac death by about 30%.

Tenormin
Lopressor
Toprol-XL
Inderal

Cucherat M. Eur Heart J 2007;28:3012

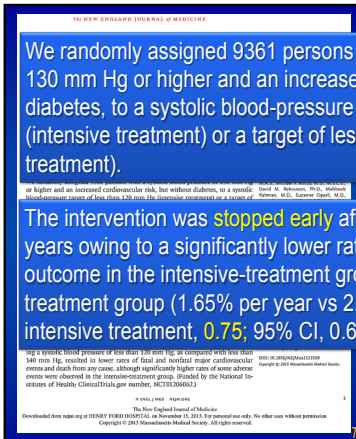
Resting Heart Rate: Lower is Better*

In general, a slower resting heart rate means a longer life – probably because a slower heart rate exerts less stress on blood vessel walls.



Studies have shown that men and women with slower resting heart rates (< 60 bpm) have fewer cardiac events and a lower risk of dying from CVD than those with faster rates (> 80 bpm)

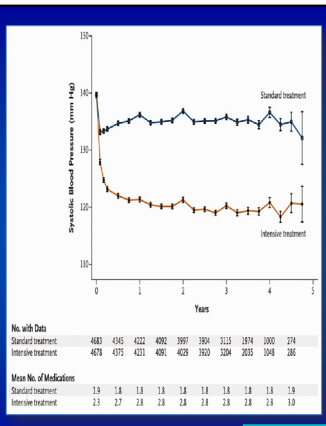
**Saxena A et al. Mayo Clin Proc 2013 (December)*

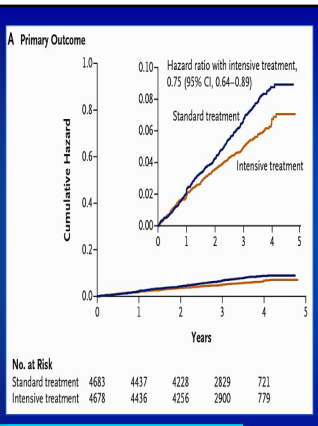


We randomly assigned 9361 persons with a systolic blood pressure of 130 mm Hg or higher and an increased cardiovascular risk, but without diabetes, to a systolic blood-pressure target of less than 120 mm Hg (intensive treatment) or a target of less than 140 mm Hg (standard treatment).

The intervention was stopped early after a median follow-up of 3.26 years owing to a significantly lower rate of the primary composite outcome in the intensive-treatment group than in the standard-treatment group (1.65% per year vs 2.19% per year; hazard ratio with intensive treatment, 0.75; 95% CI, 0.64 to 0.89; p<0.001).

This article was published on Nov. 9, 2015 at NEJM.org



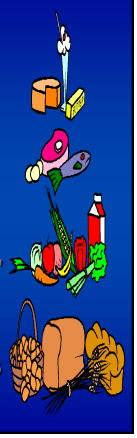


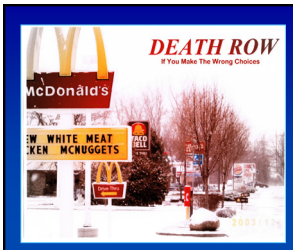
This article was published on Nov. 9, 2015 at NEJM.org

Outline

Topic 3

- Hazards of Cigarette Smoking and Secondhand Smoke
- Cardioprotective Medications
- Evidence-based Dietary Strategies
- Walking Distance/Speed: Physical Activity, Fitness, Mortality, Atrial Fibrillation, Coronary Calcium, Heart Failure, HIIT, Medical Marvels
- Genetics versus Lifestyle/ Healthy Lifestyle Factors and Life Expectancy





"Our excessive intake of meat is killing us. We fatten our cows and pigs, kill them, eat them, and then they kill us!"

William C. Roberts, M.D.

INVITED COMMENTARY

Holy Cow! What's Good for You Is Good for Our Planet

This is the first large-scale prospective longitudinal study showing that consumption of both processed and unprocessed red meat is associated with an increased risk of premature mortality from all causes as well as from cardiovascular disease and cancer.

have a spectrum of choices; it's not all or nothing.

Plant-based foods are rich in phytochemicals, bioflavonoids, and other substances that are protective. In other words, what we *include* in our diet is as important as what we *exclude*, so substituting healthier foods for red meat provides a double benefit to our health.

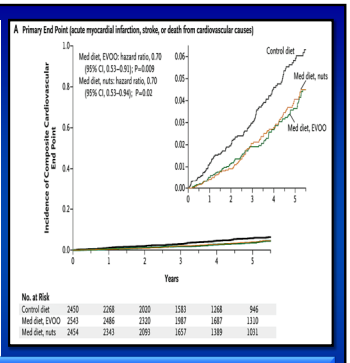
Pan et al[1] reported that adjustment for saturated fat, dietary cholesterol, and heme iron accounted for some but not all of the risk of eating red meat. Thus, other mechanisms such as nontraditional risk factors may be involved.

For example, a recent study by Smith[8] found that high-fat, high-protein, low-carbohydrate (HPLC) diets (which are usually high in red meat, such as the Atkins and Pa-

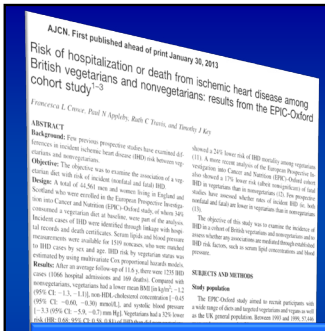
tion experts about what constitutes a healthy way of eating:

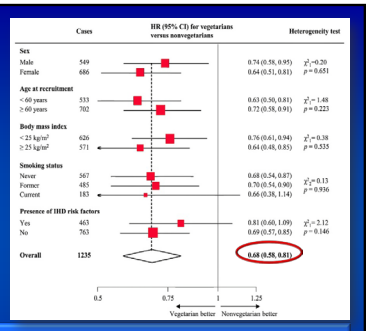
- little or no red meat;
- high in "good carbs" (including vegetables, fruits, whole grains, legumes, and soy products in their natural forms);
- low in "bad carbs" (simple and refined carbohydrates, such as sugar, high-fructose corn syrup, and white flour);
- high in "good fats" (ω-3 fatty acids found in fish oil, flax oil, and plankton-based oils);
- low in "bad fats" (trans fats, saturated fats, and hydrogenated fats);

Arch Intern Med 2012;172(7):563



Among persons at high cardiovascular risk, a Mediterranean diet supplemented with extra-virgin olive oil or nuts reduced the incidence of major cardiovascular events by ~ 30%.





Vegetarians had a 32% lower risk (HR: 0.68; 95% CI: 0.58, 0.81) of IHD than did nonvegetarians, which was only slightly attenuated after adjustment for BMI and did not differ materially by sex, age, BMI, smoking, or the presence of IHD risk factors.

Crowe FL et al. Am J Clin Nutr 2013; 1-30/2013

Trans fatty acids can adversely affect:

LDL and HDL cholesterol levels

LP(a) and triglycerides

Vascular inflammation IL-6, TNF, CRP

Trans fatty acids increase:

Coronary heart disease

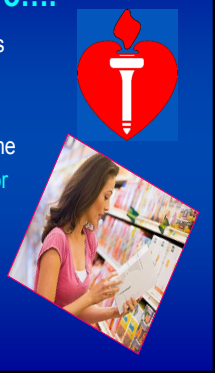
Diabetes

Mozaffarian D. et al Circulation 2012

How Much Trans Fat per Day ?
Remember : Zero isn't Zero….

The AHA recommends limiting the amount of trans fats you eat to less than 1% of your total daily calories. That means if you need 2,000 calories a day, no more than 20 of those calories should come from trans fats. Avoid foods listing hydrogenated or partially hydrogenated on the label…..

That's Less Than 2 Grams of Trans Fats a Day



How Much Salt Are You Eating?

Beware of the Sodium in these ***"Salty Six"*** Foods

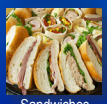

Bread and rolls


Cold cuts & Cured meats


Pizza

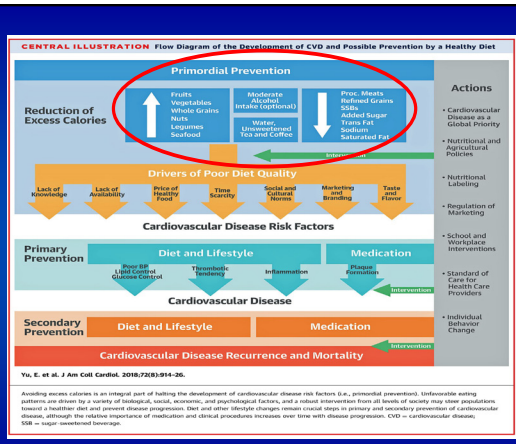

Poultry

Soup


Sandwiches

* The average American consumes ~ 3,400 mg of sodium daily – > twice the 1,500 mg recommended by the AHA. More than 75% of the sodium consumption comes from processed and restaurant foods.

Remember 1:1 Rule/Serv.

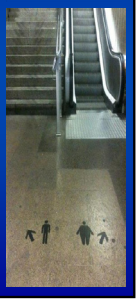


Yu, Edward Scd et al. JACC 2018; 72:914-16.

Outline

Topic 4

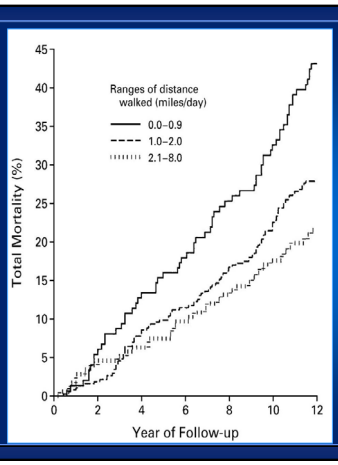
- Hazards of Cigarette Smoking and Secondhand Smoke
- Cardioprotective Medications
- Evidence-based Dietary Strategies
- Walking Distance/Speed: Physical Activity, Fitness, Mortality, Atrial Fibrillation, Coronary Calcium, Heart Failure, High Intensity Interval Training
- Genetics versus Lifestyle/ Healthy Lifestyle Factors and Life Expectancy



Effects of Walking on Mortality Among Non-Smoking Retired Men*

METHODS	707 nonsmoking retired men 61 to 81 years of age; distance walked/day
RESULTS	12-year follow-up, 208 deaths; mortality rate among the men who walked < 1 mile/day was nearly twice that among those who walked > 2 miles/day
CONCLUSIONS	Regular walking is associated with a lower overall mortality rate in older, physically capable men

**Hakim AA et al. NEJM 1998;338:94*



Hakim AA et al. NEJM 1998;338:94

How Fast does the Grim Reaper Walk? *

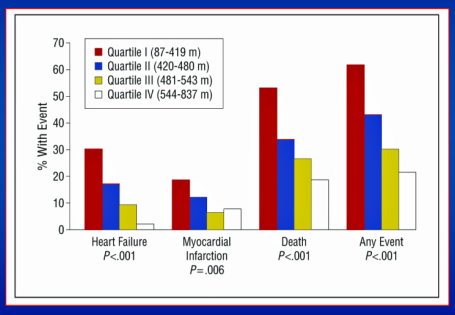
A walking speed of 0.82 m/s (2 mph) was most predictive of mortality.

Older men who walked at speeds greater than 0.82 m/s were 1.23 times less likely to encounter Death.

No men walking at speeds of 1.36 m/s (3 mph) or above were caught by Death (n=22, 1.4%), supporting the hypothesis that faster walking speeds are protective against mortality.

**Stanaway FF et al. BMJ 2011;343:d7679*

HEART & SOUL STUDY: 556 Outpatients with stable CAD, 6-minute walk test, 8-year follow-up



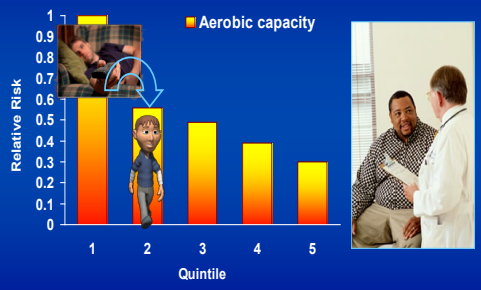
Beatty AL et al. Arch Intern Med 2012;172(14):1096-1102

Metabolic Equivalents (METs): A Measure of Fitness & Energy Expenditure

- 1 MET* = amount of O2 your body uses at rest
- Average adult has a fitness level of 6 – 10 METs; heart failure patients 2 – 5 METs; elite endurance athletes ~ 20 – 25 METs
- Each 1 MET increase in cardiorespiratory fitness is associated with a 15% reduced risk of dying from an acute cardiac event (up to ~ 10 METs)
- A treadmill test is the most accurate way to assess your MET capacity (estimated or directly measured)

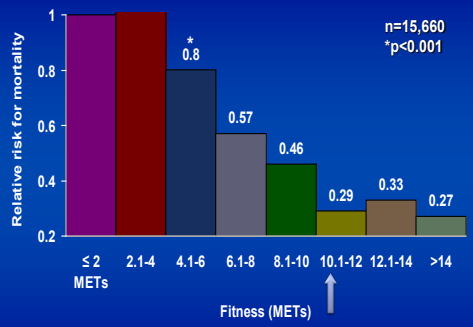
** 3.5 mL O2/kg/min*

Implications for the Medical Community: Moving Patients Out of the Least Fit, "High-Risk" Cohort (Bottom 20%, < or =5 METs)

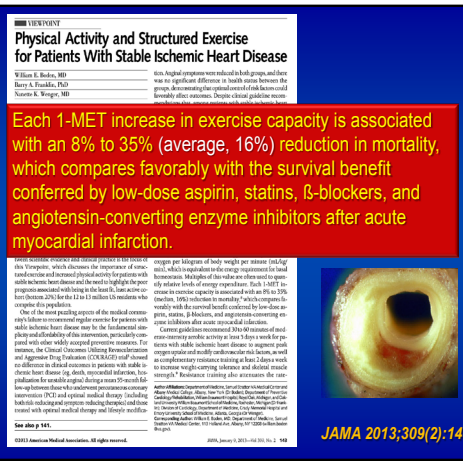


Blair SN et al. JAMA 1996;276:205
Williams PT Med Sci Sports Exerc 2001;33:754
Franklin B et al. Mayo Clin Proc 2013;88:431

Optimal Survival Benefit : > or = 10 METs



Circulation 2010;122:1637


VIEWPOINT

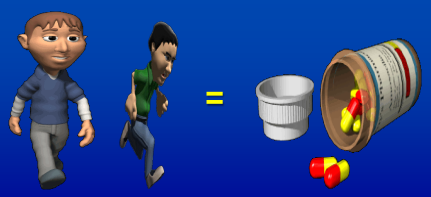
Physical Activity and Structured Exercise for Patients With Stable Ischemic Heart Disease

William E. Boden, MD
Barry A. Franklin, PhD
Nanette K. Wenger, MD

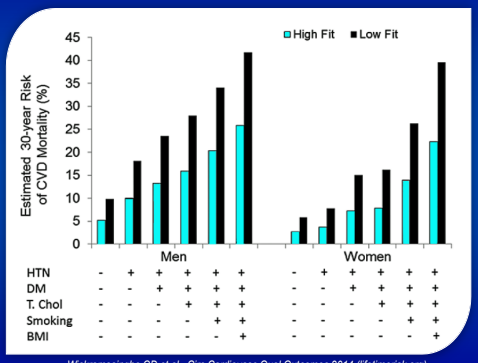
Each 1-MET increase in exercise capacity is associated with an 8% to 35% (average, 16%) reduction in mortality, which compares favorably with the survival benefit conferred by low-dose aspirin, statins, ß-blockers, and angiotensin-converting enzyme inhibitors after acute myocardial infarction.

JAMA 2013;309(2):143

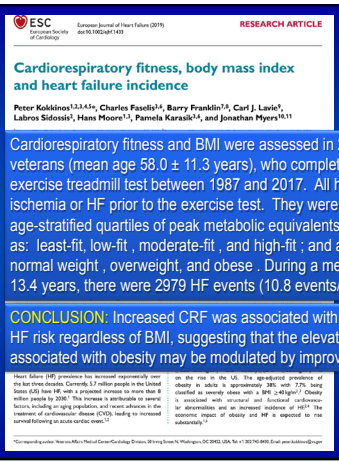
If there was a pill that you could take to cut your risk in HALF of dying from cardiovascular disease (CVD) over the next 30 years, would you take it ? There is such a pill---and its called EXERCISE.



Regardless of the Risk Factor Profile, Low Fit Men and Women have ~ 2x the Mortality



Wickramasinghe CD et al. Circ Cardiovasc Qual Outcomes 2014 (lifetimerisk.org)



Cardiorespiratory fitness and BMI were assessed in 20,254 US male veterans (mean age 58.0 ± 11.3 years), who completed a maximal exercise treadmill test between 1987 and 2017. All had no evidence of ischemia or HF prior to the exercise test. They were classified based on age-stratified quartiles of peak metabolic equivalents (METs) achieved as: least-fit, low-fit , moderate-fit , and high-fit ; and according to BMI as normal weight , overweight, and obese . During a median follow-up of 13.4 years, there were 2979 HF events (10.8 events/1000 person-years).

CONCLUSION: Increased CRF was associated with progressively lower HF risk regardless of BMI, suggesting that the elevated HF risk associated with obesity may be modulated by improved CRF.

Kokkinos P et al. Eur Journal of Heart Failure (2019) dol:10.1002/ejhf.1433

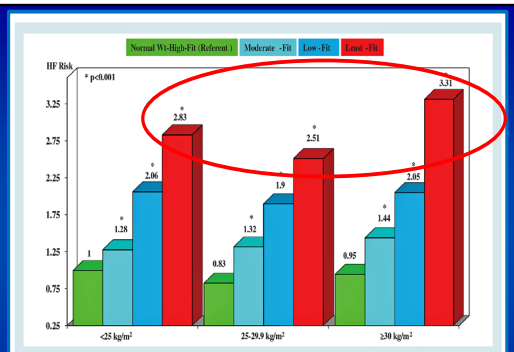
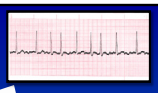


Figure 2 Risk of heart failure (HF) for cardiorespiratory fitness–body mass index interaction groups.

Kokkinos P et al. Eur J Heart Fail 2019

Extreme Exercise Increases the Risk of Atrial Fibrillation (5x)*



** O'Keefe JH et al. Mayo Clin Proc 2012;87:587-595*

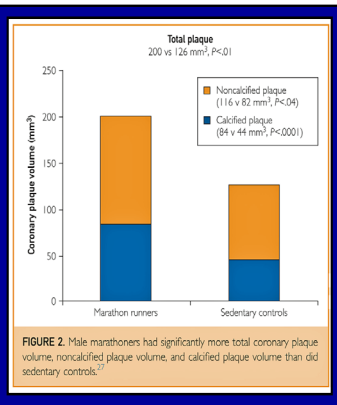
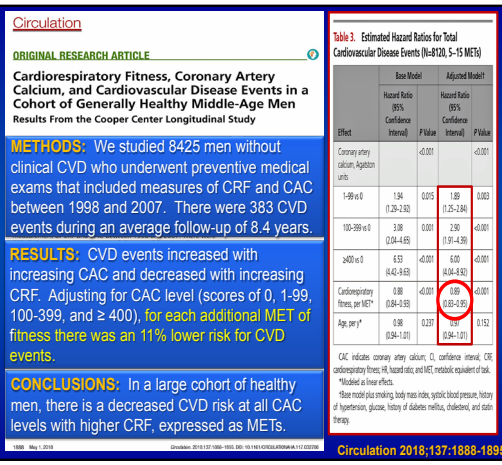


FIGURE 2. Male marathoners had significantly more total coronary plaque volume, noncalcified plaque volume, and calcified plaque volume than did sedentary controls.[27]

Schwartz RS et al. Missouri Med 2014;111:85



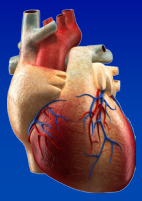
METHODS: We studied 8425 men without clinical CVD who underwent preventive medical exams that included measures of CRF and CAC between 1998 and 2007. There were 383 CVD events during an average follow-up of 8.4 years.

RESULTS: CVD events increased with increasing CAC and decreased with increasing CRF. Adjusting for CAC level (scores of 0, 1-99, 100-399, and ≥ 400), for each additional MET of fitness there was an 11% lower risk for CVD events.

CONCLUSIONS: In a large cohort of healthy men, there is a decreased CVD risk at all CAC levels with higher CRF, expressed as METs.

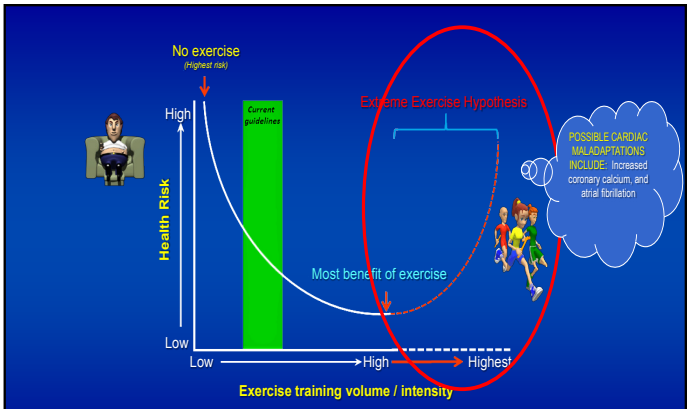
Circulation 2018;137:1888-1895

PRACTICAL IMPLICATIONS



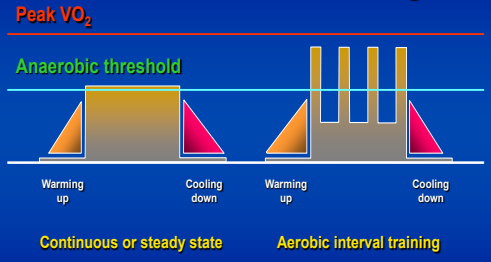
The present data suggest that extreme exercise regimens modestly increase coronary calcium and that endurance athletes with coronary artery calcium (CAC) are at higher risk for mortality and acute cardiac events compared to athletes without CAC; however, the risk for adverse cardiovascular outcomes is lower in physically active/fit persons compared to their inactive counterparts with the same CAC score.

Take Home Message: These results provide reassurance that highly active individuals with CAC can safely continue their exercise programs, provided that they remain asymptomatic.

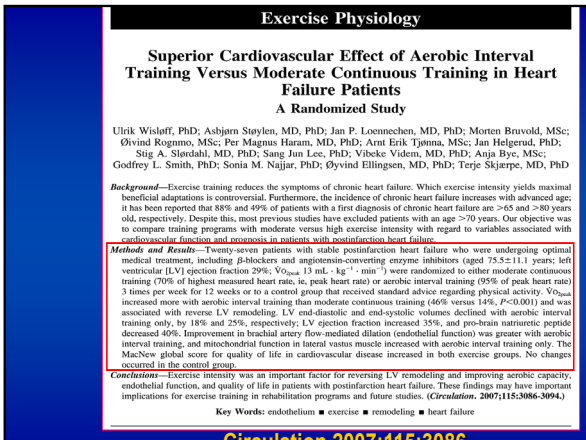


Franklin,BA et al. Circulation : Feb 2020

Conventional Versus High-Intensity Aerobic Interval Training



Archives of Cardiovascular Disease 2009;102:721



Exercise Physiology

Superior Cardiovascular Effect of Aerobic Interval Training Versus Moderate Continuous Training in Heart Failure Patients

A Randomized Study

Ulrik Wisløff, PhD; Asbjørn Støylen, MD, PhD; Jan P. Loennechen, MD, PhD; Morten Bruvold, MSc; Øivind Rognmo, MSc; Per Magnus Haram, MD, PhD; Arnt Erik Tjønna, MSc; Jan Helgerud, PhD; Stig A. Slørdahl, MD, PhD; Sang Jun Lee, PhD; Vibeke Videm, MD, PhD; Anja Bye, MSc; Godfrey L. Smith, PhD; Sonia M. Najjar, PhD; Øyvind Ellingsen, MD, PhD; Terje Skjærpe, MD, PhD

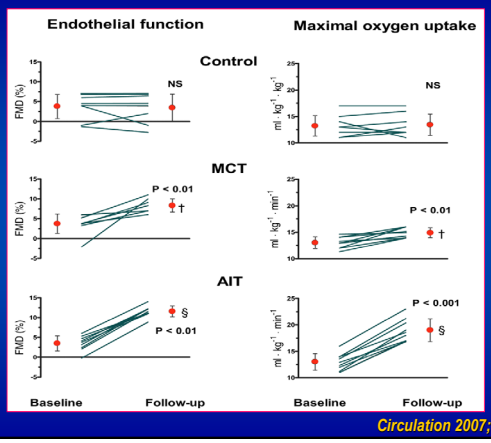
***Background*—**Exercise training reduces the symptoms of chronic heart failure. Which exercise intensity yields maximal beneficial adaptations is controversial. Furthermore, the incidence of chronic heart failure increases with advanced age; it has been reported that 88% and 49% of patients with a first diagnosis of chronic heart failure are >65 and >80 years old, respectively. Despite this, most previous studies have excluded patients with an age >70 years. Our objective was to compare training programs with moderate versus high exercise intensity with regard to variables associated with cardiovascular function and prognosis in patients with postinfarction heart failure.

***Methods and Results*—**Twenty-seven patients with stable postinfarction heart failure who were undergoing optimal medical treatment, including β-blockers and angiotensin-converting enzyme inhibitors (aged 75.5±11.1 years; left ventricular [LV] ejection fraction 29%; Vo_{2peak} 13 mL · kg^{-1} · min^{-1}) were randomized to either moderate continuous training (70% of highest measured heart rate, ie, peak heart rate) or aerobic interval training (95% of peak heart rate) 3 times per week for 12 weeks or to a control group that received standard advice regarding physical activity. Vo_{2peak} increased more with aerobic interval training than moderate continuous training (46% versus 14%, $P<0.001$) and was associated with reverse LV remodeling. LV end-diastolic and end-systolic volumes declined with aerobic interval training only, by 18% and 25%, respectively; LV ejection fraction increased 35%, and pro-brain natriuretic peptide decreased 40%. Improvement in brachial artery flow-mediated dilation (endothelial function) was greater with aerobic interval training, and mitochondrial function in lateral vastus muscle increased with aerobic interval training only. The MacNew global score for quality of life in cardiovascular disease increased in both exercise groups. No changes occurred in the control group.

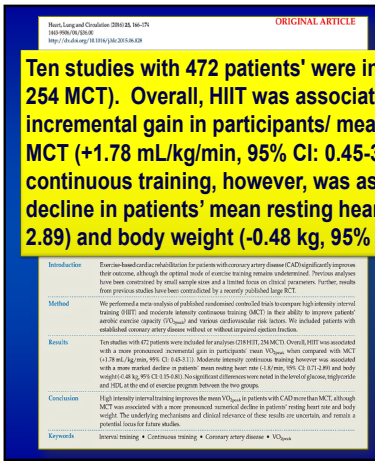
***Conclusions*—**Exercise intensity was an important factor for reversing LV remodeling and improving aerobic capacity, endothelial function, and quality of life in patients with postinfarction heart failure. These findings may have important implications for exercise training in rehabilitation programs and future studies. **(*Circulation*. 2007;115:3086-3094.)**

Key Words: endothelium ■ exercise ■ remodeling ■ heart failure

Circulation 2007;115:3086



Circulation 2007;115:3086



ORIGINAL ARTICLE

Ten studies with 472 patients' were included for analyses (218 HIIT, 254 MCT). Overall, HIIT was associated with a more pronounced incremental gain in participants/ mean VO_{2peak} when compared with MCT (+1.78 mL/kg/min, 95% CI: 0.45-3.11). Moderate intensity continuous training, however, was associated with a more marked decline in patients' mean resting heart rate (-1.8/min, 95% CI: 0.71-2.89) and body weight (-0.48 kg, 95% CI: 0.15-0.81).

Liou K et al.
Heart, Lung and Circulation
2016; 25:166-174

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

Cardiovascular Risk of High- Versus Moderate-Intensity Aerobic Exercise in Coronary Heart Disease Patients

Øivind Rognmo, Trine Moholdt, Hilde Bakken, Torstein Hole, Per Mølstad, Nils Erling Myhr, Jostein Grimsmo and Ulrik Wisløff

Circulation. published online August 9, 2012;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

FINDINGS: The absolute risk was low for high-intensity interval training (1 event per 23,182 patient-hours) and moderate-intensity training (1 event per 129,456 patient hours), but almost 6 times higher in the high-intensity group.

Benefits and Risks of High-Intensity Interval Training in Patients With Coronary Artery Disease

John C. Quindry, PhD[a,b,*], Barry A. Franklin, PhD[c,d], Matthew Chapman, MS[b], Reed Humphrey, PhD[e], and Susan Mathis, MS[b]

Exercise-based cardiac rehabilitation is integral to secondary prevention in patients with coronary artery disease. Recently, the effectiveness and "superiority" of high-intensity interval training (HIIT) is a purported time-saving alternative to "traditional" moderate-intensity continuous training (MICT) in cardiac rehabilitation. The rationale for HIIT adoption is, however, not fully substantiated in the scientific literature. Established guidelines for exercise testing and training, when carefully adhered to, reduce the likelihood of triggering a cardiac event or inducing musculoskeletal injury. Clinicians should likewise consider patient risk stratification and introduce HIIT as an alternative to MICT only after patients exhibit stable and asymptomatic responses to vigorous exercise training. Although HIIT adherence appears comparable with MICT during outpatient rehabilitation, compliance drops dramatically for unsupervised exercise. Despite the enthusiasm surrounding HIIT, its main advantage over MICT appears to be short-term exercise performance outcomes and indices of vascular function. Regarding benefits to cardiovascular disease risk factor modification, management of vital signs, and measures of cardiac performance, current evidence indicates that HIIT does not outperform MICT. Long-term outcomes to HIIT are currently uncertain and logistical constraints to HIIT incorporation need additional clarification. Based on these limited findings, derived from facilities and clinicians at the forefront of cardiac rehabilitation, the routine adoption of HIIT should be viewed cautiously. In conclusion, the current review highlights numerous specific research directives that are needed before the safety and effectiveness of HIIT can be confirmed and widely adopted in patients with known or suspected coronary artery disease, especially in unsupervised, nonmedical settings. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:1370–1377)

Table 2
Comparison of improved aerobic capacity in cardiac patients who underwent HIIT or MICT

Study lead author	HIIT prepost Δ ($ml \cdot kg^{-1} \cdot min^{-1}$)	MICT prepost Δ ($ml \cdot kg^{-1} \cdot min^{-1}$)	HIIT-MICT difference ($ml \cdot kg^{-1} \cdot min^{-1}$)
Rognmo[24]	+6.0*	+2.7*	+3.3†
Warburton[9]	+5.0*	+4.0*	+1.0
Amundsen[15]	+5.0*	+4.0*	+1.0

In conclusion, although some studies suggest that HIIT elicits slightly greater increases in CRF than moderate-intensity training, concerns regarding the safety of repeated near-maximal exercise bouts in patients with known or suspected CAD suggest that it should be cautiously prescribed, especially in unsupervised, nonmedical settings.

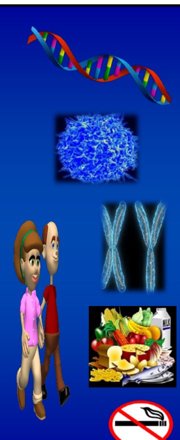
† Indicates a between-group effect was reported for the respective investigation.

Quindry JC et al. Am J Cardiol 2019;123:1370-1377 / HIIT + 1.7 ml/kg/min =1/2 MET

Outline

Topic 5

- Hazards of Cigarette Smoking and Secondhand Smoke
- Cardioprotective Medications
- Evidence-based Dietary Strategies
- Walking Distance/Speed: Physical Activity, Fitness, Mortality, Atrial Fibrillation, Coronary Calcium, Heart Failure, HIIT, Medical Marvels
- Genetics versus Lifestyle/ Healthy Lifestyle Factors and Life Expectancy



Can Bad Genes be Offset by a Healthy Lifestyle ?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease

Amit V. Khera, M.D., Connor A. Emdin, D.Phil., Isabel Drake, Ph.D., Pradeep Natarajan, M.D., Alexander G. Bick, M.D., Ph.D., Nancy R. Cook, Ph.D., Daniel I. Chasman, Ph.D., Usman Baber, M.D., Roxana Mehran, M.D., Daniel J. Rader, M.D., Valentin Fuster, M.D., Ph.D., Eric Boerwinkle, Ph.D., Olle Melander, M.D., Ph.D., Marju Orho-Melander, Ph.D., Paul M Ridker, M.D., and Sekar Kathiresan, M.D.

ABSTRACT

BACKGROUND
Both genetic and lifestyle factors contribute to individual-level risk of coronary artery disease. The extent to which increased genetic risk can be offset by a healthy lifestyle is unknown.

METHODS
Using a polygenic score of DNA sequence polymorphisms, we quantified genetic risk for coronary artery disease in three prospective cohorts — 7814 participants in the Atherosclerosis Risk in Communities (ARIC) study, 21,222 in the Women's Genome Health Study (WGHS), and 22,389 in the Malmö Diet and Cancer Study (MDCS) — and in 4260 participants in the cross-sectional BioImage Study for whom genotype and covariate data were available. We also determined adherence to a healthy lifestyle among the participants using a scoring system consisting of four factors: no current smoking, no obesity, regular physical activity, and a healthy diet.

RESULTS
The relative risk of incident coronary events was 91% higher among participants at high genetic risk (top quintile of polygenic scores) than among those at low genetic risk (bottom quintile of polygenic scores) (hazard ratio, 1.91; 95% confidence interval [CI], 1.75 to 2.09). A favorable lifestyle (defined as at least three of the four healthy lifestyle factors) was associated with a substantially lower risk of coronary events than an unfavorable lifestyle (defined as no or only one healthy lifestyle factor), regardless of the genetic risk category. Among participants at high genetic risk, a favorable lifestyle was associated with a 46% lower relative risk of coronary events than an unfavorable lifestyle (hazard ratio, 0.54; 95% CI, 0.47 to 0.63). This finding corresponded to a reduction in the standardized 10-year incidence of coronary events from 10.7% for an unfavorable lifestyle to 5.1% for a favorable lifestyle in ARIC, from 4.6% to 2.0% in WGHS, and from 8.2% to 5.3% in MDCS. In the BioImage Study, a favorable lifestyle was associated with significantly less coronary-artery calcification within each genetic risk category.

CONCLUSIONS
Across four studies involving 55,685 participants, genetic and lifestyle factors were independently associated with susceptibility to coronary artery disease. Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary artery disease than was an unfavorable lifestyle. (Funded by the National Institutes of Health and others.)

From the Center for Human Genetic Research and Cardiology Division, Massachusetts General Hospital (A.V.K., P.N., S.K.), and the Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital (N.R.C., D.I.C., P.M.R.), Boston, and the Program in Medical and Population Genetics, Broad Institute, Cambridge (A.V.K., C.A.E., A.G.B., S.K.) — all in Massachusetts; the Department of Clinical Sciences, Lund University, Malmö, Sweden (I.D., O.M., M.O.-M.); the Cardiovascular Institute, Mount Sinai Medical Center, Icahn School of Medicine at Mount Sinai, New York (U.B., R.M., V.F.); Department of Genetics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia (D.J.R.); and the University of Texas Health Science Center School of Public Health, Houston (E.B.). Address reprint requests to Dr. Kathiresan at the Center for Human Genetics Research, Massachusetts General Hospital, 185 Cambridge St., CPZN 5.252, Boston, MA 02114, or at skathiresan1@mgh.harvard.edu.

Drs. Khera and Emdin contributed equally to this article.

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4 Large-Scale Studies which included extensive genetic and lifestyle information that have followed > 55,600 adults for up to 20 years

Khera AV et al.
NEJM 11/13/2016

Methods

- **Genetic Risk Score**
  - Each participant was assigned a genetic risk score (low, intermediate, high) based on whether they carried any of the 50 gene variants associated with increased heart attack risk.
- **Lifestyle Risk Score**
  - Four lifestyle factors – no current smoking, no obesity (BMI < 30), exercise ≥ 1 time/wk, and a healthy diet → lifestyle score: favorable (3 or 4 factors); intermediate (2 factors); or, unfavorable (≤ 1 factor).

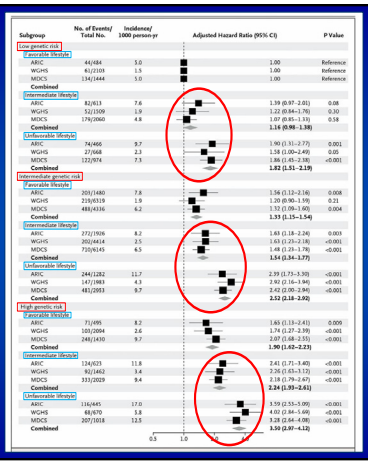
Results

Among participants at high genetic risk, a favorable lifestyle was associated with a nearly 50% lower relative risk of coronary events than an unfavorable lifestyle.

Standardized 10-year Incidence Of Coronary Events

Study Population	Unfavorable Lifestyle	Favorable Lifestyle
ARIC	10.7%	5.1%
WGHS	4.6%	2.0%
MDCS	8.2%	5.3%

Among participants in the BioImage Study, both genetic and lifestyle factors were independently associated with levels of calcium-containing plaque in the coronary arteries, and healthy lifestyle factors were associated with less extensive plaque within each genetic risk group.

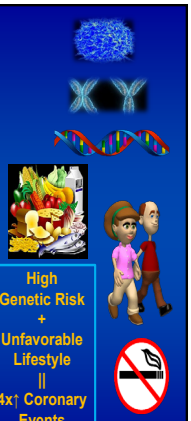


Regardless of the genetic risk [low, intermediate, or high], the biggest protective effect, by far, came from moving from an unfavorable lifestyle to one that was at least intermediate.

Khera AV et al.
NEJM 11/13/2016

Major Findings: Bad Genes ? Lifestyle Matters !

Bad genes can double the risk of heart disease, but a favorable lifestyle cuts it in half. An unfavorable or unhealthy lifestyle erases about half the benefits of good genetics. The 'deadliest combination' was when high genetic risk was paired with an unfavorable lifestyle= 4x increased risk of cardiac events.



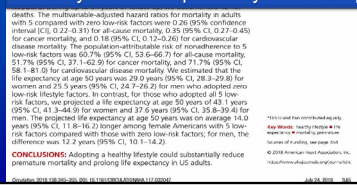
High Genetic Risk + Unfavorable Lifestyle || 4x↑ Coronary Events

Circulation

ORIGINAL RESEARCH ARTICLE

Impact of Healthy Lifestyle Factors on Life Expectancies in the US Population

Background: Americans have a shorter life expectancy compared with residents of almost all other high-income countries. We aim to estimate the impact of 5 low-risk lifestyle factors (not smoking, normal BMI, > or = 30 min/day of moderate intensity physical activity, moderate alcohol consumption, healthy diet score) on premature mortality and life expectancy in the US population.



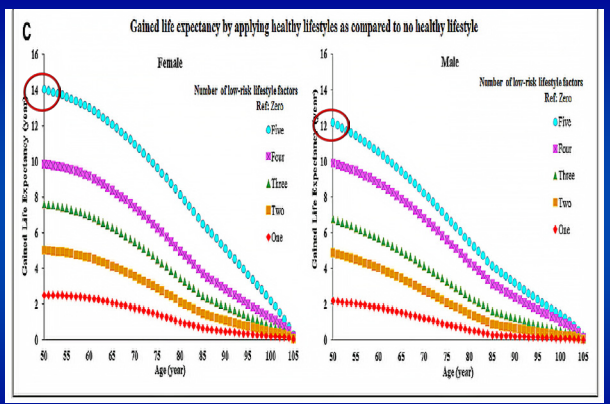
RECENT BLOCKBUSTER STUDY

Circulation 2018;137:00-00, DOI: 10.1161 Circulation/AHA, 117.032047

Results: Clinical Implications*

- During up to 34 years of follow-up, adherence to 5 low-risk lifestyle-related factors could prolong the life expectancy at age 50 years by 14.0 and 12.2 years for female and male U.S. adults compared with individuals who adopted zero low-risk lifestyle factors. The most physically active cohorts of men and women demonstrated 7-to-8 year gains in life expectancy.

Li Y et al. Circulation 2018



Li Y et al. Circulation 2018

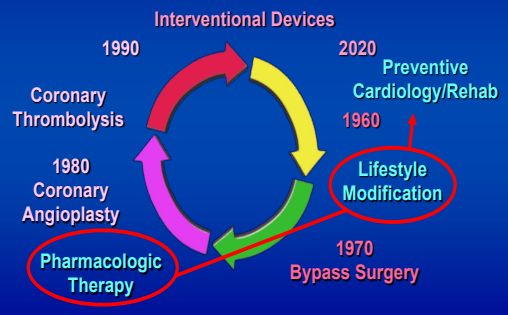
Take Home Messages

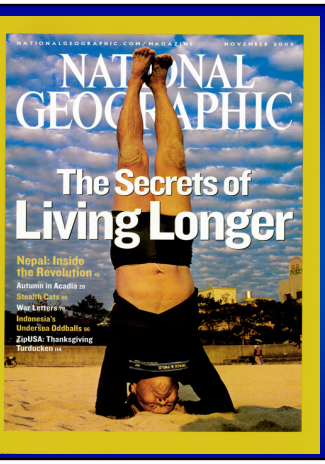
- Americans could narrow the life-expectancy gap between the U.S. and other industrialized countries by adopting a healthier lifestyle
- Prevention should be a top priority for national health policy, and preventive care should be an indispensable part of the U.S. healthcare system.

Conclusions

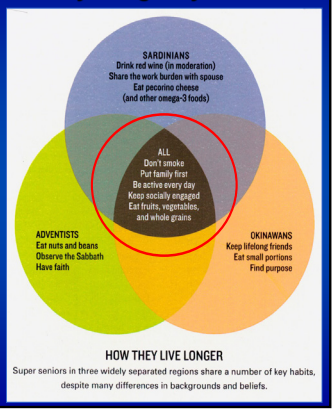
Last 5 slides

Evolutionary Treatment of Heart Disease: Value of Risk Reduction





Key Longevity Habits



Moving from Our Reactive Sick Care Model to Proactive Health Care….

Health care will soon account for $1 out of every $5 spent in the U.S. If these trends continue, health care will soon become unaffordable, unless we find ways to implement effective preventive interventions.

Marvasti FF, et al. N Engl J Med 2012;367:889

In Closing--Beyond Acute and Palliative Care…

- Contemporary healthcare providers need to become champions of achieving healthy lifestyle overhauls in the patients we serve---well beyond the acute and palliative care provided in our emergency centers, surgical suites, cath labs, hospital rooms, and physician offices. The "paradigm shift" needs to move from not only helping patients when they are ill, injured, or sick, to "helping patients help themselves (24/7) ."

SELF EVALUATION

Preventive Cardiology and Lifestyle Medicine Update

1. Two major studies have now shown that life expectancy was shortened by ~____ years in lifetime cigarette smokers.

a. 2-3
b. 5-7
c. 10-12
d. 15
e. None of the above

2. After adjusting for potential confounding variables, secondhand smoke increases the risk of coronary heart disease and cardiac events by ~_____%.

a. 5
b. 10
c. 15
d. 30
e. 44

3. Overall, commonly prescribed cardioprotective medications, including aspirin, statins, beta-blockers, and ACE-inhibitors individually confer an average risk reduction of ____% in the secondary prevention of coronary artery disease.

a. 13
b. 23
c. 35
d. 45
e. >50

4. According to a widely cited meta-analysis, the benefit of drugs modifying the resting and exercise heart rate (e.g., beta-blockers) is strongly related to the magnitude of reduction in resting heart rate. Each 10 beat/min reduction in resting heart rate is estimated to reduce the relative risk of cardiac death by ___%.

a. 5
b. 10
c. 15
d. 20
e. 30

5. A practical rule-of-thumb to facilitate smarter food selections relative to sodium content is:

a. The “0.5 mg-of-sodium-per calorie rule”
b. The “1 mg-of-sodium-per calorie rule”
c. The “2 mg-of-sodium-per calorie rule”
d. The “3 mg-of-sodium-per calorie rule”
e. None of the above

6. To reduce the risk of cardiovascular disease, researchers recommend that patients increase the daily consumption of:

a. Fruits and vegetables
b. Whole grains
c. Processed meats
d. Trans fat
e. Two of the above

7. T/F - When a high genetic risk of premature heart disease is combined with an unfavorable or unhealthy lifestyle, there is an ~10-fold increased risk of cardiac events.

8. T/F - According to a recent blockbuster study, adherence to 5 low-risk lifestyle factors (not smoking, normal BMI, ≥30 min/day of exercise, moderate alcohol intake, healthy diet score) could prolong the life expectancy at age 50 years by 14.0 and 12.2 years for female and male U.S. adults compared with their counterparts who had none of these low-risk lifestyle factors.

Answer Key: 1. C, 2. D, 3. B, 4. E, 5. B, 6. E, 7. F, 8. T

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Joseph W. Shannon, Ph.D., of Columbus, Ohio, has a doctorate in counseling psychology and over 30 years of clinical experience as a psychologist, consultant and trainer. An expert in understanding and treating a broad range of mental disorders, he has appeared on several television programs including CBS', *Morning Show*, and *PBS: Viewpoint*. Dr. Shannon has developed and presented training programs for medical, allied medical, mental health and substance abuse professionals in the United States and Canada consistently earning exemplary ratings for presenting key insights and practical approaches with clarity, enthusiasm and humor.

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Preventing Burnout by Managing Stress

Stress is a multi-faceted response of the body to a perceived demand or threat. While some stress is inevitable and even positive, unhealthy stress can undermine physical, emotional and spiritual health and well-being.

The primary objective of this thought-provoking seminar is to help professional caregivers learn how to recognize and address the causes of unhealthy stress. More specifically, as a result of attending this program, participants will be able to:

1. Understand the role of perception in creating and avoiding stress;
2. Identify specific physical, psychological, cognitive and behavioral symptoms of unhealthy stress;
3. Identify primary and secondary causes of stress;
4. Understand the role of internal pressure and anxiety in creating and sustaining stress over time;
5. List and describe the 6 critical factors that determine the severity of stress; and
6. Utilize 12 specific strategies for reducing stress and preventing burn-out.

STRESS MANAGEMENT AND BURN-OUT PREVENTION FOR HELPING PROFESSIONALS

I. Introduction

A. Definition: A non-specific response of the body to a perceived threat, danger or demand.

B. Stress can actually be positive – e.g., life would be pretty dull/uneventful without stress; stress can create unique challenges and opportunities which can foster growth, etc.

C. Some degree of stress is with us most of the time. It comes from cognitive, emotional and physical activity.

D. Stress is unique and personal; "Perception is critical…"

E. Learning how to reduce or manage stress is an essential skill to ensure a healthy, balanced life.

II. Specific symptoms of unhealthy stress

A. Physical

1. Pupils dilate, blurred vision
2. Dry mouth, difficulty swallowing
3. Muscle aches and tension
4. Faster, irregular breathing; heart pumps faster
5. Blood pressure rises; flushed face
6. More adrenalin is released into blood stream
7. Digestion slows down; stomach may become queasy; ulcers may develop; waning appetite
8. Excessive sweating
9. Nervous rash, allergies
10. Sexual difficulties
11. Fatigue, physical exhaustion
12. Sleep difficulties, insomnia
13. Tension headaches

B. Emotional/Psychological Symptoms

1. Anxiety, fear
2. Anger, irritability, "shortness" with others
3. Feeling out of control
4. "Burn Out"
5. Depressive symptoms
6. Feeling "trapped" or immobilized

C. Cognitive Symptoms

1. Difficulty concentrating
2. Day dreaming
3. Irrational thinking
4. Unable to leave job worries/problems at office

D. Behavioral Symptoms

1. Poor work performance
2. Procrastination
3. Conflict with co-workers or authority figures
4. Excessive tardiness or absenteeism
5. Compulsive/addictive disorders, e.g., compulsive overeating, alcohol dependency, etc.
6. Excessive checking of emails, "tweets" and other social media, to the point where it disrupts forward momentum with other tasks.

III. Causes of Unhealthy Stress

A. Primary causes:

1. You have physical limitations that create an inordinate number of challenges in your day-to-day life.
2. You are mentally ill. The nature of your mental illness compromises your ability to manage stress.
3. Your mental illness prompts you to create unnecessary "drama" and stress for yourself and others; e.g., "Cluster B" personality disorders.
4. Work related issues:
   a. Work overload, i.e., the amount of the work is unreasonable.
   b. Too little to do, i.e., you're bored.
   c. Personality conflict with supervisor or colleagues
   d. Nature of the job itself, e.g., you work in a high-volume E.R.,
   e. You hate your job; e.g., it's not your "passion".
   f. The work environment is toxic.
   g. Your specific skill set is not a good match for the job in question.
   h. You do not have a clear idea of what your responsibilities are.
   i. You have difficulty keeping up with the "learning curve" at work.

B. Other sources of stress:

1. You are not balancing your professional responsibilities with a meaningful personal life; you may be a "work-a-holic".
2. You have unrealistic expectations of yourself and never feel like you're doing enough.
3. You receive little or no positive feedback from those closest to you.

4. You play multiple roles and feel overwhelmed.
5. You lack skills for managing time and multiple tasks effectively.
6. You have personal problems (which may impact the work situation in a negative way).
7. You are living with someone who is mentally ill and/or a substance abuser who refuses to seek treatment.
8. You lack a positive system of support.
9. Unemployment/financial stressors
10. There is little or no happiness/joy in your life.

C. Single greatest source of stress: the tremendous internal pressure and anxiety that we create for ourselves. We create this through:

1. Worrying/ruminating about situations that are beyond your control.
2. Perfectionism – e.g., expecting too much of yourself and others.
3. Competition – e.g., turning every encounter into a win-lose situation
4. Self-criticism – e.g., focusing only on your perceived faults rather than strengths
5. Insecurity – you look inordinately to others to provide emotional security.
6. Unverified assumptions – e.g., you assume the worst about the motives, intentions of others.
7. Powerlessness – e.g., you fail to see the choices that are available to you.
8. Hurrying – e.g., constantly pushing yourself to perform better, "smarter" and faster.
9. Comparisons – e.g., you compare your achievements, or lack of them, to those of others.
10. Pessimism – e.g., you typically expect the worst from life.
11. Unrealistic expectations:
    - "I should never be inconvenienced…"
    - "I'm always entitled to special treatment…"
    - "Life should be easy, trouble-free…"
    - "I must be well-liked/approved of by all…"
    - "If we're in a relationship, I should always be your #1 priority."

IV. Factors which determine severity of stress

A. Predictability

e.g., "Can I anticipate what I will have to deal with on a given day?"

B. Perception of competency

e.g., "Do I believe that I am skilled enough to cope with demands?"

C. Availability of social support

e.g., "Are there trustworthy, reliable people who will assist me if I need help?"

D Cognitive evaluation of what's going on

e.g., "As I approach this challenging situation what is my mindset?"

E. Control over duration

e.g., "Can this stressful situation be resolved in a timely way?"

F. Personality factors

e.g., "What aspects of my core personality style help/impede me with this challenging situation?"

V. Effective Coping Strategies

A. Assess your current level of stress/wellness.

B. Examine unhealthy mindsets/expectations that are undermining your wellness.

C. Engage in aerobic exercise for at least 30-40 minutes, 3 to 4 times weekly.

D. Focus on proper nutrition vs "dieting"

1. Choose well-balanced meals from the four food groups.
2. Eliminate sugar, high fructose corn syrup and white flour from diet.
3. Limit fatty foods and foods high in cholesterol.
4. Limit salt.
5. Eat more fiber, e.g., fruits and vegetables.
6. Increase your intake of high-protein foods, e.g., fish, poultry.

E. Talk about what's stressing you out with a loved one or trusted friend.

F. Know your limits and set them firmly and consistently, e.g., saying "No".

G. Schedule time for rest, relaxation, play.

H. Turn off your cell phone, I-pad, computer.

I. Learn how to manage your time more effectively.

J. Assess any job-related skill deficits and address these via specialized training.

K. If possible, limit major changes, i.e., avoid making too many major changes in your life at one time. Allow for a period of adjustment for each major change.

*L. Pursue training in meditation, yoga and other mindfulness strategies. Empirically, this has been found to be the number one strategy for enhancing resilience and overall health.

VI. Questions, Closure

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APPENDIX A

THE HOLMES – RAHE SCHEDULE OF LIFE EVENTS*

Instruction. This survey attempts to identify significant recent events in your life which may relate to your adaptation. Review the list of life events listed below. If you have experienced any of these life events in the past 12 months circle the individual event described.

	LIFE EVENT	MEAN VALUE
1.	Death of spouse	100
2.	Divorce	73
3.	Marital separation from mate	65
4.	Detention in jail or other institution	63
5.	Death of a close family member	63
6.	Major personal injury or illness	53
7.	Marriage	50
8.	Being fired from work	47
9.	Marital reconciliation with mate	45
10.	Retirement from work	45
11.	Major change in the health or behavior of a family member	44
12.	Pregnancy	40
13.	Sexual difficulties	39
14.	Gaining a new family member (e.g., through birth, adoption, oldster moving in, etc.)	39
15.	Major business readjustment (e.g., merger, reorganization, bankruptcy, etc.)	39
16.	Major change in financial state (e.g., a lot worse off or a lot better off than usual)	38
17.	Death of a close friend	37
18.	Changing to a different line of work	36
19.	Major change in the number of arguments with spouse (e.g., either a lot more or a lot less than usual regarding child rearing, personal habits, etc.)	35
20.	Taking on a mortgage greater than $150,000 (e.g., purchasing a home, business, etc.)	31
21.	Foreclosure on a mortgage or loan	30
22.	Major change in responsibilities at work (e.g., promotion, demotion, lateral transfer)	29
23.	Son or daughter leaving home (e.g., marriage, attending college, etc.)	29
24.	In-law troubles	29
25.	Outstanding personal achievement	28
26.	Spouse beginning or ceasing work outside the home	26
27.	Beginning or ceasing formal schooling	26
28.	Major change in living conditions, (e.g., building a new home, remodeling, deterioration of home or neighborhood)	25
29.	Revision of personal habits (dress, manners, associations, etc.)	24
30.	Troubles with the boss	23
31.	Major change in working hours or conditions	20
32.	Change in residence	20

33.	Changing to a new school	20
34.	Major change in usual type and/or amount of recreation	19
35.	Major change in church activities (e.g., a lot more or a lot less than usual)	19
36.	Major change in social activities (e.g., clubs, dancing, movies, visiting, etc.)	18
37.	Taking on a mortgage or loan less than $150,000 (e.g., purchasing a car, TV, freezer, etc.)	17
38.	Major change in sleeping habits (e.g., a lot more or a lot less sleep or change in part of day when asleep)	16
39.	Major change in number of family get togethers (e.g., a lot more or a lot less than usual)	15
40.	Major change in eating habits (e.g., a lot more or a lot less food intake, or very different meal hours or surroundings)	15
41.	Vacation	13
42.	Christmas, other major holidays…	12
43.	Minor violations of the law (e.g., traffic tickets, jaywalking, disturbing the peace, etc.)	11

_____

*From: T.H. Holmes & R.H. Rahe, "The Social Readjustment Rating Scale", Journal of Psychosomatic Research, Volume II, 1967.

SOCIAL READJUSTMENT RATING SCORE

Scoring. Add the mean value of all circled items in the Social Readjustment Rating Scale.

Enter your Total Raw Score here:_____

Interpretation Studies by Holmes, Rahe et al. suggest that people who experience more numerous and/or more serious recent changes in their personal life may be more vulnerable to illness. The underlying assumption is that when people's lives are relatively stable with few changes, less illness will be found. This survey approach has held up well in a wide range of samples from different cultures and countries. While it is impossible to make accurate predictions on an individual basis research suggests the following statistical probabilities:

LIFE CHANGE SCORE FOR PREVIOUS YEAR	PROBABILITY OF ILLNESS WITHIN NEXT TWO YEARS
Less than 150 (low stress)	Low
150 – 199 (mild stress)	30%
200 – 299 (moderate stress)	50%
300 or more (major stress)	80%

APPENDIX B

Ten Tips to Help You Cope with Job Stress

1. **Take charge of your situation.** To the extent possible, set and re-set priorities. Take care of important (and difficult) things first. Organize your time.

2. **Be realistic about what you CAN change.** Don't doom yourself to frustration and failure. Do what's possible. Accept the rest.

3. **Take one step at a time.** Divide each project into manageable steps. Decide on a first step. Do it. Feel better?

4. **Be honest with colleagues.** This includes the boss. Make it plain you feel in a bind. Chances are others are feeling the same. Don't just complain. Be constructive and make practical suggestions for improvement.

5. **Let your employer help.** Many companies help their employees deal with the effects of stress through diet, smoking and alcohol clinics, corporate fitness programs and personal counseling and employee assistance programs. Find out what's available to you.

6. **Slow down.** Learn to say "no". Drop activities that are not crucial.

7. **Recognize danger signals.** Learn the symptoms of job stress and take action as soon as they appear to be getting out of hand.

8. **Take care of your physical health.** It increases your stress tolerance and stamina. Eat and sleep sensibly. Cut down on alcohol, tobacco and drugs. Get plenty of exercise.

9. **Learn to relax.** Find a safety valve, whether it is a sport, hobby, music, reading or just walking.

   Use it to create a "bridge" between work and home life.

10. **Don't neglect your private life.** Work out a schedule which allows you to do justice to both work and personal life. Stick to it.

(Source: Channing Bete publication "What Everyone Should Know about Job Stress" and pamphlet "Coping with Your Job" from the National Mental Health Association.)

APPENDIX C:

STRESS (on the job) 13 REASONS

1. Inadequate time to complete a job to one's satisfaction.
2. Lack of a clear job description or chain of command.
3. Absence of recognition or reward for good job performance.
4. Inability or lack of opportunity to voice complaints.
5. Many responsibilities but little authority or decision-making capability.
6. Inability to work with superiors, associates or subordinates because of basic differences in personality, values and/or goals.
7. Lack of control or pride over the finished product.
8. Job insecurity due to pressures from within the organization, or the possibility of a takeover or merger.
9. Prejudice and bigotry due to age, gender, race or religion.
10. Unpleasant environmental conditions, cigarette smoke and other air pollution, crowding, noise, exposure to chemicals, commuting difficulties and inadequate/nonworking equipment.
11. Not being able to use personal talents or abilities effectively or not to their full potential.
12. Problems at home, such as family worries, financial problems or alcohol/drug/gambling problems.
13. The "FUD Factor": fear, uncertainty and doubt

SELF EVALUATION

Preventing Burnout by Managing Stress

1. Stress is:

a. A non-specific response of the body to a perceived demand or threat.
b. Affected by one's perceptions.
c. To some degree with us most of the time.
d. All of the above.

2. Which of the following is not a primary cause of stress?

a. A positive, optimistic mindset or world view
b. Physical limitations that create inordinate challenges
c. Mental illness which compromises your ability to manage stress
d. Work-related issues, such as work overload or conflict with your boss/ supervisor

3. Which of the following does not impact the level or severity of stress that you experience?

a. Not balancing your personal and professional lives
b. A supervisor who provides ongoing support and positive feedback
c. Living with someone who is mentally ill and/or an active substance abuser
d. You are expected to play multiple roles and feel overwhelmed.

4. Internal pressure that can worsen stress and anxiety includes which of the following factors?

a. Rumination about situations that are beyond your control
b. Perfectionistic expectations of self or others
c. Insecurity
d. Hurrying
e. All of the above

5. Which of the following factors does not determine the severity of stress?

a. Predictability
b. Perception of competency
c. Gender
d. Control over duration

6. Specific coping strategies for reducing stress and burn-out include all but which of the following?

a. A diet rich in high-fructose corn syrup and white sugar
b. Well-balanced meals from the four food groups
c. Decrease your intake of high-protein foods.
d. "A" and "C" are not recommended.

7. Which of the following is a helpful guideline for lowering your stress?

a. Know your limits and set them firmly and consistently.
b. Avoid physical exercise as it may deplete necessary energy reserves.
c. Focus on "dieting" vs "proper nutrition".
d. Do not burden others with your problems and stress; "suck it up…"

8. Which of the following statements is true?

a. You can avoid burn-out by setting aside sufficient time for rest, relaxation and recreation.
b. Training in meditation, yoga and other mindfulness strategies significantly lowers unhealthy stress.
c. If possible, it is a good idea to limit major changes.
d. All of the above are true.

9. Which of the following is not a source of job-related stress?

a. Inadequate time to complete the job satisfactorily
b. A clear job description and chain of command
c. Prejudice, bigotry due to age, gender, etc.
d. Fear, uncertainty and doubt

10. Which of the following is not an emotional/psychological symptom of stress?

a. Blood pressure rises; flushed face
b. Anxiety and fear
c. Irritability or anger
d. Depression, despair

Answer Key: 1. D, 2. A, 3. B, 4. E, 5. C, 6. D, 7. A, 8. D, 9. B, 10. A

Herman P. Houin, MD, FACS

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You may contact Dr. Houin with your questions and comments at 313-982-8355, or by email at HHouin@Yahoo.com.

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Diagnosing and Treating Common Hand Problems and Injuries

Observations

- Most common hand injuries/ infections can be treated completely or temporized in ER or office
- Most common conditions are easily diagnosed
- Keep treatments simple, comfortable and safe
- Stabilize patient when needed for referral to specialist

HAND INJURIES

INDICATIONS FOR IMMEDIATE SURGERY:

HIGH PRESSURE INJECTION INJURY

PEDIATRIC FLEXOR TENDON SHEATH INFECTION

SEVERE CRUSHING INJURY

REPLANTATION

EXAM

MOTION / MOBILITY/SENSATION

ANATOMY IS KEY TO DIAGNOSIS AND TREATMENT

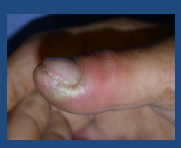
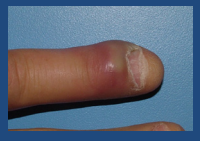
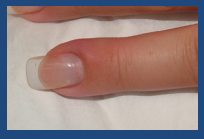
PRECISION TREATMENT REQUIRES A PRECISE KNOWLEDGE OF ANATOMY AND FUNCTION

INFECTIONS

- PARONYCHIA
- FELON
- FLEXOR TENDON SHEATH
  - **Kanavel's Four Cardinal Signs**
    - **intense pain**
    - **flexion posture**
    - **uniform swelling**
    - **percussion tenderness**

PARONYCHIA

A paronychia is an abscess of the proximal and / or the lateral nail folds. When it extends laterally, fingertip necrosis can result from pressure within the neurovascular spaces formed by longitudinal fibrous septae.

LOCAL ANESTHESIA

- EPINEPHRINE USE IN HANDS HAS HAD A BAD RAP FOR MANY YEARS.
- EPINEPHRINE HAS BEEN PROVEN TO BE SAFE IN SEVERAL SERIES.
- USE OF EPINEPHRINE MAKES A TOURNIQUET UNNECESSARY IN MOST HAND CASES.

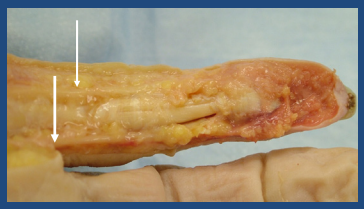
LOCAL ANESTHESIA

- WORKHORSE COMBO:
  - WRIST BLOCK
    - 1% LIDOCAINE / 0.25% MARCAINE WITH EPINEPHRINE
    - 10 ML WILL DO A TOTAL BLOCK
  - LOCAL INFILTRATION OF THE INCISION OR WOUND
    - 1% LIDOCAINE WITH EPINEPHRINE

DIGITAL BLOCK ANESTHESIA

ANATOMY

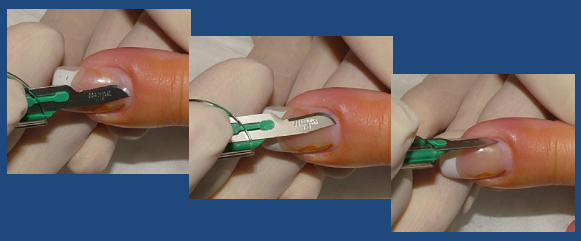
THE DIGITAL NERVES ARE BLOCKED WHERE THEY LIE ADJACENT TO THE FLEXOR SHEATH AT THE MP FLEXION CREASE



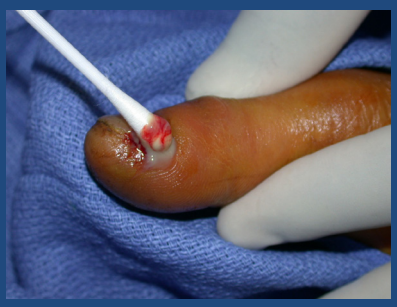
DIGITAL BLOCK ANESTHESIA TECHNIQUE

INJECT 5-10 ML 1% LIDOCAINE +/- EPINEPHRINE IS INJECTED ON THE DORSUM OF THE FINGER AND INJECT TO PALMAR SIDE. NEEDLE LESS PAINFUL TO INSERT THRU DORSAL SKIN

THE TANGENTIAL ORIENTATION OF THE KNIFE FOLLOWS THE CONTOUR OF THE FINGERNAIL AS THE PARONYCHIA IS INCISED.



REMEMBER TO CULTURE



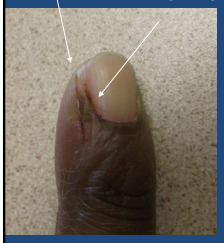
WARM WATER SOAKS FOUR TIMES A DAY AS DEMONSTRATED BELOW. AT HOME A PAPER CUP IS RECOMMENDED AS AN EASY WAY TO AVOID INJURY AND CONTAMINATION

THE FINGER IS DRESSED WITH BACITRACIN OINTMENT AND A SMALL GAUZE HELD IN PLACE WITH A STRIP OF COBAN.

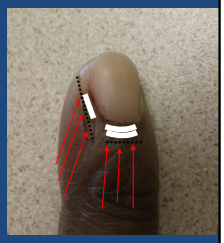
HOW NOT TO DO IT !!

I & D INCISION PARALLEL TO THE LATERAL NAIL FOLD

AREA OF NECROSIS



THIS TYPE OF INCISION CUTS OFF THE BLOOD SUPPLY TO THE LATERAL NAIL FOLD --- AND IF DORSAL: THE PROXIMAL NAIL FOLD



Felon

- Palm side tip infection
- Incise directly into pus
- Use longitudinal incision to avoid nerve injury

Ring Removal

- Don't Delay
- Don't Cut Ring unless necessary

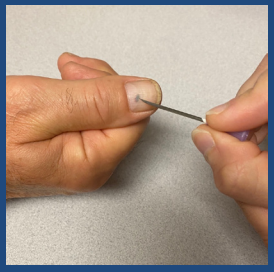
- 2 String technique-100% success rate- Pass two threads (sutures) through ring with needle reversed. Soap on finger then spin ring with threads while pulling distally

RING REMOVAL WITHOUT CUTTING

- Pass 2 sutures under ring
- Soap Finger
- Spin ring with sutures
- while pulling distally

Painful Subungual Hematoma

- ONLY NEED PIN HOLE IN NAIL TO RELIEVE PRESSURE
- ROTATE NEEDLE TIP AS DRILL BIT UNTIL DROP OF BLOOD SIGNALS NAIL PENETRATION
- PATIENT WILL LOVE YOU

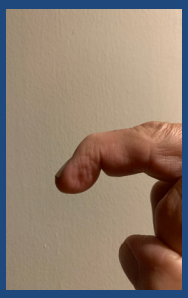


BURNS

- PARTIAL THICKNESS- ALOE CREAM Q3H
- DEEP PARTIAL THICKNESS=BLISTERED- ALOE Q3H; IF BLISTERS RUPTURE CONVERT TO TOPICAL ANTIBIOTIC
- FULL THICKNESS-TOPICAL ANTIBIOTIC/SURGERY IF LARGE AREA

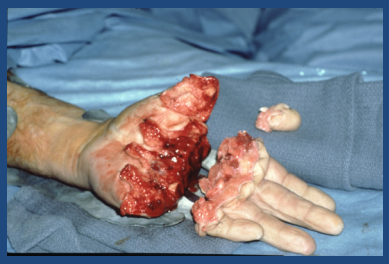
MALLET FINGER

- SPLINT IN FULL EXTENSION FOR 6 WEEKS: MUST MAINTAIN IN EXTENSION AT ALL TIMES
- ONE JOINT FLEXION MEANS RESTARTING AT DAY ONE



REPAIRS

- SUTURE
- GRAFTS
- FLAPS

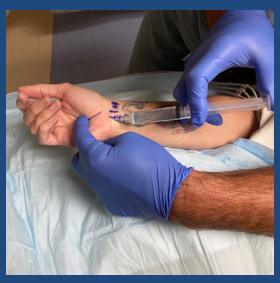


Anesthesia

- Wrist block adequate for most hand procedures
- May supplement wrist block with local containing epinephrine to minimize bleeding and need for tourniquet

Wrist Block

- Median Nerve Block- deep to Palmaris Longus tendon
- Ulnar to PL tendon
- Aim to base of ring finger
- Feel for fluid with finger pressing distal to carpal ligament



Wrist Block

- Ulnar Nerve—Deep to FCU tendon and get dorsal branch 1cm proximal to ulnar styloid

Wrist Block

- Superficial Radial Nerve- below cephalic vein and distal to Brachioradialis tendon

ANESTHETIC

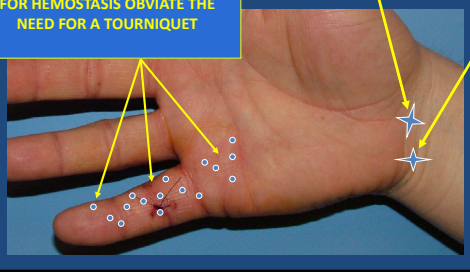
WRIST BLOCK AND LOCAL INFILTRATION

2.

DROPS OF 1% LIDOCAINE WITH EPINEPHRINE INJECTED ALONG THE COURSE OF THE BRUNER INCISION FOR HEMOSTASIS OBVIATE THE NEED FOR A TOURNIQUET

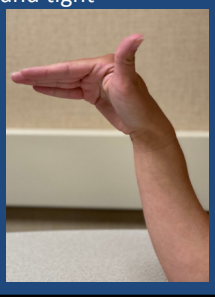
1.

1% LIDOCAINE / 0.25% MARCAINE: MEDIAN AND ULNAR NERVE *WRIST BLOCKS*

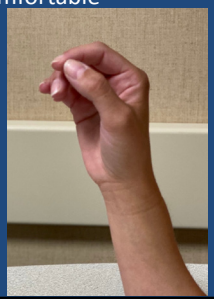


Hand Splinting to maximize Ligament

- Position of function Ligaments at full length and tight



- Position of Comfort Ligaments loose and comfortable



If Swelling, Infection or other planned Delay

Double Kerlix Dressing and Elevation

Will keep patient comfortable while waiting for referral to specialist and edema resolves

Double Kerlix Dressing acts as splint for fractures which allows for swelling occur without allowing movement or pain to occur causing

Grasping the Kerlix leaves ligaments in loose position of Comfort

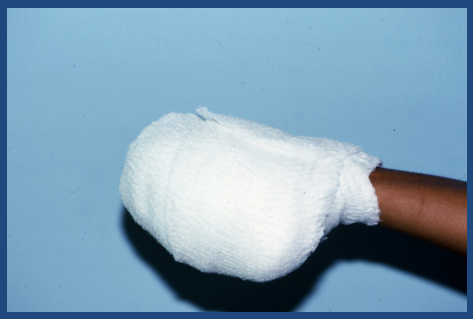
GRAB A KERLIX

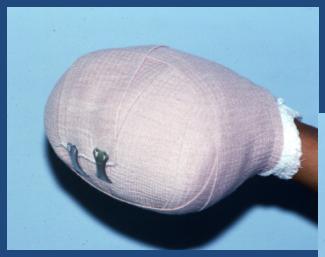
WRAP IN THE DIRECTION OF THE FINGERS AROUND THE BASE OF THE FIRST METCARPAL

NOT TIGHT AROUND THE BASE OF THE HAND

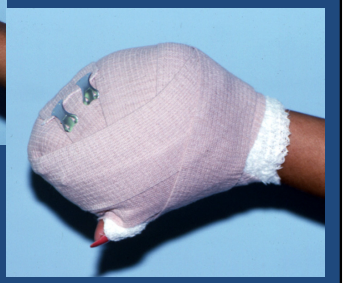
THEN THROUGH THE FIRST WEB SPACE

USE UP THE REST OF THE KERLIX BACK OVER THE FINGERS

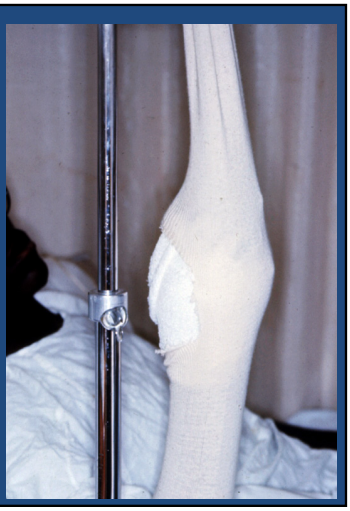




SNUG BUT NOT TIGHT ACE WRAP APPLIED IN THE SAME PATTERN



Elevation in cast sleeve keeps gravity on your side and is very comfortable for patient

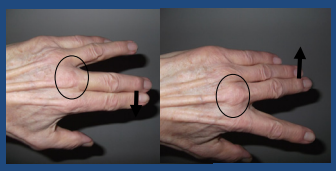


SPLINT CONCEPTS

- SPLINT ONLY WHAT IS REQUIRED TO AVOID STIFFNESS OF NON-INJURED DIGITS
- DETERMINE WHAT IS REQUIRED AND DESIGN THE SPLINT TO DO THE JOB

FINGER SPLINTING
LATERAL MOBILITY OF MP VS IP JOINTS

MP JOINT EXTENDED – COLLATERAL LIGAMENTS LOOSE = LATERAL MOTION



MP JOINT FLEXED – COLLATERAL LIGAMENTS TIGHT = LITTLE LATERAL MOTION

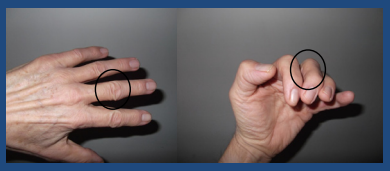
RETINACULAR TISSUES CONTRACT

MP JOINTS SHOULD BE SPLINTED IN FLEXION TO KEEP THE LIGAMENTS STRETCHED TO ALLOW FLEXION

NOT STRAIGHT WHICH STIFFENS THE MPJs AND PRLONGS HAND THERAPY

FINGER SPLINTING
LATERAL MOBILITY MP VS IP JOINTS

IP JOINTS HAVE LITTLE LATERAL INSTABILITY WHEN EXTENDED



SO:

SPLINT IP JOINTS IN POSITION OF FUNCTION WHEN POSSIBLE

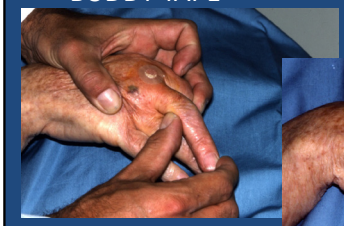
NOT FLEXED WHICH MAKES INITIATION OF HAND THERAPY MUCH MORE DIFFICULT

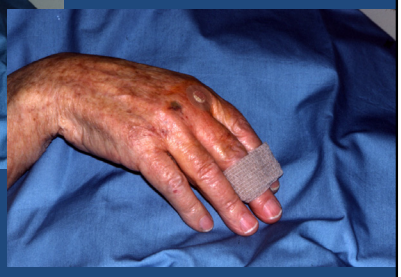
SPLINT FOR MALLET INJURY
"STATIC SPLINT"

SPLINTS

- BUDDY TAPE

"DYNAMIC"





HUMAN BITE INJURIES

SUSPECT --- IDENTIFY ---TREAT

IF THERE IS A STRONG SUSPICION OF A HUMAN BITE --- TREAT AS A HUMAN BITE; A DELAYED PRIMARY CLOSURE CAN ALWAYS BE SAFELY DONE LATER.

- WRIST BLOCK OR LOCAL ANESTHESIA
- SURGICAL HAND WASHING
- SALINE IRRIGATION
- IV ANTIBIOTICS
- **CDU OR FOLLOWUP *NEXT DAY***
- ORAL ANTIBIOTICS
- NO SUTURES UNLESS ADEQUATE IRRIGATION/DEBRIDMENT
- DOUBLE KERLIX GIVES BEST FINGER POSITION

AMPUTATIONS

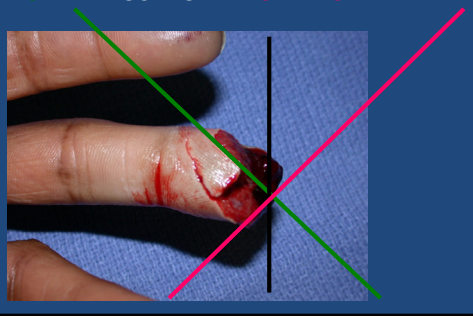
- FINGERTIP AMPUTATIONS
  - FAVORABLE : VOLAR PAD REMAINS
  - GUILLOTINE : VERTICAL LOSS
  - UNFAVORABLE : VOLAR PAD GONE
  - WHAT TO DO WITH BONE

AMPUTATIONS

- FINGERTIP AMPUTATIONS
  - GENERAL RULE:
    - ANY AREA UNDER **1 CM²** WILL HEAL BY WOUND CONTRACTION AND EPITHELIALIZATION
    - WITH LESS SCARRING AND BETTER SENSATION THAN WITH A DISTAL GRAFT OR FLAP
    - **IF PATIENT HAS TISSUE CAN REPLACE AS SKIN GRAFT**
    - **SHORTEN BONE IF NEEDED**

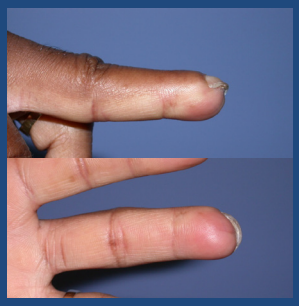
AMPUTATIONS

- FINGERTIP AMPUTATIONS
  - FAVORABLE GUILLOTINE UNFAVORABLE



AMPUTATIONS

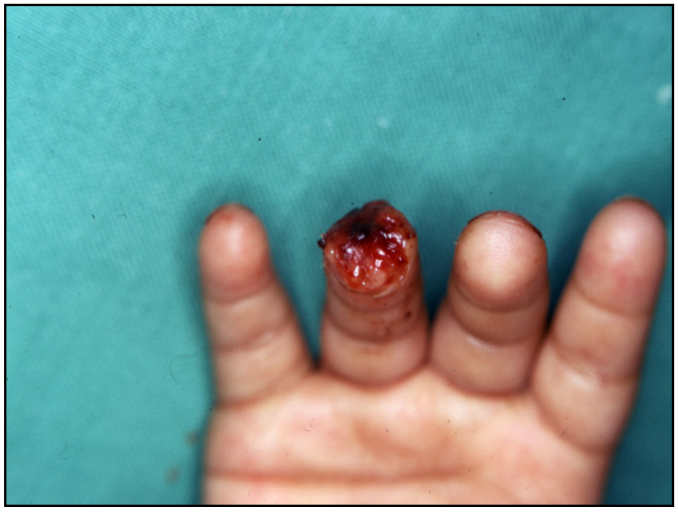
- FINGERTIP AMPUTATIONS
  - GUILLOTINE



PEDIATRIC FINGERTIP AMPUTATIONS

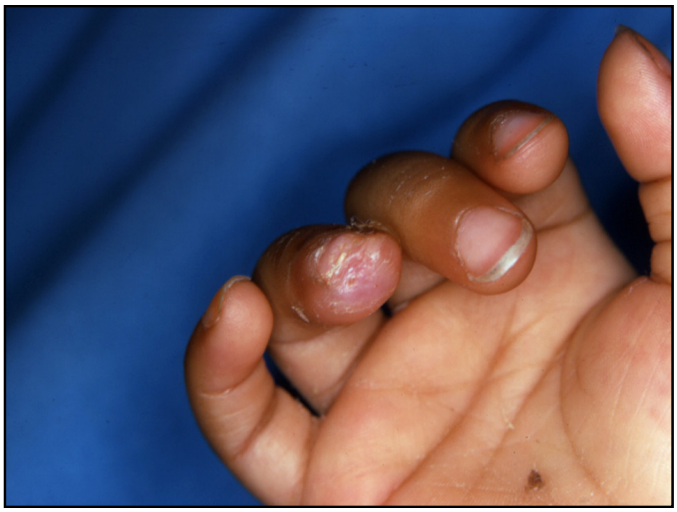
This 18 m o toddler pinched off the end of the RMF fingertip in a kitchen cabinet.

THE BONE IS SHOWING !

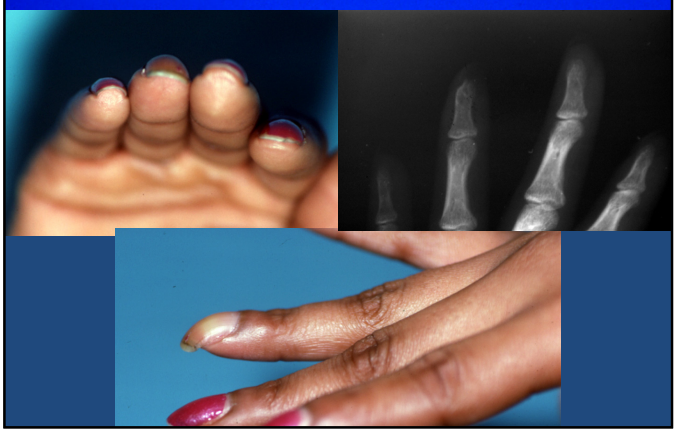


SO WHAT ?

One month later . . . .



Twelve years later . . . .



UNFAVORABLE AMPUTATION:
WHAT TO DO WITH THE RECOVERED TIP

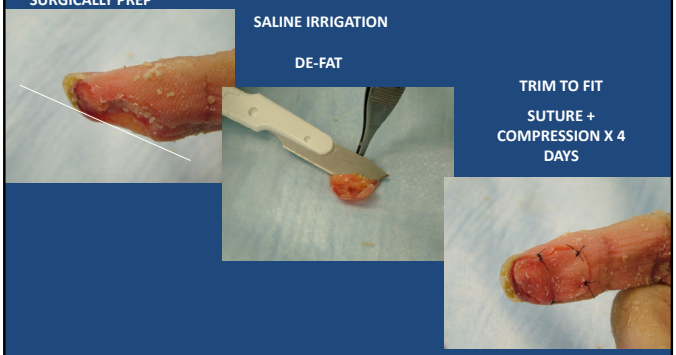
SURGICALLY PREP

SALINE IRRIGATION

DE-FAT

TRIM TO FIT

SUTURE + COMPRESSION X 4 DAYS



Replantations

- THUMB
- MULTIPLE DIGITS
- STABLE PATIENT

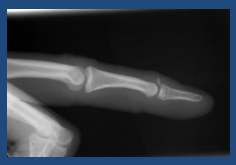
- REPLANTATIONS
  - PROCESS FOR OR/REFERRAL QUICKLY.
  - AMPUTATED PART IN MOIST SALINE GAUZE IN PLASTIC ON ICE BUT NOT SUBMERGED.
  - EVALUATE REST OF DIGIT / HAND FOR SUITABILITY FOR REPLANTATION
    - CRUSHING OR AVULSION INJURIES QUESTIONABLE

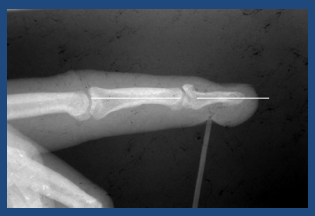
TRAUMA

- Distal phalangeal fractures and fingernail anatomy

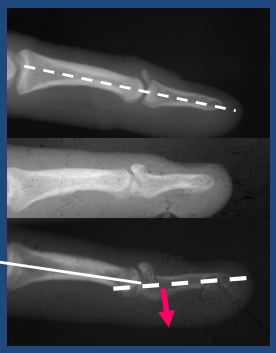
  – CASE ILLUSTRATIONS →

MALLET FRACTURE





MALLET FRACTURE
30% RULE



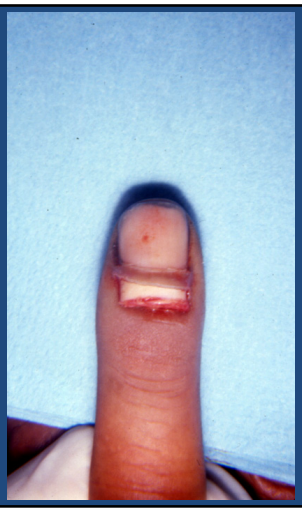
IF THE SMALL FRACTURE FRAGMENT INVOLVES MORE THAN 30% OF THE ARTICULAR SURFACE OF THE DISTAL PHALANX, THEN THERE WILL BE A GOOD CHANCE THAT THE COLLATERAL LIGAMENTS WILL BE INVOLVED RESULTING IN *SUBLUXATION* OF THE DISTAL PHALANX...AN OPERATIVE REDUCTION AND FIXATION WILL BE REQUIRED.

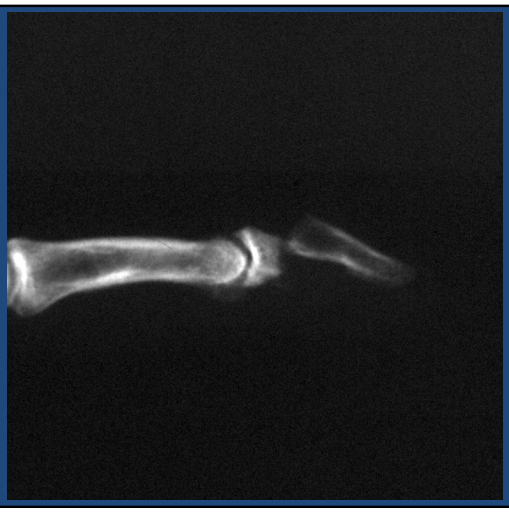
OTHERWISE SPLINT IN A STACK SPLINT FOR 8 WEEKS FULL TIME AND TWO MORE WEEKS AT NIGHT.

A 39 y o man had a crushing injury to the RMF.

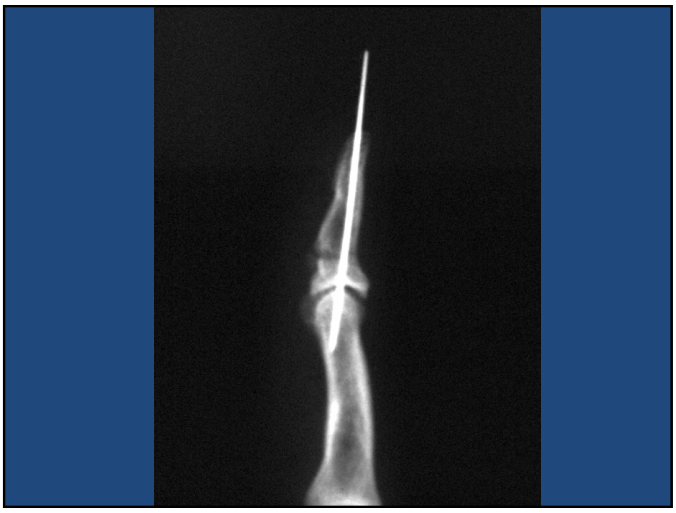
Exam reveals a dorsal displacement of the proximal nail over the proximal nail fold.

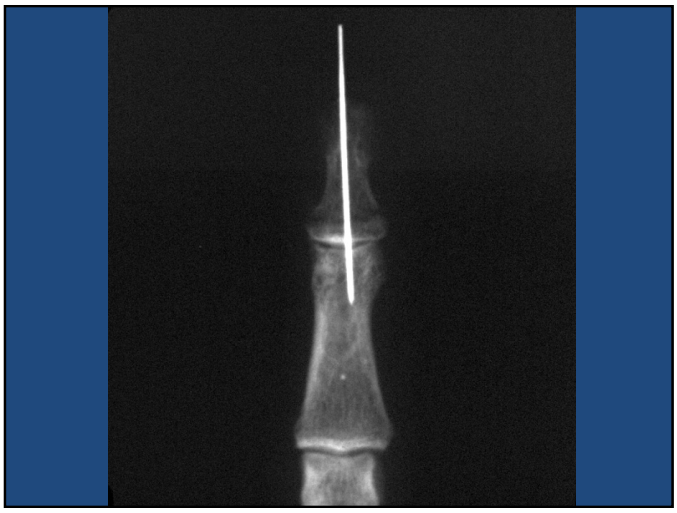
Xrays show a transverse fracture of the base of the distal phalanx with dorsal displacement and volar angulation of the distal fragment.





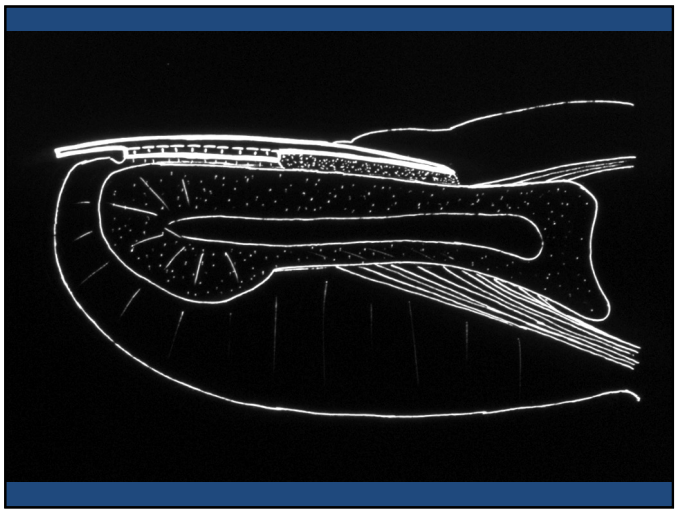
Treatment:
a. Leave alone. Let nail grow.
b. Pop nail into anatomic position and splint.
c. Remove nail plate, K-wire.
d. Replace nail and K-wire fragments.
e. Extend wound to visualize fracture fragments for open reduction and K-wire fixation.





Was this necessary?

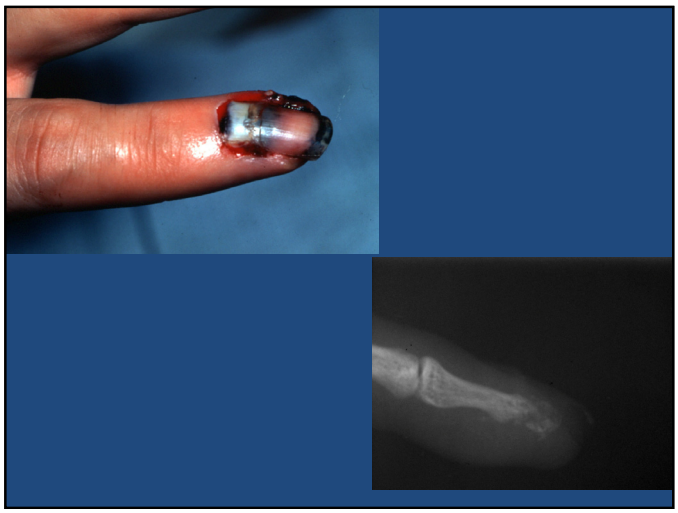
Lets check the anatomy. . . .



A more typical door-closing-on-fingertip injury.

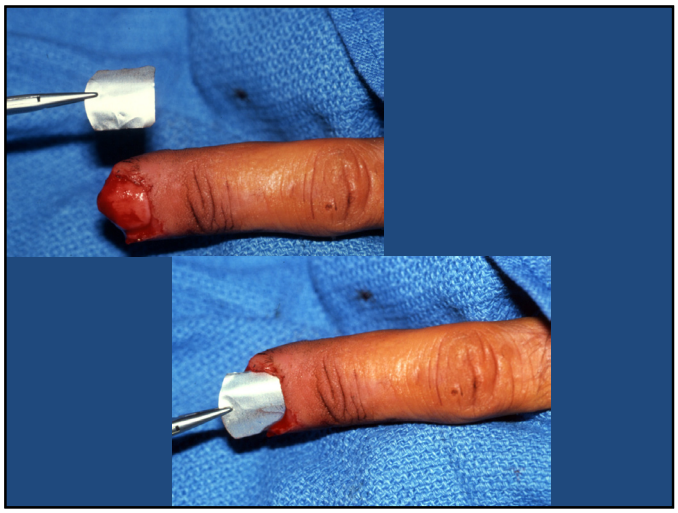
Note the pink nail over the sterile matrix.

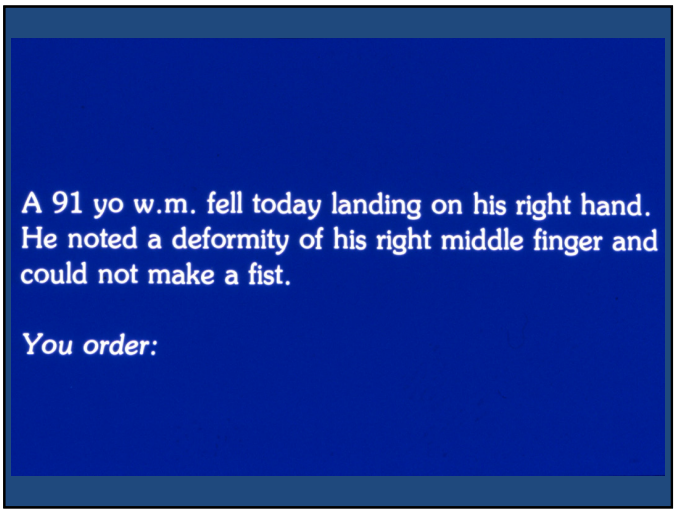
TREATMENT OPTIONS . . . . .

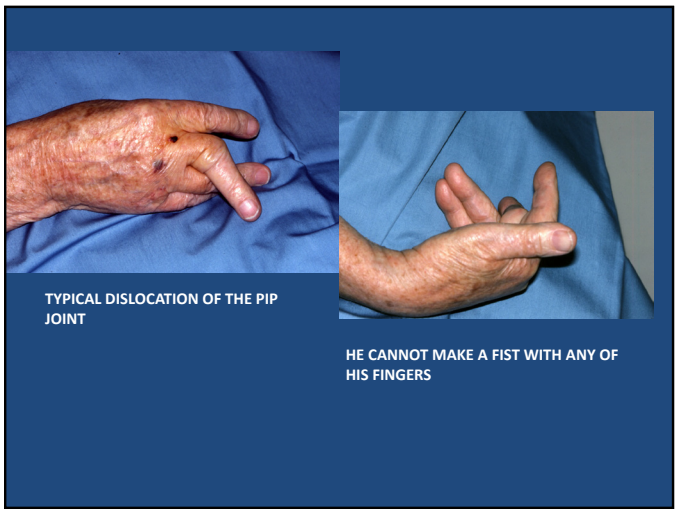


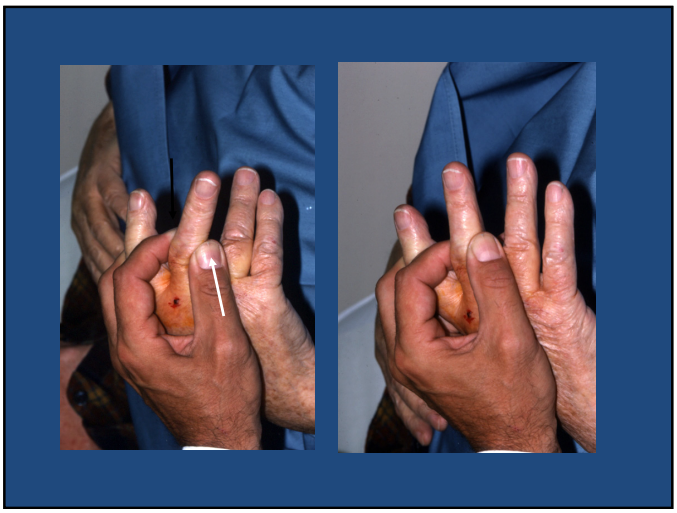

USE CLAMP AS A SHOEHORN
MATTRESS SUTURE THRU PROXIMAL NAIL FOLD TO HOLD IN PLACE


WHAT IF THE NAIL IS GONE?

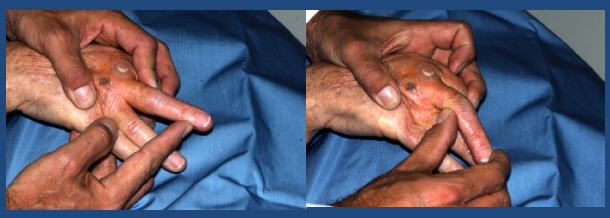



A 91 yo w.m. fell today landing on his right hand. He noted a deformity of his right middle finger and could not make a fist.
You order:

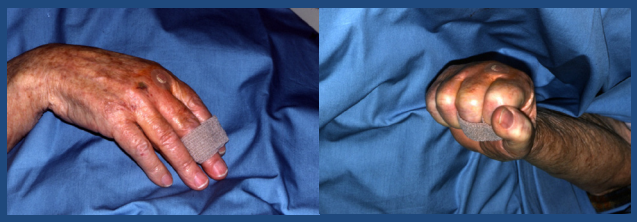

TYPICAL DISLOCATION OF THE PIP JOINT
HE CANNOT MAKE A FIST WITH ANY OF HIS FINGERS



COLLATERAL LIGAMENT STRESS TESTING



BUDDY TAPE SPLINT TO PROTECT THE RADIAL COLLATERAL LIGAMENT THROUGHOUT THE RANGE OF FINGER MOTION

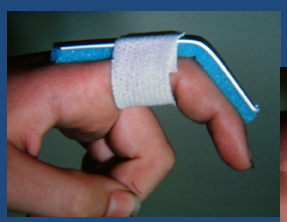


VOLAR PLATE AVULSION FRACTURE

THE EXTENSION BLOCK SPLINTS USED FOR

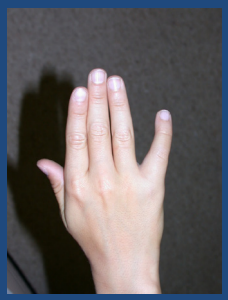
VOLAR PLATE AVUSLION FRACTURES

PREVENT HYPEREXTENSION RE-INJURY WHICH COULD LEAD TO SWAN NECK DEFORMITIES WHICH ARE INFINITELY HARDER TO TREAT.

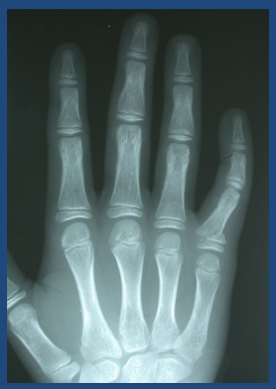


"LIMITED MOTION DYNAMIC SPLINT"

EPIPHYSEAL FRACTURE



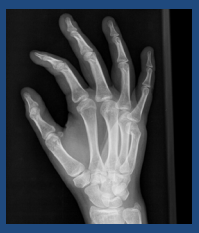
TYPE II



REDUCTION TECHNIQUE: FLEX THE MP JOINT

- FLEXION OF THE MP JOINT REDUCES ITS MOBILITY BY TIGHTENING THE COLLATERAL LIGAMENTS.
- THE COLLATERAL LIGAMENTS ATTACH TO THE SMALL FRAGMENT NEXT TO THE JOINT
- THE ANGULATED LARGER/DISTAL FRAGMENT CAN THEN BE LEVERED INTO POSITION AGAINST A STABLE SMALL FRAGMENT.

BOXER'S FRACTURE



REDUCE IF >45 DEGREES

IF THE BOXERS ANGULATION DEFORMITY RECURS WHEN THE PRESSURE IS TAKEN AWAY

THEN TREATMENT SHOULD BE A DOUBLE KERLIX ELEVATION AND REFERRAL

IF REDUCTION STABLE SPLINT IN POSITION OF FUNCTION

FULL FUNCTION WITHOUT REDUCTION IS THE NORM IF LESS THAN 45 DEGREES OF ANGULATION

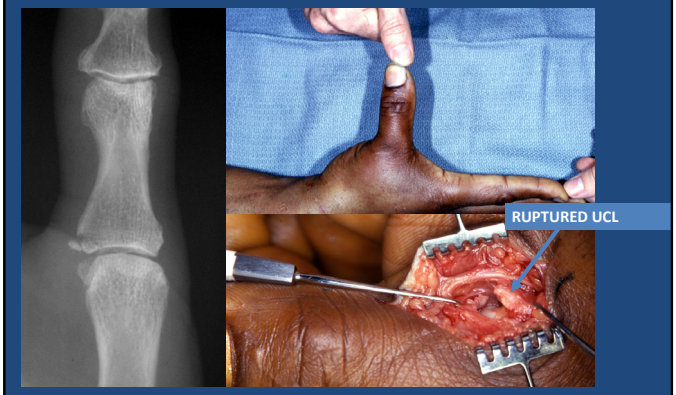
"FRACTURE INSTABILITY"

- **SHORT LEVER ARM**
  - BOXERS
- **COMMINUTION**
  - PROXIMAL PHALANGEAL
- **UNFAVORABLE ANGLE**
  - BASE OF FIFTH METACARPAL
- **TENDON PULL**
  - BASE OF FIFTH METACARPAL
- **SPIRAL**
  - METACARPAL SHAFT
- **LACK OF TENDON/LIGAMENT SUPPORT**
  - BOUTONNIERE
  - GAMEKEEPERS

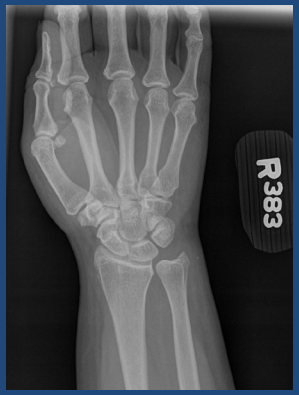
IN THESE SITUATIONS:

ATTEMPTS AT REDUCTION AND SPLINT FIXATION ARE NOT EFFECTIVE AND A WASTE OF TIME----REFER TO SURGEON

GAMEKEEPER'S FRACTURE



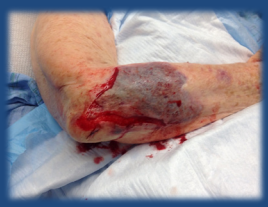
SCAPHOID FRACTURE

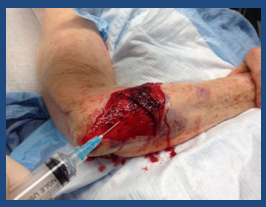


LACERATION REPAIRS

1. **WOUND CARE**
   - **DETERMINE VIABILITY**
2. **WHEN TO CLOSE**
   - **CLEAN**
   - **EASY**
   - **NOT A HUMAN BITE**
3. **ANTIBIOTICS**
   - **CONTAMINATED**
   - **HUMAN BITE**
   - **TENDON OR BONE EXPOSED**

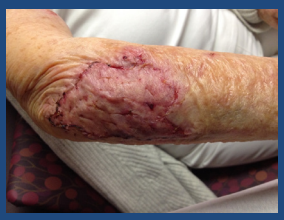
Avulsion Injuries





Thin avulsed skin flap with length to width greater than 1:1 need to convert to Full thickness skin graft by cutting remaining attachment

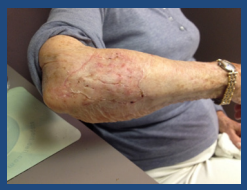
Flap converted to Graft

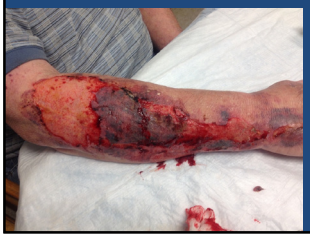


100% graft take at 5 days

Managing Thin avulsion Flaps

- Flap converted to graft





Flap repaired as laceration

CONCLUSION

- MANY COMMON INJURIES CAN BE TREATED WITHOUT SPECIALIST
- ATTENTION TO ANATOMY AND DETAILS LEADS TO BETTER TREATMENT
- REGIONAL BLOCKS ALLOW COMFORTABLE CARE FOR PATIENTS AND PHYSICIANS
- ELEVATION KEEPS EDEMA AWAY AND PATIENTS COMFORTABLE

SELF EVALUATION

Diagnosing and Treating Common Hand Problems and Injuries

True/False

1.___ Nerves that block skin sensation in the hand are median, ulnar and peroneal

2.___ Mallet finger injury can be a fracture or tendon rupture

3.___ PIPJ dislocations are usually reduced easily

4.___ Human bite injuries require extensive debridement and irrigation

5.___ All fingertip amputations require surgery

6.___ Pediatric Flexor Tendon Sheath Infection is a surgical emergency

Answer Key: 1. F, 2. T, 3. T, 4. T, 5. F, 6. T

Commander John J. Burke

John J. Burke, of Cincinnati, Ohio, retired as the Commander of the Greater Warren County, Ohio, Drug Task Force and of the Southern Ohio High Intensity Drug Trafficking Area (HIDTA) in 2015, an operation which included focus on pharmaceutical diversion. He is president of Pharmaceutical Diversion Education, Inc. (PDE), a company providing education and training to health professionals, law enforcement, and regulatory agents on the issues of prescription drug abuse, and the balance required between pain management and drug diversion.

Commander Burke has been a law enforcement officer for 49 years and in 1990 was asked to establish the Cincinnati Police Department's Pharmaceutical Diversion Squad, one of the first units of its kind in the United States, where he pioneered the development of policies and procedures unique to the investigation of prescription drug abuse. He lectures nationally, has authored a monthly column on drug diversion in *Pharmacy Times* magazine for the past 15 years, and is the past president of the National Association of Drug Diversion Investigators. In 2015 he co-founded the International Health Facility Diversion Association and is the current President of this non-profit organization which provides training and networking for healthcare facility diversion professionals with the link available at www.ihfda.org

You may contact Commander Burke at (513) 623-3278 or, by email at Burke@rxidversion.com.

Commander John J. Burke
Phone: 513-623-3278
Email: burke@rxdiversion.com

Prescription Drug Diversion: Safeguarding Your Practice

PHARMACEUTICAL DIVERSION EDUCATION INC.

- John Burke, President & Owner
- www.rxdiversion.com
- Provide prescription drug education to health professionals, law enforcement, & the general public
- Provide expert witness testimony
- Coordinate and present conferences on abuse and diversion of Rx drugs in health facilities

TYPICAL DRUG SEEKER

- Total goal is to scam you out of medication
- Rx addict every bit as overwhelmed as heroin and cocaine addicts
- Waking hours are devoted to planning on how they will get their drugs
- You are the #1 gate keeper!
- Keeping your guard up while remembering only 10-15% of your PTS are drug seekers

TYPICAL RX DRUG SEEKER

- Rx drug seeker loves to compliment the prescriber
- May compliment your practice, staff, or even family if photos available
- Maintains best of behavior to start
- May feign ignorance and deliberately mispronounce Rx drug name

TYPICAL RX DRUG SEEKER

- When confronted by prescriber, attitude and mood will likely change
- Becomes agitated
- May try and make a scene at your practice
- Threatens lawsuit
- Will leave abruptly once they realize their behavior is not working
- Fresh victim's down the street!

NEW PATIENT FORM QUESTIONS

- When is the last time you saw a physician?
- What prescribers have you seen in the past year?
- When is the last time you were prescribed an Rx drug?
- List name of all drugs you have been prescribed in the past year.
- Staff should ensure all questions are answered

NEW PATIENT TO THE PRACTICE

- Notify PT a couple of days prior to appointment
- Remind them of their appointment
- Remind them to bring a photo ID along with insurance info
- Staff should copy photo ID and place in permanent medical files
- Remind them photo ID is for their protection!

NEW PATIENT PROCEDURE

- Obtain medical history from former prescribers
- Do not assume that photocopied medical records brought by PT are valid!
- Perform physical exam appropriate to complaint
- Contact and talk with prior prescribers if deemed necessary

NEW PATIENT PROCEDURE

- Check Prescription Monitoring Programs!
- Your state and bordering states if possible
- Make yourself available to ER physicians and their concerns when appropriate
- Make a copy of all CS scripts and put them in the permanent medical files
- Take careful note of who and how PT was referred to your practice

STAY ALERT FOR PHYSICAL SIGNS OF ADDICTION

- Inflamed nasal passages
- Constant running nose
- Track arms (arms, wrist, neck, between toes and fingers)
- "Skin Popping" (irregular or round scars like smallpox vaccinations)
- Obvious impairment in office by PT or companion

SAFEGUARDING YOUR PRACTICE

- Thoroughly document history, physical, & treatment plan
- Document all diversion issues of PT
- If not documented, like it never happened!
- Schedule tests appropriate to complaint and require they be completed!
- Consider referral to pain specialist
- Not mandatory to give a CS on first visit

DEALING WITH SUSPECT PT

- Periodic urine screens mandatory
- Should be witnessed! (clean urine, Whizzinator)
- Pill counts
- CS Rx should indicate if non-CS was also written
- Have staff check with Rph on filling of non-CS scripts

LIMITING CS DOSES IN RESIDENCE

- Family member or care giver may be diverting
- Limit number of CS in household
- CII drug can be subject to "Do not fill until" program (90 day supply)
- All three scripts dated on day they are written
- DO NOT post date scripts!

PROTECTING THE PRACTICE FROM DIVERSION

- Write out script (alpha and numeric) quantity and strength
- Do not leave refill space blank
- Consider serialized prescriptions and record or copy into medical records
- Consider tamper resistant prescriptions
- Consider electronic prescriptions when available to you

PROTECTING THE PRACTICE FROM DIVERSION

- Use your script pad for prescribing ONLY!
- Acetone (fingernail polish remover) can be used to alter your scripts
- Ball point pens should be avoided (roller ball etc.)
- Do not sign scripts in advance or print CS drug on same
- Treat Rx pads like your personal check book

PROTECTING THE PRACTICE FROM DIVERSION

- Take Rph concerns seriously
- Rph has a "corresponding responsibility" to make sure script is legitimate
- Collaborate with Rph for better PT care and more complete info for you
- Make your local Rph part of the pain management team

PROTECTING THE PRACTICE FROM DIVERSION

- Listen to your office staff!!
- They oftentimes see a very different side of the PT
- May be first to identify the PT as a drug seeker
- Drug seeking PT's oftentimes let their guard down with the front office staff
- Post no early refill notice in waiting room and enforce it

BE SUSPICIOUS OF

- Unusual interest or knowledge in CS
- Requests for specific CS
- PT always in a hurry
- PT who refuses or constantly delays testing you have ordered
- PT unwilling to try non- Rx solutions to their pain
- PT unwilling to see pain specialist

BE SUSPICIOUS OF

- Over friendly or complimentary PT
- PT disinterested in non-CS drug alternatives
- PT claims allergy to virtually all non-CS
- PT only interested in obtaining medication, not getting better

BE SUSPICIOUS OF

- Consistent early refill requests on CS
- Rx drugs stolen
- Require police report
- Advise PT that you only allow this once
- Rx drugs missing- dog ate them, dropped in toilet, etc.

BE SUSPICIOUS OF

- PT unable to recall past office or clinic where treated last
- Unwilling or unable to identify past prescriber
- PT unwilling to give permission for past medical records
- Claims to be from out of town and needs Rx refill only

BE SUSPICIOUS OF

- PT who fills CS script only! (Notation for Rph)
- PT who always wants appointment at the end of the day
- PT who shows up at end of the day for an appointment and needs meds!

PAIN AGREEMENTS

- Also called “contracts”
- Educates PT to potential abuse of Rx drugs
- May prevent/reduce family or caregiver diversion inside household
- One physician- one pharmacy
- No refills after hours
- Go to ER if persisting pain

PAIN AGREEMENTS

- PT should know that Rx not to be shared with anyone
- Doing so likely violates state and federal law
- You may conduct witnessed urine screens (make sure opiate you are prescribing is being screened)
- May conduct pill counts

PAIN AGREEMENTS

- You may contact law enforcement if crimes are committed
- State law may require you to report illegal activity
- May refuse to prescribe CS due to PT non-compliance
- May dismiss PT due to non-compliance of pain agreement

ADDICTION/DEPENDENCE

- Addicts can be in pain
- Addicts can be treated for pain by prescriber
- Do not prescribe CS if PT indicates he/she is addicted (3 day rule)
- Dependent PT's can be tapered
- Very closely monitor PT with prior addiction (urine screens, pill counts, etc.)
- Document thoroughly!

PATIENT EDUCATION

- PT's receiving CS for the first time need drug education
- Instructions on how to take the drug
- Instructions on potential abuse/misuse by friends, family members, visitors, etc.
- Educational written instructions to PT
- Have PT view video explaining pitfalls and answer short quiz to ensure they paid attention

PATIENT EDUCATION

- Instruct PT to not keep CS in medicine cabinet
- PT should be advised to secure CS somewhere in their residence
- PT should understand that their family, neighbors, and/or friends may seek out their CS medication
- Visitors- carpet cleaners, painters, movers, etc. may be drug-seekers

PATIENT EDUCATION

- Make PT's aware that teenagers in the house may use or distribute these drugs to classmates
- PT should understand that their CS are prescribed to them only!
- PT should understand that providing their CS to others may result in catastrophic results in other persons of which you may become liable

PATIENT EDUCATION

- PT should be advised to report any problems with the diversion of their CS Rx's to the prescriber
- Dispose of unused, unneeded, or outdated Rx drugs promptly
- PT should seek out drop box locations or local take back programs
- PT needs to do their part to reduce Rx abuse

DON'T-

- Be known as an easy mark for drug seekers (will make your practice undesirable to legitimate PT's and cause police scrutiny)
- Tolerate repeated violations of pain agreements
- Refuse to prescribe appropriate medication to legitimate PT's!

DO-

- Develop a rapport and report drug diversion to local LE
- Encourage police administrators to address the issue
- Encourage local prosecutors to address the issue
- Attempt to become a mentor to LE
- Treat legitimate pain PT's appropriately

WHY GET INVOLVED?

- Rx drug seekers will consume much of your time
- Keeps you from legitimate PT's
- Lack of addressing the issue of diversion will only increase the problem
- Perpetuates PT's addiction of trafficking by ignoring the problem
- Attracts police scrutiny of your practice

REMEMBER-

- Aggressively pursue Rx drug diverters
- Not illegal to be deceived- only to continue prescribing after you know you are being deceived!
- Vast majority of your PT's are legitimate
- Usually less than 10% of your PT's are showing signs of drug diversion

REMEMBER-

- Vast majority of your PT's need your help, including pain relief
- Do not allow Rx drug seekers to negatively impact your relationship with legit PT's.
- Good pain management requires a balance between reducing diversion and providing legitimate patients with appropriate pain care

SELF EVALUATION

Prescription Drug Diversion: Safeguarding Your Practice

1. The #1 gatekeeper to addressing drug diversion is:

a. Prescriber
b. Pharmacist
c. Police
d. Addict

2. T/F - Concerning the new PT form- staff should ensure most questions are answered by the PT.

3. T/F - If the PT wants a controlled substance on their first visit, the prescriber should always accommodate them.

4. In dealing with a suspect PT, what precautions should you take as a prescriber?

a. Periodic urine screens
b. Pill Counts
c. Query prescription monitoring program
d. All of the above

5. T/F - Your script pad should only be used for prescribing and work excuses.

6. Be suspicious of a PT who does the following:

a. Consistent early refill requests
b. Claims allergies to all non-controlled substances
c. Is brought to appointment by a relative
d. Requests appointments early in the day
e. A&B

7. T/F - Safest place for a PT to keep their controlled substances is in their medicine cabinet.

Answer Key: 1. A, 2. F, 3. F, 4. D, 5. F, 6. E, 7. F

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Defining, Diagnosing and Treating Heart Failure

CHF (HFrEF) 1^0 Care Roadmap 2019

Non-Invasive Disease-Modifying Rx

ACE/ARB	Hydralazine/ISDN
Beta-Blocker	Ivabradine
Aldosterone Antagonist	Valsartan/Sacubitril

Sx-Modifying Rx

Diuretics Digoxin

Common Modifiable Comorbidities

Anemia, HTN, T-4, Thiamine, Alcohol, COPD, CAD

Lifestyle & Immunizations

Na^+/H_2O, Weight, Exercise, FluVax, PneumoVax

HFrEF Disease-Modifying Interventions

ACE
ARB
Beta Blocker
Aldosterone Antagonist
Hydralazine/Isosorbide
Ivabradine
ARB/Sacubitril

Cardiac Rehab
Exercise

ICD
CRT

Home Visits
Frequent Visits
Phone Support

CHF Vocabulary

Old Terminology	Current Terminology
CHF	Heart Failure (HF)
Systolic Dysfunction EF <40%	HF with Reduced Ejection Fraction HFrEF ('Heff-Reff')
Diastolic Dysfunction EF >50%	HF with Preserved Ejection Fraction HFpEF ('Heff-Peff')

HF: Functional Definition

A clinical syndrome that occurs when cardiac output is inadequate for tissue metabolic requirements

HF: Pathophysiologic Definition

- Clinical syndrome resulting from structural or functional impairment of ventricular filling or ejection of blood.
  - Exercise Intolerance (dyspnea & fatigue)
  - Fluid Retention (NOT everyone; ≠CHF)
- Cardiac output(CO) ≠ tissue metabolic needs
  - Sustained Sympathetic Activation
  - Sustained RAAS activation

Clyde W. Yancy et al. Circulation. 2013;128:1810-1852

NYHA Functional Classification (HF & Angina)

- CLASS I. No undue symptoms on ordinary activity. No limitation of physical activity
- CLASS II. Slight to moderate limitation of activity (IIs-IIm); patient comfortable at rest
- CLASS III. Marked limitation of activity; patient comfortable at rest
- CLASS IV. Discomfort with any physical activity; symptoms may exist even at rest

NYHA Functional Classification (SOMA)

S CLASS I. **S**trenuous activity → Sx
O CLASS II. **O**rdinary ADL → Sx
M CLASS III. **M**inimal activity → Sx
A CLASS IV. **A**ny activity/at rest → Sx

ACCF/AHA Stages of HF		NYHA
A	At high risk *but* Asymptomatic + NO structural heart disease	∅
B	Structural heart dz *but* Asymptomatic	I
C	Structural heart dz with current or prior symptoms	I-IV
D	Refractory HF	IV

Clyde W. Yancy et al. Circulation. 2013;128:1810-1852c

Heart Failure The Hemodynamic Malignancy

"The prognosis of affected individuals is dismal, as fewer than 50% of these people survive 5 years from the time of initial Dx"

Mulrow C. JAMA 1987;259(23):3422-3425

Heart Failure The Hemodynamic Malignancy

"Mortality from CHF is high, averaging 30% within the 1st year, 50% by 3-4 years, and 80% by 6-10 years"

Anderson J. Modern Medicine 1987;55(May)

Heart Failure: The Hemodynamic Malignancy

A Prospective Cohort Study (n=558)

- Total mortality at 5 years
  - Systolic Dysfunction = 42%
  - Diastolic Dysfunction = 25%

MacCarthy PA, et al Prognosis in HFpEF BMJ 2003;327:78-9

Family Practice, 2017, Vol. 34, No. 2, 161–168
doi:10.1093/fampra/cmw145
Advance Access publication 27 January 2017

Epidemiology

Survival following a diagnosis of heart failure in primary care

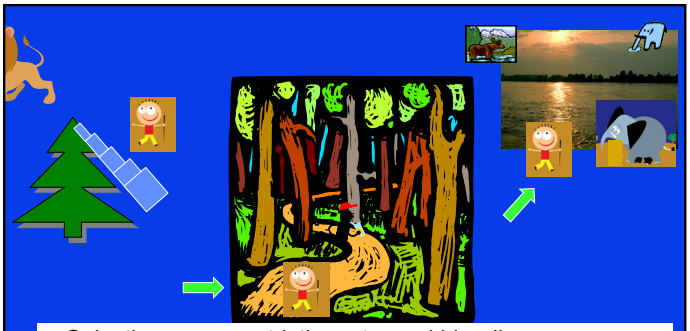
Clare J Taylor[a,*], Ronan Ryan[b], Linda Nichols[b], Nicola Gale[c], FD Richard Hobbs[a,†] and Tom Marshall[b,†]

- UK 1^0 Care patients with new Dx (n = 54,313)
- Followed 1998-2012
- Survival:
  - 1 Year: 81.3%
  - 5 Years: 51.5%
  - 10 Years: 29.5%

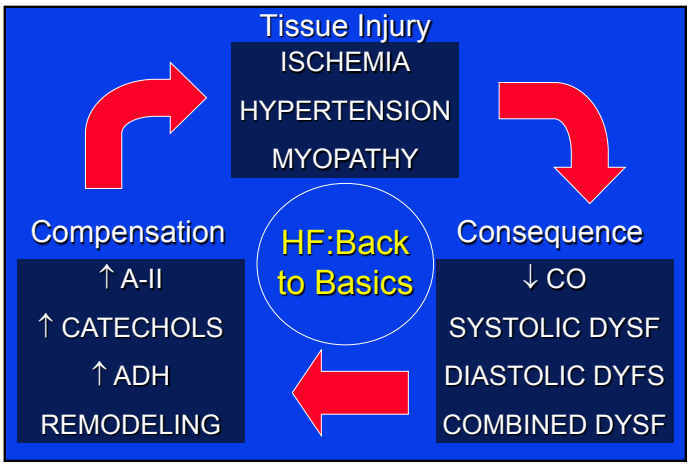
PATHOPHYSIOLOGY

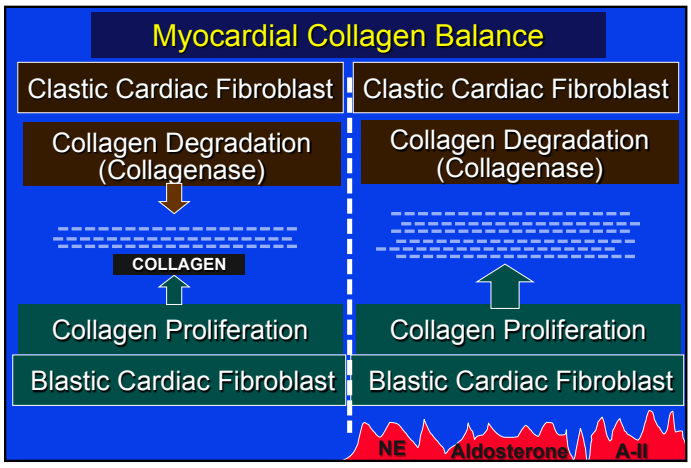
RAAS To The RESCUE!!

- A-II: Selective Vasoconstriction
- NE: Vascular Tone, Heart Rate, Contractility
- Aldosterone: Salt, Water retention, Thirst

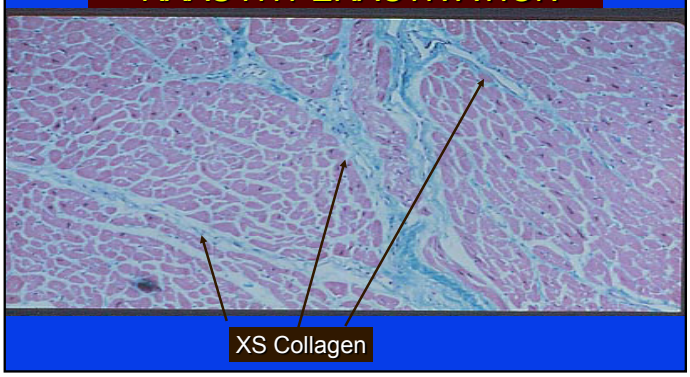


- Selective vasoconstriction: stopped bleeding
- Flow maintained to muscles, heart, brain
- 4 quarts low: ↑ heart rate, contractility
- Insensitive fluid losses stemmed (saliva, sweat, urine)
- Thirsty





RAAS HYPERACTIVATION



BNP

- BNP = brain natriuretic peptide
- Originally: brain natriuretic peptide (first isolated in porcine brain)
- synthesized (but not stored) in ventricular myocytes
- Ventricular stress →↑ BNP

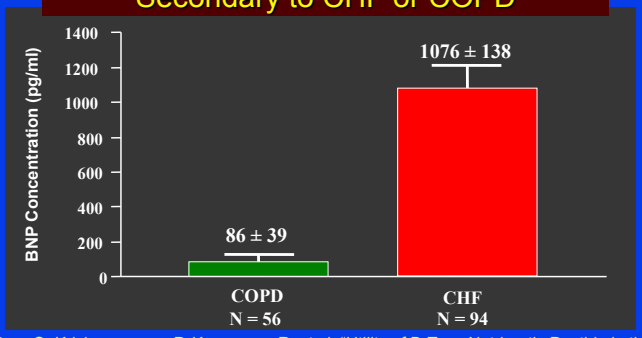
Cheung BM, Kumana CR. "Natriuretic Peptides-Relevance in Cardiovascular Disease" JAMA. 1998;280(23):1983-1984

BNP : Diagnostic Clinical Role

- STUDY: Unselected dyspnea pts presenting to VA (n=250)
- METHOD: compare BNP (rapid bedside test) with cardiologist assessment of Dx

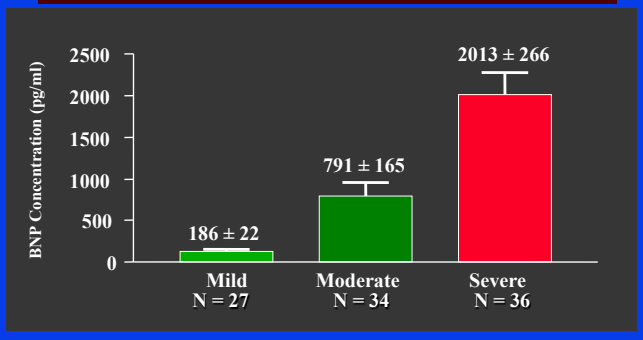
Dao Q, Krishnaswamy P, Kazanegra R, et al "Utility of B-Type Natriuretic Peptide in the Dx of CHF in an Urgent-Care Setting" J Am Coll Cardiol 2001;37:379-85

BNP Levels in Patients With Dyspnea Secondary to CHF or COPD



Dao Q, Krishnaswamy P, Kazanegra R, et al "Utility of B-Type Natriuretic Peptide in the Dx of CHF in an Urgent-Care Setting" J Am Coll Cardiol 2001;37:379-85

BNP: Degree of CHF Severity



Dao Q, Krishnaswamy P, Kazanegra R, et al "Utility of B-Type Natriuretic Peptide in the Dx of CHF in an Urgent-Care Setting" J Am Coll Cardiol 2001;37:379-85

BNP to Guide CHF Rx

- STUDY: Pts with systolic dysfunction in Cardiology HF clinic, NYHA II-IV, EF <40% (n=60)
- GOAL: BNP <200 vs clinical heart failure score <2
- METHOD: 'Standard' clinical assessment vs BNP Q 3 months X 1 year

Troughton RW, Frampton CM, Yandle TG,et al "Rx of heart failure guided by N-BNP concentrations" Lancet 2000;355:1126-30

HEART-FAILURE SCORING SYSTEM

Orthopnea	0.5
PND	1.0
↓Exercise tolerance	0.5
Resting Sinus tachycardia	0.5
JVP >4cm	0.5
Hepatojugular reflex +	1.0
S-3 Heart Sound	1.0
Basal crackles	1.0
Hepatomegaly	0.5
Peripheral edema	0.5

Troughton RW, Frampton CM, Yandle TG,et al "Rx of heart failure guided by N-BNP concentrations" Lancet 2000;355:1126-30

BNP vs Clinical Evaluation to Guide CHF Rx: Results

- Total CV events (death, hospital admission, or worse HF): 19 vs 54 (p=0.02)
- At 6 months 27% BNP vs 53% traditional had experienced a first CV event
- LV function, QOL, Renal Fx, adverse events ≅

Troughton RW, Frampton CM, Yandle TG,et al "Rx of heart failure guided by N-BNP concentrations" Lancet 2000;355:1126-30

BNP to Guide CHF Rx: Interpretation

"N-BNP guided Rx of heart failure reduced total CV events, and delayed time to first event compared with intensive clinically guided Rx."

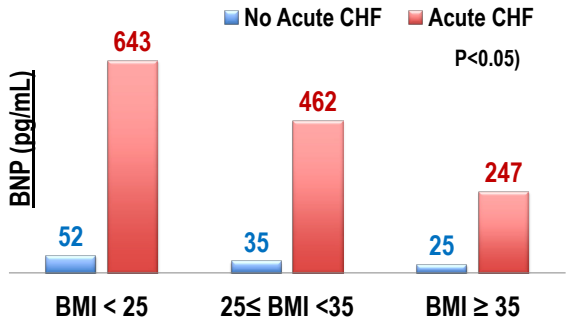
Troughton RW, Frampton CM, Yandle TG,et al "Rx of heart failure guided by N-BNP concentrations" Lancet 2000;355:1126-30

Breathing Not Properly (BNP) Study: Dx and Prognosis

- Prospective Obs. study; n=1,586 w/ Ac. SOB
- 2 Dx Methods compared to Cardiologist Dx
  1. NHANES and Framingham criteria for Dx CHF
  2. BNP
- OUTCOME:
  - Single BNP more accurate than criteria scores for Dx of CHF
  - pts whose 30d BNP level was > discharge BNP level were at highest risk for decompensation/readmission

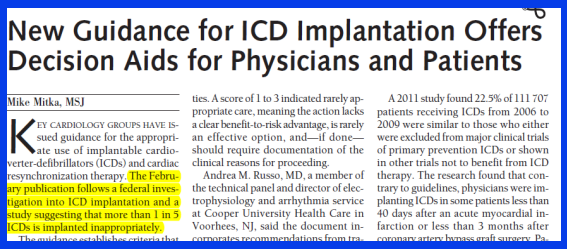
Maisel AS, Daniels LB. Breathing Not Properly 10 Years Later: What We Have Learned and What We Still Need to Learn. *J Am Coll Cardiol*.2012;60(4):277-282.

BNP Study: Obesity and BNP Levels



Daniels LB, Clopton P, et al. How Obesity Affects the Cut-Points for B-Type Natriuretic Peptide in the Diagnosis of Acute Heart Failure. Am Heart J. 2006;151(5):999-1005.

Why Should I have to Learn All the Treatments?



New Guidance for ICD Implantation Offers Decision Aids for Physicians and Patients

Mike Mitka, MSJ

KEY CARDIOLOGY GROUPS HAVE ISsued guidance for the appropriate use of implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy. The February publication follows a federal investigation into ICD implantation and a study suggesting that more than 1 in 5 ICDs is implanted inappropriately.

ties. A score of 1 to 3 indicated rarely appropriate care, meaning the action lacks a clear benefit-to-risk advantage, is rarely an effective option, and—if done—should require documentation of the clinical reasons for proceeding.

Andrea M. Russo, MD, a member of the technical panel and director of electrophysiology and arrhythmia service at Cooper University Health Care in Voorhees, NJ, said the document incorporates recommendations from tra-

A 2011 study found 22.5% of 111 707 patients receiving ICDs from 2006 to 2009 were similar to those who either were excluded from major clinical trials of primary prevention ICDs or shown in other trials not to benefit from ICD therapy. The research found that contrary to guidelines, physicians were implanting ICDs in some patients less than 40 days after an acute myocardial infarction or less than 3 months after coronary artery bypass graft surgery. Pa-

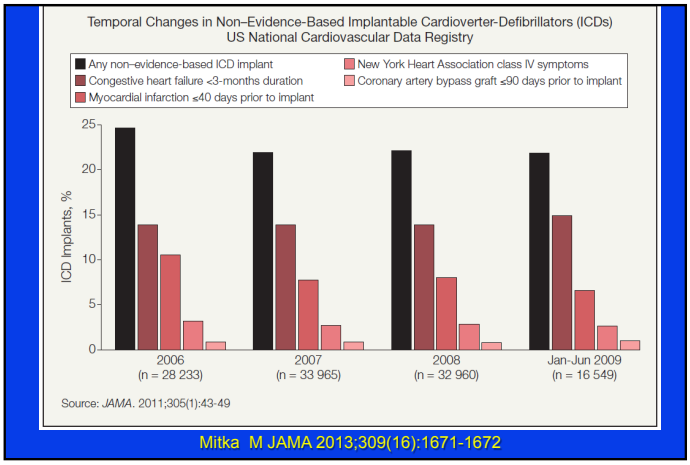
Mitka M JAMA 2013;309(16):1671-1672

WHY

verter-defibrillators (ICDs) and cardiac resynchronization therapy. The February publication follows a federal investigation into ICD implantation and a study suggesting that more than 1 in 5 ICDs is implanted inappropriately.

Mitka M JAMA 2013;309(16):1671-1672

Just Because The Consultant is a CARDIOLOGIST Doesn't Mean That All The Right Stuff Happens All The Time



Mitka M JAMA 2013;309(16):1671-1672

HFrEF Disease-Modifying Interventions

ACE
ARB
Beta Blocker
Aldosterone Antagonist
Hydralazine/Isosorbide
Ivabradine
ARB/Sacubitril

Cardiac Rehab
Exercise

ICD
CRT

Home Visits
Frequent Visits
Phone Support

Treating Hypertension to Prevent HF

Aggressive blood pressure control:

Decreases risk of new HF by ~ 50% 56% in DM2

Aggressive BP control in patients with prior MI:

Decreases risk of new HF by ~ 80%

Lancet 1991;338:1281:1281-5 (STOP-Hypertension).
JAMA 1997;278:212-6 (SHEP).
UKPDS Group. UKPDS 38. BMJ 1998;317:703-713.

Heart Failure Society of America

BP Control

- Long-term tx of both systolic and diastolic HTN reduces risk of HF by ~ 50%
  - 2013 ACCF/AHA HF Guidelines
- SPRINT Trial (n=9,361)
  - Non DM pts with HTN were ~40% less likely to develop HF if treated to a goal SBP <120 compared to a SBP goal <140

The SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015;373:2103-2016

Sodium Restriction?

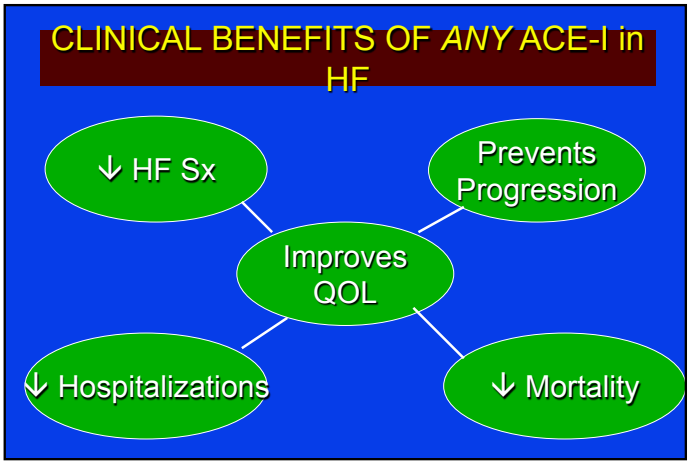
- Obs. study: 902 pts NYHA II-III; Systolic or Diastolic HF
- METHOD: Na+ intake assessed over 36 months using a food freq. questionnaire; pts classified as either Na+ Restricted (<2500mg/d) or Unrestricted (≥2500 mg/d).
- OUTCOME: composite of death or HF hospitalization

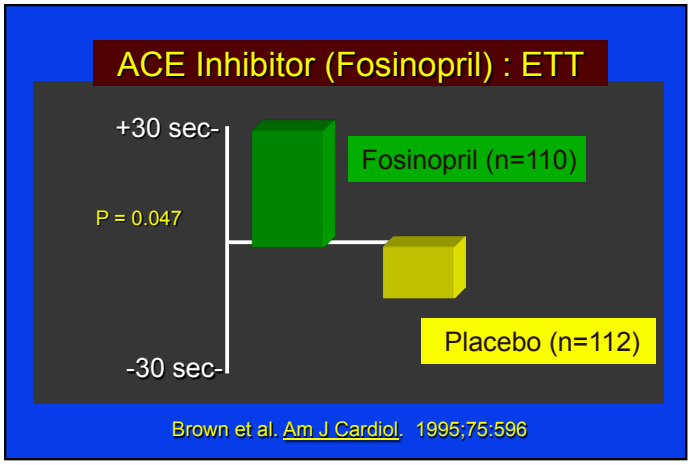
Doukky R, Avery E, Mangla A, et al. Impact of Dietary Sodium Restriction on Heart Failure Outcomes. *JCHF.* 2016;4(1):24-35.

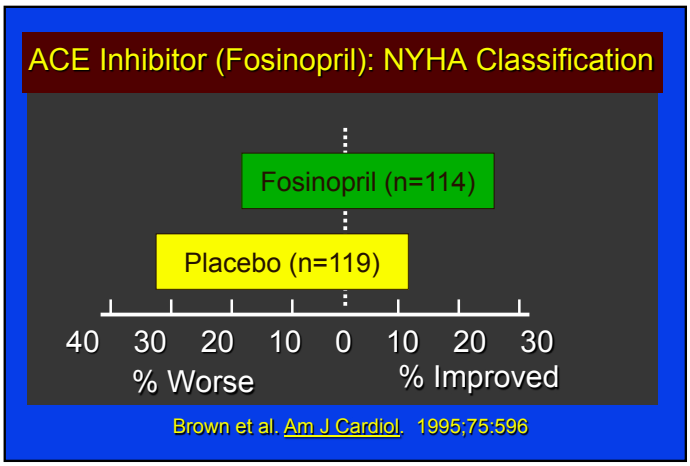
Sodium Restriction?

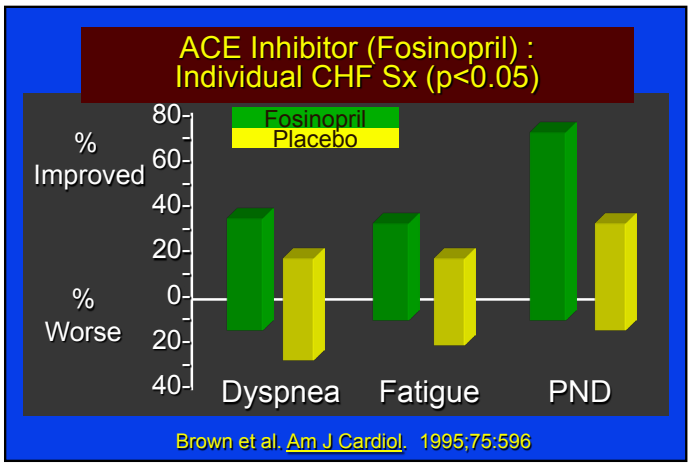
- Na+ Restriction → **Higher Risk of HF hospitalization** or **death** (42% v 26%; HR 1.85; p=0.004)
- Highest risk increase in those not taking ACE/ARB (HR 5.78; P=0.002) and NYHA II (HR 2.36; P=0.003)
- ACCF/AHA SOR for Na+ restriction downgraded
  - Class I (recommended) →Class IIa (reasonable)

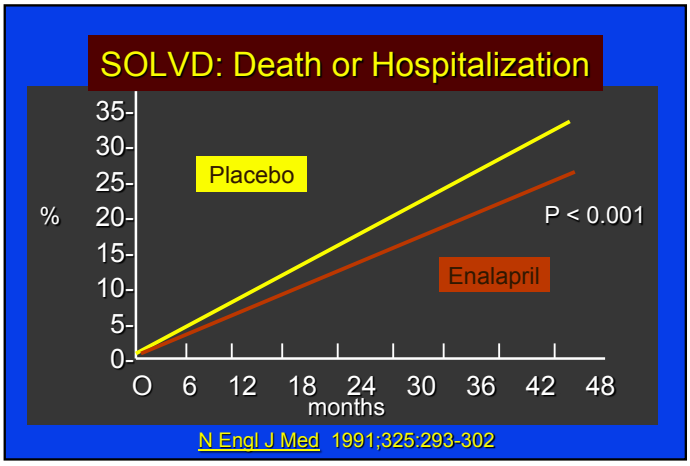
Doukky R, Avery E, Mangla A, et al. Impact of Dietary Sodium Restriction on Heart Failure Outcomes. *JCHF.* 2016;4(1):24-35.

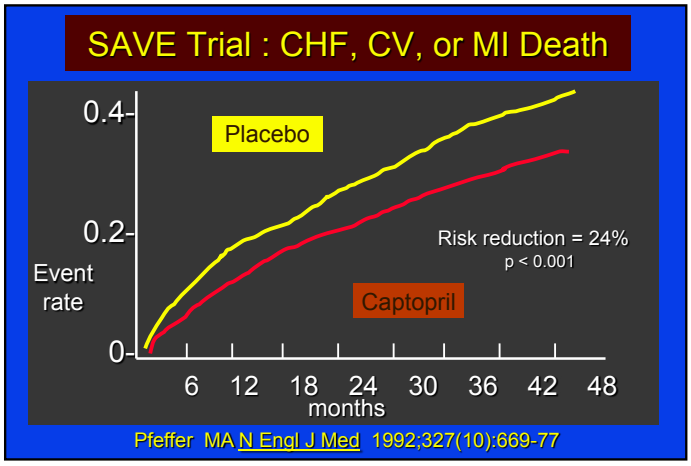

CLINICAL BENEFITS OF *ANY* ACE-I in HF
↓ HF Sx
Prevents Progression
Improves QOL
↓ Hospitalizations
↓ Mortality


ACE Inhibitor (Fosinopril) : ETT
+30 sec-
-30 sec-
P = 0.047
Fosinopril (n=110)
Placebo (n=112)
Brown et al. Am J Cardiol. 1995;75:596


ACE Inhibitor (Fosinopril): NYHA Classification
Fosinopril (n=114)
Placebo (n=119)
40 30 20 10 0 10 20 30
% Worse
% Improved
Brown et al. Am J Cardiol. 1995;75:596


ACE Inhibitor (Fosinopril) : Individual CHF Sx (p<0.05)
Fosinopril
Placebo
% Improved
% Worse
80
60
40
20
0
20
40
Dyspnea
Fatigue
PND
Brown et al. Am J Cardiol. 1995;75:596


SOLVD: Death or Hospitalization
%
35
30
25
20
15
10
5
0
Placebo
Enalapril
P < 0.001
O 6 12 18 24 30 36 42 48
months
N Engl J Med 1991;325:293-302


SAVE Trial : CHF, CV, or MI Death
0.4
0.2
0
Event rate
Placebo
Captopril
Risk reduction = 24%
p < 0.001
6 12 18 24 30 36 42 48
months
Pfeffer MA N Engl J Med 1992;327(10):669-77

ACE Inhibitors & CHF

- Meta-analysis 32 trials (n = 7,105)
- Most pts severe CHF (EF < 35-40%) Rx ≥ 8 weeks

RESULTS	ACE	PLACEBO
• Mortality	15.8%	21.9%
• Hospitalization or death	22.4%	32.6%

- NO APPRECIABLE DIFFERENCE AMONG STUDY DRUGS (ALL ACE = EFFICACY)

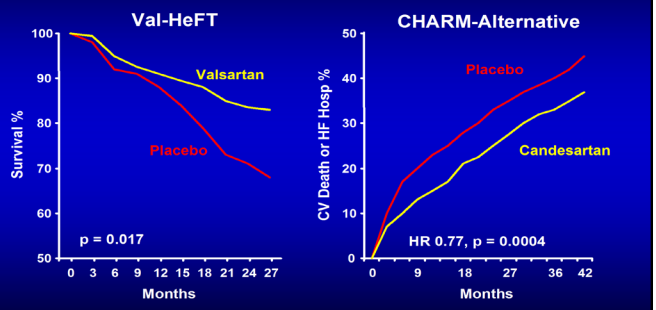
JAMA 1995; 273:1450

2013 ACCF/AHF HF Guidelines: ARBs

"ARBs are recommended in pts w/ HF*r*EF w/ current or prior Sx who are ACEI intolerant, to reduce morbidity and mortality." **(Class I Rec; LOE: A)**

Clyde W. Yancy et al. 2013 ACCF/AHA HF Guideline. *Circulation*. 2013;128:1810-1852.

ARBS in Patients Not Taking ACE Inhibitors: Val-HeFT & CHARM-Alternative



Heart Failure Society of America

Maggioni AP et al. JACC 2002;40:1422-4.
Granger CB et al. Lancet 2003;362:772-6.

2013 ACCF/AHA HF Guidelines: Beta-Blockers (BB)

"1 of the 3 BBs proven to reduce mortality (**bisoprolol, carvedilol, metoprolol succinate**) is recommended for **ALL pts** w/ current or prior symptoms of HF*r*EF to reduce morbidity and mortality."

(Level of Evidence: A)

Clyde W. Yancy et al. 2013 ACCF/AHA HF Guideline. *Circulation*. 2013;128:1810-1852.

The Additional Value of Beta Blockers Post-MI: CAPRICORN

Studied impact of beta blocker (carvedilol) on post-MI patients with LVEF ≤ 40% already receiving contemporary treatments, including revascularization, anticoagulants, ASA, and ACEI:

- All-cause mortality reduced (HR = 0.077; p = 0.03)
- Cardiovascular mortality reduced (HR = 0.75; p = .024)
- Recurrent non-fatal MIs reduced (HR =.59; p = .014)

Dargie HJ. Lancet 2001;357:1385-90.

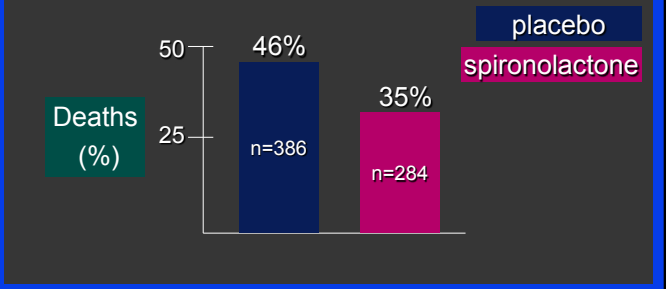
Heart Failure Society of America

RALES: Spironolactone in Severe Heart Failure

- STUDY: NYHA III-IV CHF, EF <35% (n =1663)
- INCLUSION: on ACE + loop diuretic with (+ dig or vasodilators OK), K+ < 5.0, Cr < 2.5
- Rx: spironolactone 25 mg QD vs placebo X 3 years

Pitt B, Zannad F, Remme W. et al "The Effect of Spironolactone on Morbidity and Mortality in Pts with Severe Heart Failure" N Engl J Med. 1999;341(10):709-17

Spironolactone in Severe Heart Failure: Results



Pitt B, Zannad F, Remme W. et al "The Effect of Spironolactone on Morbidity and Mortality in Pts with Severe Heart Failure" N Engl J Med. 1999;341(10):709-17

Spironolactone in Severe Heart Failure

"Blockade of aldosterone receptors by spironolactone, in addition to standard therapy, substantially reduces the risk of both morbidity and death among pts with severe heart failure."

Pitt B, Zannad F, Remme W. et al "The Effect of Spironolactone on Morbidity and Mortality in Pts with Severe Heart Failure" N Engl J Med. 1999;341(10):709-17

Spironolactone in Severe Heart Failure : Results

	Spironolactone	Placebo
Hospitalizations	260 pts	336 pts
NYHA class ↑	41%	33%
NYHA class ↓	38%	48%
Hyperkalemia	2% ⇔ (NS)	1%
Gynecomastia	10% ⇔	1%

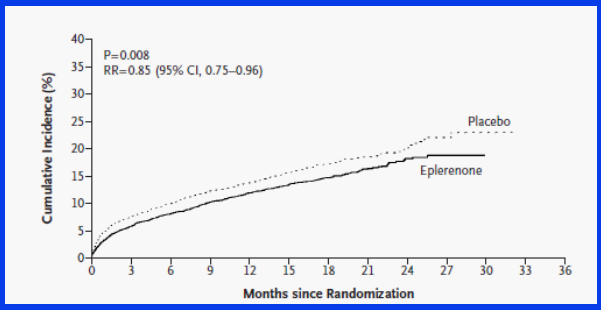
Pitt B, Zannad F, Remme W. et al "The Effect of Spironolactone on Morbidity and Mortality in Pts with Severe Heart Failure" N Engl J Med. 1999;341(10):709-17

EPHESUS
Eplerenone Post-Acute MI HF Efficacy and Survival Study

- Study: RDBPCT in Post-MI HF pts
- Rx: eplerenone 25-50 mg/d vs placebo X 16 months (n=6,632)
- Outcomes:
  - All-cause mortality
  - CV Death
  - CV Hospitalizations

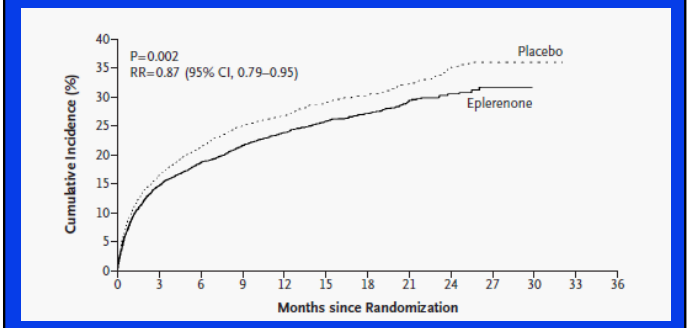
Pitt B et al NEJM 2003;348:1309-1321

EPHESUS: All Cause Mortality



Pitt B et al NEJM 2003;348:1309-1321

EPHESUS: CV Death or CV Hospitalization



Pitt B et al NEJM 2003;348:1309-1321

Aldosterone Antagonist in HF*r*EF

"Clinicians should strongly consider the addition of the aldosterone receptor antagonists spironolactone or eplerenone for *all patients* with HFrEF already on ACEI (or ARBs) and BBs."

-2013 ACC/AHA Guidelines

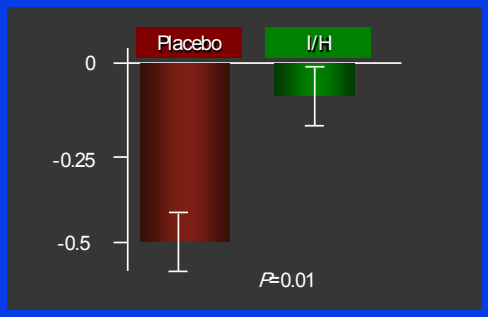
Clyde W. Yancy et al. 2013 ACCF/AHA HF Guideline. *Circulation*. 2013;128:1810-1852.

A-HeFT

- STUDY: Black patients with CHF, NYHA III-IV (n=1050) followed 18 months
- PREMISE: Previous CHF trials→ beneficial I/H effects in black subgroup
- Rx: isosorbide dinitrate/hydralazine 37.5mg/20 mg one t.i.d. → two t.i.d.

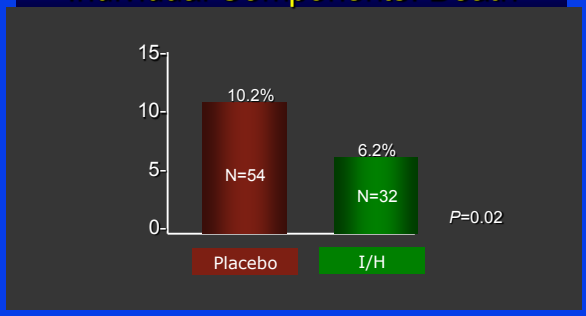
Taylor AL, Ziesche S, Yancy C, et al "Combination of ISDN and Hydralazine in Blacks with Heart Failure" N Engl J Med 2004;351:2049-57

A-HeFT: Primary Endpoint



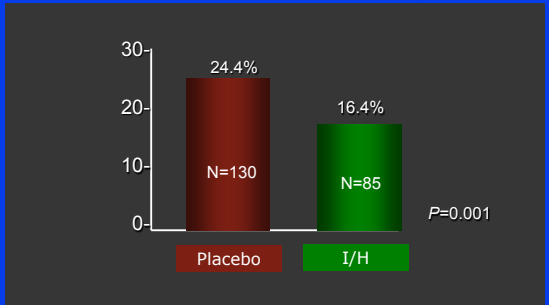
Taylor AL, Ziesche S, Yancy C, et al "Combination of ISDN and Hydralazine in Blacks with Heart Failure" N Engl J Med 2004;351:2049-57

A-HeFT Composite Score Individual Components: Death



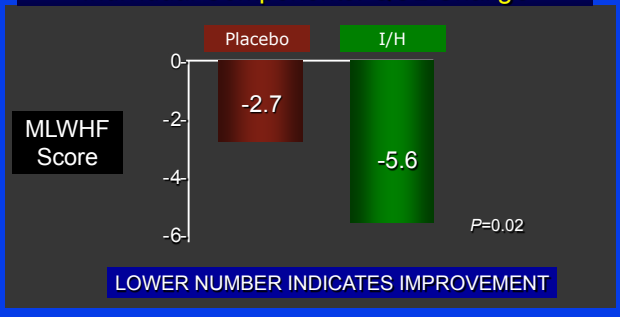
Taylor AL, Ziesche S, Yancy C, et al "Combination of ISDN and Hydralazine in Blacks with Heart Failure" N Engl J Med 2004;351:2049-57

A-HeFT Composite Score Individual Components: 1st HF Hospitalization



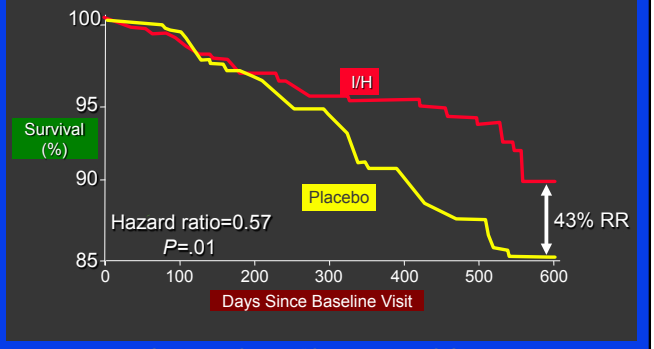
Taylor AL, Ziesche S, Yancy C, et al "Combination of ISDN and Hydralazine in Blacks with Heart Failure" N Engl J Med 2004;351:2049-57

A-HeFT Composite Score Individual Components: QOL Change



Taylor AL, Ziesche S, Yancy C, et al "Combination of ISDN and Hydralazine in Blacks with Heart Failure" N Engl J Med 2004;351:2049-57

A-HeFT: Mortality



Taylor AL, Ziesche S, Yancy C, et al "Combination of ISDN and Hydralazine in Blacks with Heart Failure" N Engl J Med 2004;351:2049-57

A-HeFT: Adverse Events

	I/H	Placebo	*P* Value
Headache (all)	47.5%	19.2%	<0.001
Headache (severe)	5.2%	0.9%	
Dizziness	29.3%	12.3%	<0.001
HF Exacerbation	8.7%	12.8%	0.04
HF Exacerbation (severe)	3.1%	7.0%	0.005

Taylor AL, et al N Engl J Med 2004;351:2049-57

20113 ACCF/AHA Recommendation

"The combination of ISDN/H is recommended for pts self-described as AA w/ NYHA III-IV HF*r*EF receiving optimal tx w/ ACEI/B-blkers."

(*Level of Evidence: A*)

Clyde W. Yancy et al. 2013 ACCF/AHA HF Guideline. *Circulation*. 2013;128:1810-1852.

Ivabradine (Corlanor)

- Selective Inhibitor of the "funny channel (I_f)" which modulates SA pacemaker → ↓ Sinus Rate
- Does not effect atrial conduction, AV node, or ventricles → no effect on contractility
  - Difference from BB and CCB
- Reduces HR by ~ 10 bpm → ↓ cardiac workload

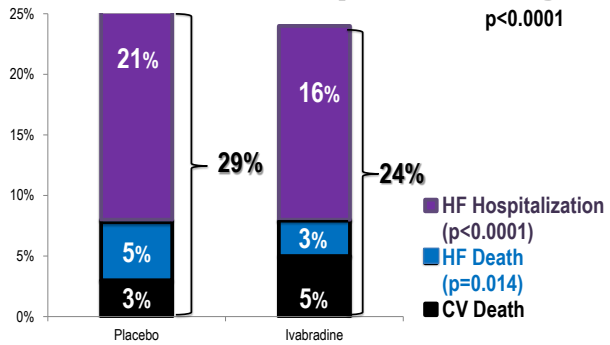
Colucci, WS. Use of beta blockers and ivabradine in heart failure with reduced ejection fraction. In: UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA. (Accessed on March 31, 2016).

SHIFT Trial: Systolic Heart Failure tx with I_f Inhibitor Ivabradine Trial

- RCT; 6558 pts w/ HF Sx and LVEF ≤ 35%
  - HR ≥ 70bpm
  - HF Admission in previous year
  - On background GDMT *(ACE/ARB, BB, Aldo Antagonist)*
- 1° Outcome: CV Death or Hosp for worsening HF

Swedberg, Karl et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. The Lancet , Volume 376 , Issue 9744 , 875 – 885.

SHIFT: CV Death *or* Hosp for Worsening HF



Swedberg, Karl et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. The Lancet , Volume 376 , Issue 9744 , 875 – 885.

SHIFT Trial: Ivabradine in Chronic HF

- No increase Serious AES
  - –Increased Sx'tic Bradycardia (5% vs 1%)
  - –Increased Visual side effects (3% vs 1%)
- Conclusion: HR reduction w/ Ivabradine ↓CV Mortality and Hospitalizations for pts with persistent HF Sx, HF > 70bpm on background tx

Swedberg, Karl et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. The Lancet , Volume 376 , Issue 9744 , 875 – 885.

Sacubitril-valsartan

- Sacubitril = neprilysin inhibitor
- Neprilysin inhibition → ↑ vasoactive peptides → vasodilatation, natriuresis/diuresis, ↓ LV remodeling
- Indicated for NYHA II-IV HF*r*EF in place of ACE/ARB
- Increased risk of angioedema w/ concurrent ACEI

Colucci, WS and Pfeffer MA. Use of angiotensin II receptor blocker and neprilysin inhibitor in HF with reduced EF. UptoDate, Gottlieb SS (Ed), UpToDate, Waltham, MA. (Accessed on April 12, 2016).

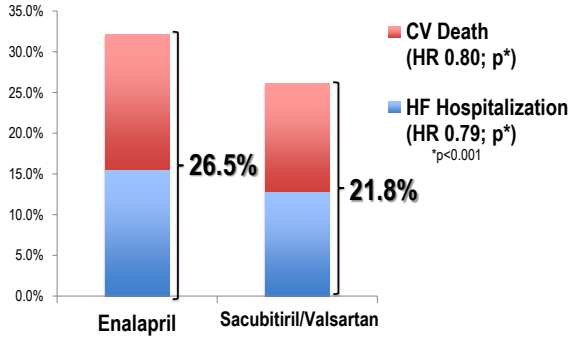
PARADIGM-HF: Sacubitril-valsartan in HF*r*EF

- 8442 HF NYHA II-IV and EF ≤ 40%
- Randomized to:
  - –Sacubitril + Valsartan 200mg BID
  - –Enalapril 10mg BID
- 27 months
- OUTCOMES:
  - –1° Outcome: Composite CV death or HF Hosp
  - –2° Outcomes: CV Death; All-Cause Death

McMurray JJV et al. N Engl J Med 2014;371:993-1004

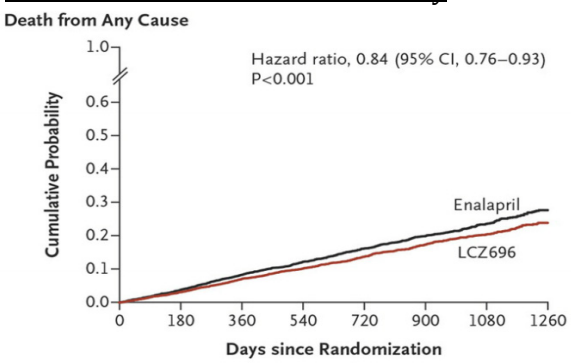
PARADIGM-HF: 1° Outcome

(CV Death or HF Hospitalization; HR 0.80, p*)



McMurray JJV et al. N Engl J Med 2014;371:993-1004

PARADIGM-HF: All-Cause Mortality



McMurray JJV et al. N Engl J Med 2014;371:993-1004

HF Guideline Recommendations: ICD (Implantable Cardioverter-Defibrillator)

- 1° SCD prevention in pts > 40 days Post-MI, on GDMT and expected survival > 1 yr:
  - –nonischemic DCM or ischemic heart disease w/ **EF ≤ 35%, NYHA II-III Sx** (*LOE: A*)
  - –w/ **EF ≤ 30%, NYHA I Sx** (*LOE: B*)
- **Refer to cardiology when EF ≤ 35%**

Clyde W. Yancy et al. 2013 ACCF/AHA HF Guideline. *Circulation*. 2013;128:1810-1852.

MADIT-II: Multictr Automatic Defib Implantation Trial II

Prophylactic ICD compared w/ standard of care led to 31% RRR in all-cause mortality in post-MI pts w/ EF ≤ 30%

-Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med. 2002;346:877–83.

MADIT-CRT Trial

- CRT-ICD decreased risk of HF event in aSx pts (NYHA I-II) w/ LVEF ≤30% and wide QRS (≥130ms)
  - –1 Outcome: All-cause death or Nonfatal HF event (ICD-CRT 17.2% vs ICD alone 25.3%; HR 0.66; p=0.001)

Moss AJ, Hall WJ, et al. Cardiac-Resynchronization Therapy for the prevention of Heart Failure Events, N Engl J Med 2009; 361:1329-1338.

HF Guidelines: Cardiac Resynchronization Therapy (CRT)

- CRT is indicated for pts w/ EF ≤ 35%, NSR, LBBB, QRS ≥150ms, and NYHA class II-IV Sx on GDMT
  - –May consider in non-LBBB pattern, QRS duration 120-149ms, Afib
- **Refer to cardiology when EF ≤ 35%**

Clyde W. Yancy et al. 2013 ACCF/AHA HF Guideline. *Circulation*. 2013;128:1810-1852.

Thiamine and CHF

- 30 CHF pts on Lasix ≥ 80 mg/d chronically
- Rx thiamine IV X 1 week + 200mg/ d PO X 6 weeks vs placebo
- Results of thiamine compared to placebo:
- LV end diastolic function ↑ 22%
- diuresis & Na^+ excretion improved
- NYHA class ↓ from 2.6-2.2

Shimon A, Almog S, Vered Z, et al, "Improved LV Function after Thiamine Supplementation in Pts with CHF" Am J Med 1995; 98:485-490

Thiamine and CHF : Postulates

- Subclinical thiamine deficiency (furosemide known to deplete thiamine)
- diuretic effect of thiamine
- direct cellular thiamine effect
- Commentary: Because the adverse effects were few, and the benefits potentially great, thiamine supplementation could be useful.

Shimon A, Almog S, Vered Z, et al, "Improved LV Function after Thiamine Supplementation in Pts with CHF" Am J Med 1995; 98:485-490

CHF (HFrEF) 1^0 Care Roadmap 2019

Non-Invasive Disease-Modifying Rx

ACE/ARB	Hydralazine/ISDN
Beta-Blocker	Ivabradine
Aldosterone Antagonist	Valsartan/Sacubitril

Sx-Modifying Rx

Diuretics Digoxin

Common Modifiable Comorbidities

Anemia, HTN, T-4, Thiamine, Alcohol, COPD, CAD

Lifestyle & Immunizations

Na^+/H_2O, Weight, Exercise, FluVax, PneumoVax

SELF EVALUATION

Defining, Diagnosing and Treating Heart Failure

1. The old terminology of 'systolic heart failure' has been replaced with

a. HFrEF (Heart failure with reduced ejection fraction)
b. HFpEF (Heart failure with preserved ejection fraction)
c. OCHF (Output-compromised heart failure)
d. FCHF (Filling-compromised heart failure)

2. 5-year mortality after a new diagnosis of heart failure with current standard care therapy is approximately

a. 10%
b. 20%
c. 30%
d. 50%

3. The sustained sympathosis of Heart Failure with Reduced Ejection Fraction (HFrEF) is typified by all of the following characteristics except

a. Increased norepinephrine
b. Increased angiotensin II
c. Increased aldosterone
d. Decreased generation of myocardial collagen

4. In a COPD patient presenting to the ED with dyspnea, a high BNP level indicates his dyspnea is more likely from

a. Heart Failure
b. COPD
c. Anemia
d. Anxiety

5. ACE inhibitors are considered 1st line treatment of HFrEF. Which statement is correct

a. Ramipril is the most effective ACEi
b. Lisinopril is the most effective ACEi
c. Enalapril is the most effective ACEi
d. All ACEi appear to be equally effective

6. Which beta blocker has NOT been shown to reduce mortality in HFrEF?

a. bisoprolol
b. metoprolol
c. carvedilol
d. propranolol

7. According to the 2013 ACC/AHA Heart Failure Guidelines, aldosterone blockers (e.g., spironolactone, eplerenone) should be considered

a. only for HFrEF patients with Ejection Fraction <20%
b. only for HFrEF patients with Ejection Fraction <15%
c. for all HFrEF patients
d. only for HFrEF post-ICD (implantable cardiovertor defibrillator) patients

Answer Key: 1. A, 2. D, 3. D, 4. A, 5. D, 6. D, 7. C

Ike Z. Devji, Esq.

Ike Z. Devji, Esq., of Phoenix, Arizona, has been solely focused on asset protection and wealth preservation planning for the last 14 years. He and his colleagues have protected over $5 billion in personal assets for a national client base that includes thousands of successful physicians, as well as business owners and entrepreneurs. Mr. Devji is a noted national educator (CME, CLE, and CE), an author with over 300 nationally published bylines, and a frequent speaker, having taught thousands of doctors, lawyers, and advisors on asset protection and risk management, in addition to being a contributing author to multiple books and a dozen medical journals. He is AVVO rated "10.0 Superb" for nine years in a row and is included in "Arizona's Finest Lawyers" among other distinctions.

You may contact Mr. Devji with any questions or comments at (602) 808–5540, by email at id@thewealthy100.com, or through his website at www.ProAssetProtection.com.

Holistic Asset Protection: Identifying and Protecting Against Practice Risks

You have significant professional risk as a physician, but you are also potentially an executive, a parent, a business owner, a compliance officer, a breadwinner, the driver of vehicle, the owner of a home and other real estate and bear liability for a number of other serious risks that are commonly overlooked

Having experienced help in properly identifying as many of these other, non-malpractice related risks as possible and addressing them proactively both personally and professionally is a key part of any defensive strategy. Here are some of the most common risk factors, and while this list is by no means complete, **I'd guess that more than half the risk factors below apply to the majority of people reading this.**

RISK FACTORS OF THOSE NEEDING ASSET PROTECTION

- They are high net worth, high liability, or they soon will be (i.e. new doctor, rookie athlete, new business owner)
- They drive a vehicle and/or own a home
- They are a board member, officer or director of a public or private business
- They are a board member of a charitable, school private foundation or other board
- They have assets that would be difficult to replace if lost or reduced
- They have employees
- They own their own business
- They have professional liability
- They own liability generating assets like investment real estate
- They are highly visible locally or nationally and are perceived to hold substantial wealth
- They have children, spouses and other extended family in their homes and driving their vehicles
- They are selling a business and replacing recurring income with a single lump sum

Other Significant Threats to Your Wealth, It's Not Just About *Lawsuits*.

- Economic Conditions
- Decreasing Compensation and Insurance Reimbursement Rates
- Changing Healthcare Business Models and Consolidation
- Hostile Litigation System
- Social and political variables that threaten wealth
- Increasing Overhead and Liability Insurance Costs (payroll, healthcare, etc.)
- Decreases in Liability Insurance Protection (due to large awards, *consent to settle* and *defense inside the limits* clauses in current coverage)

SECTION ONE: What Exactly is "Asset Protection"?

This can understandably be a confusing term for consumers, especially given that it's currently a fashionable marketing phrase used by everyone from insurance and annuity salesmen to loss prevention specialists and, perhaps even worse, a wide variety of both lawyer and non-lawyer "promoters" advancing various legal and financial legal schemes of subjective value.

For our purposes here, the term "Asset Protection" refers to the holistic legal practice of proactively managing your assets, risk and liabilities, both personal and professional.

It's also at, the broadest level, a combination of four core disciplines that protect individuals and their assets from hostile attack, waste and spoilage. These include:

- Insurance (including liability, life, health, disability, etc.)

- Legal Tools
- Financial Planning
- Proper Tax Planning

Asset Protection is Always PROACTIVE

It cannot be strongly enough emphasized that **prevention always beats treatment** with legal and financial exposures; **the best asset protection is always preventative and proactive.** Timing is crucial and of the essence; you may be legally unable to act, (fraudulent conveyance, voidable transaction, etc.) or at best, end up with results that are more expensive and less predictable if you wait and try to manage *crisis* instead of *risk*.

Litigation is managing crisis, bankruptcy is managing crisis as just two examples. **Even the best asset protection strategies *will fail* against a known and preexisting exposure and create additional financial and legal risk up to the level of being *criminal*.**

How Is "Asset Protection" Different from Traditional "Estate Planning"?

Traditional Estate Planning is **"death planning"** that controls who gets your assets when you pass, how they are administered, who is appointed to manage your estate, and in some cases, helps mitigate your estate tax exposure. This year, a married couple can pass roughly the first **$22.8 Million dollars** of their estate **(or roughly $11.4 million each)** to anyone they like **free of federal estate tax or "death tax"** as referred to by politicians. There is no estate tax on assets passed between spouses.

- **ASSET PROTECTION** is **LIFE PLANNING;** how you can help ensure that you and your family get to keep the wealth **DURING** your life and that it will ultimately be there to actually go to your estate plan and protect your heirs at the end of your life as well
- Most People omit a good **LIFE PLAN** and plan only for their death
- Successful, high risk professionals like **physicians need both,** and they need to work *together*

YOUR REVOCABLE LIVING TRUST IS NOT ASSET PROTECTION
THIS IS ONE OF THE MOST COMMON FINANCIALLY FATAL MISTAKES MADE BY DOCTORS

-Many medical professionals mistakenly rely on their **REVOCABLE LIVING TRUST (RLT)** as Asset Protection. **IT ISN'T.** These individuals usually have their homes, investments and other valuables in the name of the RLT.

-The RLT is ZERO Asset Protection of **your assets,** from **your creditors,** during **your life,** as it is REVOCABLE – the court will simply order you to revoke and tender the assets;

-The RLT is a **great estate planning tool** and is a tool you probably should have, but it has a specific purpose and job to do for you.

Asset Protection Is a System of Layers

Think of asset protection they way you teach your patients about wellness; it's a system and **lifestyle that requires** some discipline and good habits in **four core areas.**

• A culture of good habits, procedures, accountability and compliance, starting with **you**. Avoiding or eliminating higher risk behavior often starts with having good, professionally drafted, legally compliant policies and procedures on a variety of risk management issues and consistently implementing and enforcing them uniformly. **There is no more dangerous and ineffective manager than one who is conflict averse or who wants to be everyone's friend.** Leadership requires that you help everyone be and do their best by managing them actively and creating expectations and boundaries.

• Proactively managing all your predictable risks, not just those related to medial malpractice. We won't dwell on this issue beyond this; medical malpractice lawsuits are a real threat and no matter what various experts tell you about statistics, how many actually go trial, and etc. we have seen the devastating first hand effects of these claims and the best way I can share my concern on this issue, no matter how remote a risk you feel it may be, is this; **what if it is you?** Are

you emotionally, legally and financially prepared for a claim or judgment that could potentially stop your income, cost you your hospital privileges or practice, trigger a payor audit and take seven figures off your life's work and net worth? Most physicians are not.

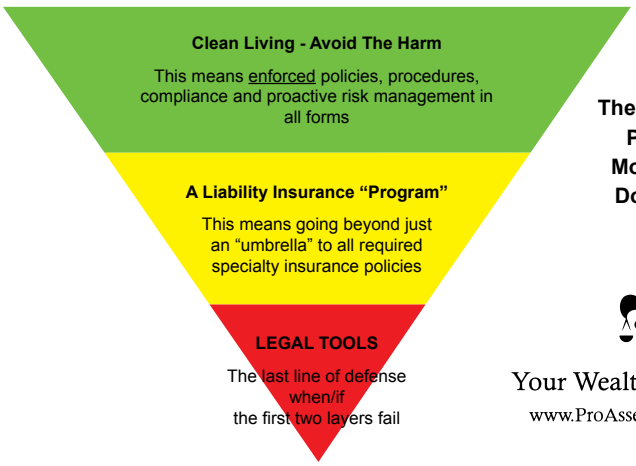
• **Insurance, all the right kinds and in the right amount.** Insurance needs to be thought of as an **"insurance program"**, not a line item and works as a system of overlapping coverage. Most physicians have an overly simplified vision of what they should have in place, mainly some form of professional liability insurance typically a "1-3" policy meaning $1MM per occurrence and $3MM aggregate. As an attorney I advise physicians to buy, "Every dollar you can afford, then have a back-up plan."

This goes far beyond your professional liability or malpractice insurance and includes half a dozen or more varieties of specialty insurance that can be well covered with the help of a top-notch property and casualty (P&C) insurance agent. **A word of caution, having an asset protection plan consisting of defensive legal tools in place without the complimentary insurance, commonly known as "going bare" is never the best idea and if nothing else, subjects you the exposure of massive legal fees for defense costs which are easily six figures.**

• **Defensive legal structures.** There will inevitably be gaps in the number of things that can be covered or the dollar limit to which you can insure yourself. Do not ever rely on your "umbrella" policy as effective universal coverage. This is where all the trusts, LLCs, partnerships, corporate structures and estate-planning techniques that we lawyers are so fond of come into play. You must have good policies and procedures, insurance against instances those fail and have a legal back up plan if the first two layers fail.

Remember that asset protection is fact specific and use your facts. Every doctor seeking asset protection must have a thorough review of her own assets, have her personal and professional risks identified and have tools and solutions implemented by a qualified and experienced professional. **In other words, the familiar pattern of exam, diagnosis and then personalized treatment.** There may be a reasonable and proven course of treatment for any particular problem, but your advisors should always know what the problems are **before** they start proposing specific solutions.

Below is my "Asset Protection Pyramid", as explained above, the first and largest layer of defense is behavioral and risk management related, the second layer is an insurance program that covers as many risks as possible and the last line of defense is comprised of well proven defensive legal structures that attorneys like myself add to the picture and ideally help you implement along with the first two layers. "Just" providing either legal services or selling insurance or consulting on a compliance program on their own are ineffective and in some cases may be malpractice. Make sure your planner is informed about all these areas and makes them part of your comprehensive plan. If all they talk about is the specific trust, insurance, or service they sell, get better help. It is the strength and redundancy of all three of these layers that creates an effective wealth preservation plan and you must have all three to have effective and predictable results.



The Asset Protection Pyramid - What Most Lawyers Still Don't Understand

Your Wealth, Made *Safer*
www.ProAssetProtection.com

What Does Asset Protection Achieve?

- Reduces the economic incentive to sue, or aggressively pursue you beyond insurance
- Creates an incentive to settle within limits of applicable liability coverage if there is real liability – HELPS MAKE YOUR INSURANCE WORK
- Legally separates personal and business assets and liability as they should be
- Protects you from the internally generated liability of certain assets, like real estate
- Adds additional surety and control to assets that will be distributed at your death by your estate plan

SECTION TWO: SPECIFIC RISKS

Acknowledging Medical Malpractice Risk: It is Real, and Common:

A common mistake by doctors is failing to think beyond the obvious (and very real) threat of medical malpractice risk. As significant as this risk is for every doctor in America, it's not the only, or even the most predictable and recurring exposure you face. The 2017 Medscape Malpractice Report, surveyed 4,000 doctors across the country in different specialties and is a close reflection of what we've seen from many other sources for years. **Fifty-five percent** of physicians surveyed had been named in a malpractice lawsuit and nearly **half of those who had been sued said other physicians were also named in the same lawsuit.** Nearly **half of all those sued** also said they've **been named in between two to five malpractice suits** each and nearly 60% said they were surprised by the lawsuit.

Who Gets Sued?

The following ten specialties had the highest number of malpractice lawsuits:

- Surgery – 85%
- OB-GYN and women's health — 85%
- Otolaryngology — 78%
- Urology — 77%
- Orthopedics — 76%
- Plastic surgery/aesthetic medicine — 73%
- Radiology — 70%
- Emergency medicine — 65%
- Gastroenterology — 62%
- Anesthesiology — 61%

Why Are They Sued?

The top five reasons physicians were sued for malpractice are:

- Failure to diagnose/delayed diagnosis — 31 percent
- Complications from treatment/surgery — 27 percent
- Poor outcome/disease progression — 24 percent
- Failure to treat/delayed treatment — 17 percent
- Wrongful death — 16 percent

Non-Medical Business Risks

Directors and Officer's (D&O) Liability

The scope of the liability for doctors is wider than most realize. You have all of the conventional medical practice related issues such as HIPAA compliance, Medicare and Medicaid billing regulations, and of course the policies and procedures related to care delivery itself. Add to that responsibility for issues ranging from waste disposal and employment policies to accounting and tax reporting and you begin to see the tip of the iceberg we are trying to avoid and protect you against.

Practice owners, managers and employed physicians all potentially face this risk regardless of their actual title. We most commonly see executive titles like president, vice-president, CMO, director, but many practice owners are the defacto CEO,

compliance director etc. and bear **personal liability for acts or omissions** that injure a patient, employee, the healthcare organization and itself and its other members and of course your partners. **Doctors in group practice routinely sue each other and the groups' board over various issues.**

D&O Liability Also Exists Outside Your Practice

This exposure applies not just to medical practices and related businesses like labs and medical supply, research and medical device and technology companies but also to a variety of **other businesses that seek to include doctors on their boards** and executive management teams for their knowledge, prestige and connections. Realize this liability extends beyond the business world into service on private foundations, **hospital boards,** charitable boards, and even boards of religious institutions.

Two Main D&O Liability Defense Strategies

D&O Insurance

- This risk is not adequately covered by your personal umbrella policy, general business liability insurance or medical malpractice insurance
- The policy should be wide in scope and have high limits, ideally seven figures.
- Ideally this is a stand-alone policy with separate limits, not just a rider on an existing policy that shares limits
- It should also cover intracompany disputes

Indemnity Agreements from Organizations You Serve

This should be a written agreement, that is negotiated in advance as a condition of your board membership, executive service and etc. **This agreement should ideally address at least three key issues:**

- Limit or waive your **internal liability** for your official acts, with reasonable exceptions for fraud and intentional acts that violate your fiduciary duties
- Require the **organization to bear the costs of your defense** for any claims arising from said service
- **Require the organization to insure you** as described above

Employee Related Liability

- Most common and likely exposure
- You are 5 times more likely to be sued by an employee than for any other reason
- **Average sexual harassment verdict is $530K #metoo**
- EEOC website brags of 100's of millions of dollars collected EACH YEAR from people like you
- Suing more often winning more often, winning more money
- Many cases come down to a popularity contest
- Is there really such a thing as a jury of **your** peers?

The stakes here are high on two fronts; first, the awards themselves can be financially devastating, with sexual harassment verdicts, as one example, regularly reaching hundreds of thousands of dollars. **Second**, the **costs of legal defense** alone can drive a medical practice out of business, easily reaching six figures in short time — without including the potential dollar value of any award that may be obtained against the physician.

The risk is growing
According to a recent EEOC press release the agency collected nearly $400 million in fines in 2013 alone — the largest collections year in the history of the EEOC — and receives close to 100,000 complaints a year.

The most common causes of these complaints, in order, are; **retaliation** under all the statutes (about 40 percent); followed by **race discrimination** (about 33 percent); **sex discrimination**, including sexual harassment and pregnancy discrimination (roughly 27 percent); and discrimination based on **disability** (about 25 percent). Both race and disability discrimination claims increased as a percentage of all charges.

You MUST Have EPLI insurance

EPLI *(employment practices liability insurance)* is another indispensable and overlooked line of defense for every employer. It covers a variety of employment related risks to you and your practice as an employer and can cover both defense costs and damages. Again, use an expert and **get high limits, a low limit rider added to your medical malpractice policy that shares limits is not enough.** Get seven figures in coverage.

Have a professionally drafted employment manual

We consistently find that medical practices have one of the three following bad scenarios at play with their employment policies and manuals, which should be custom drafted, state specific, formal, written, distributed to all employees and enforced:

We have NO formal manuals.
We have generic manuals of speculative value that are not specific to our business and how it operates (i.e., we got it free off the Internet or from a buddy in another state.)
We have a custom manual but have NOT implemented it, distributed it to our staff in a formal way, or consistently enforced it.

Data Breach and Cyber Liability Exposure

- Penalties more onerous and expensive than ever and carry heavy statutory penalties and fines
- You are responsible for both healthcare (HIPAA) and financial info like SS#'s and credit card info
- Hacking is an international business, they target people who have the most/best info
- Offices are more "connected" than ever, the liability extends to every tablet, smartphone, laptop and even your equipment like faxes, printers, scanners and etc.
- Beware of equipment disposal issues and practices

RAC AUDITS – MEDICARE / MEDICAID AND OTHER THIRD-PARTY PAYORS WANT THEIR MONEY BACK FROM YOU

- The govt. collected more than $1 Billion in refunds from doctors last year
- Auditors are paid on contingency of up to 12.5% of what they take back from you
- An audit could wipe out a small practice with audit and defense costs and the LABOR that may be called for
- They can request up to 400 files every 45 days
- This does not even mention the INCOME DISRUPTION
- This is a revenue retention exercise meant to fight fraud, but often "runs over" compliant practices

Drug Based Treatment Liability

Medical specialties that use drug-based treatments administered by the physician's office as a routine part of their treatment regimes face some additional risks as well. This usage presents several expanding liability issues that require serious proactive risk management.

Using specialty-compounded drugs is increasingly common, one recent report says they **account for a full 6 percent of medical-error claims,** and so are the associated risks for medical practices. A recent case that made national headlines involved the unknowing use of infected epidural steroid compounds by pain management practices across the country. Over 200 patients across more than twelve states came suffered meningitis infection and a variety of other serious ailments with nearly 50 causalities.

Drug-injury lawsuit websites makes it clear that the administering doctor is part of the lawsuit chain in such circumstances. One website reads, in part, **"The doctors who prescribed (or administered) the drug that injured you may also be liable for your injuries because they are part of the chain of distribution of the drug."** Having and enforcing a drug-quality policy regardless of whether you work in pain management, cardiology, or any other specialty is vital. Regardless of actual fault or causation lawsuits always seek deep, easy pockets like yours for redress.

Steps to Protect Your Patients and Practice

Remember that many insurance programs you bill for treatment, including the use of drugs, require that all pharmaceuticals are sourced from licensed U.S. providers. If you use and bill for tainted drugs that do not meet these conditions you have both the risk of injury to the patient and the potential to face a Medicare fraud claim, another exceptionally onerous issue that will have to be litigated and defended separately if you think you can prove you were an "innocent purchaser".

REAL ESTATE: Managing Premises Liability Risk

One common issue we see surprise medical professionals is the liability they face as the owners or operators of a physical facility that is open to the public. This issue extends beyond your office to your home and other investment real estate as well and is more common than you think.

How Great is The Risk?

Slip and fall accidents requiring medical treatment, as just one example of a premises liability, happen half a million times a year and account for some 1500 emergency visits a day. Such accidents are the leading cause of work related injuries and even deaths, causing an estimated 25,000 deaths a year and follow only auto accidents as the leading accidental cause of death in the U.S. Judgments for such injuries can be financially devastating and range from relatively small amounts to millions of dollars for death and permanent or disfiguring injuries.

Whose Injuries Are You Responsible For?

Pretty much everyone's, but to differing degrees and standards of care. Loosely paraphrased, if you created, knew or should have known of dangerous conditions and allowed them continue or failed to provide warnings, you may be on the hook.

The law breaks the "duty of care" for property owners and operators down as follows, from highest to lowest liability:

- **Invitees** are generally defined as those on the property by express or implied invitation for a business purpose.
- **Licensees or guests** are persons on the property at the express or implied invitation for a social purpose. A higher degree of care is typically due to a child guest.
- **Trespassers** are defined as persons on the property without actual or implied permission. A higher degree of care may be owed to trespassing children under the attractive nuisance doctrine.

Risk Management Issues To Address Today

Being proactive about **maintenance and safety issues** is vital, especially during months where water and ice pose additional and often unseen risks that arise over the course of a single day or less or cause even durable property like stairs, railings and sidewalks and parking lots to deteriorate. A good maintenance program including **a record of what was done and when it was inspected** is a good start and will help prove-up the fact that you make serious efforts to inspect and maintain the property for any safety related conditions. **Both owners and tenants share this risk, so don't assume that you are off the hook if you lease a property, especially if the condition is in an area you limit access to or control completely.** Likewise if you are property owner that leases to others, don't assume dangers the tenant creates will not flow up to you.

The first level of defense is as always a good liability insurance policy with limits that are adequate to cover the true scope of the liability as outlined above. I instruct my clients that **$1 Million is the bare minimum** in bodily injury a commercial insurance policy should cover and should ideally be higher and backed up by a higher limit umbrella policy.

Some Specific Examples: Are there dangerous conditions in your office or have you allowed patients or employees to create them?

- Tree branch falls on expensive, collector car in Doctor's parking lot on windy day. Doctor sued for diminution in value of auto due to the improper maintenance of landscaping on her property;
- Employee of medical practice moves warning signs and a bucket covering a hole in the floor that a contractor was working on then the same day, steps in hole, injures foot and sues her employer;
- We've seen a variety of lawsuits where very heavy people have also been injured by falling when a chair, bench or

toilet broke under their weight. These lawsuits sometimes even include an emotional distress claim;
- Large flat screen TV installed in waiting area of high-end dentist office was accidentally pulled over by children toddler, falling on top of a toddler and injuring him severely.
- Elderly medial office patient was injured by the expensive bicycles of two patients who asked the front desk for permission to bring them inside because of fears that they'd be stolen. The senior citizen tripped over the bikes upon entering and injured his knee and had his cheek pierced by a section of the bike's brake cable that barely missed his eye;
- Inattentive mother leaving doctor's office lets child run out from between parked cars and is child injured by vehicle driven by another patient. Doctor sued for contributory negligence in not having enough warnings and speed bumps in his very small parking lot;

As you can see from these examples, wherever possible liability is going to be attributed to the practice that is often seen as a more exciting "deep pocket" corporation than just another patient. It makes more financial sense to the lawyers (as one real example) to sue a doctor's office for not having enough signs and speed bumps in their parking lot than it does to sue the retired widow on a fixed income who hit a child in the parking lot.

Someone in the practice should be responsible for a variety of issues like cleaning crew schedules, waiting room construction and furniture selection, public access to electricity or electronics with electrocution risks, including medical devices that can cause harm, access to dangerous materials including biohazards, drugs and chemicals like cleaning products that may be stored in a bathroom cabinet (restaurants are famous for this unsafe practice) or other publicly accessible space as just a few specific examples. Considering outsourcing this, at least for an initial review of issues to correct or watch for. Professional safety inspectors can be hired to walk your facility from the parking lot to the exam room and look for potential issues. I've also suggested clients walk through the entire facility as if they are childproofing it (another common issue) while making sure they wouldn't limit access by a handicapped person. Issues we overlook and think of as simple can get complicated relatively quickly.

ADA Compliance Liability – Is your facility "Accessible"?

Properly addressing this issue covers basics like having the legally required handicapped-accessible parking and restrooms all the way through specific legal requirements for the construction of public spaces like entrances, thresholds, pathways, elevators, counters, even your practice signage. Lawsuits on this issue have hit businesses across the United States and can be generated by people who are not even your patients when a scout spots a condition that is not ADA complaint as the basis for a lawsuit. Specialists in ADA compliance are available in nearly every jurisdiction to inspect your facility and provide list of violations and the required corrective actions. What "fully abled" people take for granted surprises even physicians and there's a significant ROI from a risk management perspective as the relatively small costs of a compliance review are always less than the cost of responding to an ADA complaint or lawsuit. This is especially true given that fact that some states provided ADA plaintiffs punitive damages, attorney's fees and fines and on top of that your practice will still have to make the changes legally required.

A Word About Equipment Disposal Liability

Medical practices replacing obsolete computer and electronic equipment must safely and securely dispose of a variety of devices including:

- Networked printers, faxes, scanners, etc.
- Computer servers and arrays
- Devices that combines hardware and software for a specific function, medical or administrative
- Networking equipment
- Electronic data storage devices and backups
- Desktop and laptop computers, tablets and smartphones that have been used to access or relay protected data

Computers themselves were listed last and pose only the most obvious threat to the financial and HIPAA-protected information that every medical office in the United States stores and is legally responsible for. The partial list of other devices that store and transfer this data illustrates the true size of the exposure that practices must deal with. Just one example of just how

onerous the a liability the equipment itself can be is that a printer can have thousands of patient's PPI and treatment data stored in its memory.

You Can't Just Throw Them Away or Donate Them

You may donate and perhaps take a tax deduction for certain peripherals after determining if they pose a storage risk or not, (things like mice, keyboards, and monitors are the most basic examples), but the computers themselves and most other devices that transfer, copy, or store data present a serious exposure to your business. Your responsibility does not end when it goes out the door.

Automobile Accident Exposure

- Automobile accidents are a real, common and significant source of liability. By some figures there roughly **11 million automobile accidents** in the U.S. every year that cause **40,000 fatalities** and many serious and permanent injuries.
- I routinely get calls from people looking for protection from an accident they, their spouse, children or some other individual has been involved in while driving their vehicle.
- Because of their pre-existing liability I usually have to turn them away or exclude the event they called for help with, acting after the accident is FRAUD and no educated planner should do any planning without
- Fatalities routinely generate seven-figure judgements and as physicians you likely know the costs associated with extended medical care, rehab and etc.
- **Worse, MANY clients come to me with their car and their spouse's vehicle leased or titled in the name of their business or the corporate entity that owns it;**
- In most cases, this has been done at the suggestion of the CPA, who has correctly told the Doctor that this is a great way to get a tax deduction;
- Unfortunately, if you, your spouse, child, nanny or anyone who has your keys gets into an accident **you have jeopardized the source of your income by making your practice the vehicle's owner and a defendant in the suit.**

Which of the following would you be most excited about suing if you were a personal injury attorney?

a. John Smith
b. Dr. Smith
c. **Smith and Associates Medical Specialists Inc.**

This one of several areas where a **personal liability umbrella policy** is vital. You should have a minimum of $1 Million in umbrella coverage on your home and automobile and that coverage should ideally include **"UIM and UM"** which stands for underinsured and uninsured driver protection for you in case the person who hits you is underinsured or uninsured. It's also vital that you don't rely on your umbrella as a one-step asset protection, it isn't. It covers some very specific risks, mainly issues related to your **home and autos only** and typically will not help you with any unrelated professional risks.

Protect Yourself Against Divorce Risk, Two Major Defenses:

1. Get a prenup;
2. Keep your pre-marital property separate
    - Doctors of BOTH sexes don't get pre-nups because they fall victim to emotional blackmail. "If you really loved me you wouldn't ever ask me to sign it". THIS IS A LIE.
    - The odds of a **second marriage** ending in divorce are over 65 percent and climb to 75 percent in a third marriage.
    - Moreover, you will have less time to earn, save, and rebuild wealth than you did the first time around in a substantially more demanding medical business climate.
    - I routinely talk to doctors who have had years of high income and who amassed significant wealth but didn't investigate protecting it until they had already lost half or more of their hard-earned net worth to a divorce. When I ask if they had a pre-nup the response is nearly always the same, in fact alarmingly identical, "We didn't have anything when we got married, we ended up successful and never thought it would happen to us…"

Parental Liability

Because physicians are attractive litigation targets for many issues (due to their perceived wealth) they must understand that their liability concerns and defensive planning need to go substantially beyond their medical practice. Parents are generally responsible for the intentional and negligent acts of their children through the age of 18, although a few states extend that liability even further through "age of majority" laws that extend parental liability beyond age 18.

In some cases, this liability may be *civil*, where the risk is financial (and which should also be considered in your "asset protection risk factor" analysis). One common example I've faced with many clients who are parents is being sued for an accident caused by a teen driver that involved extensive property damage, death, or serious injuries to others.

In other cases, the liability may also be *criminal*, for both affirmative actions on your part including those that contributed to the delinquency of a minor and in other cases for your negligence, failure to act, or failure to properly supervise.

Just a few of the many examples of <u>common</u> parental liability include:

- Access to firearms and acts of violence including school shootings
- Auto accidents and misuse of boats, ATVs etc.
- Cyber and In-person bullying, harassment and assaults
- Abuse, possession and/or distribution of controlled substances, including what's in your home bar and medicine cabinet
- Vandalism and destruction of property
- Sexual crimes including sexting, alleged statutory rape (two sixteen-year-olds dating)

EXIT RISK

Watch Your Tail (Coverage). The first and most obvious example of this failure is not being adequately insured for traditional malpractice, E&O or D&O coverage (as appropriate) *after you sell or retire.*

This takes the form of "tail" insurance at or above the same level of coverage they carried while running the business. This is important for several reasons; the obvious one is the liability of a claim itself, the second is that the damage the claim can do to you and how aggressively it will be pursued is actually magnified when you are no longer in business. The costs of defense alone can put many sellers at a disadvantage or back them into a corner where they have to settle a claim they shouldn't have.

Cash-rich sellers are more vulnerable to any litigation or liability than ever before because:

- They are *more liquid* than ever before
- They have replaced a *recurring income stream* with a *single lump sum* that has to last them "forever"
- The fact that they sold their business and, in many cases, the dollar amount they received are usually a poorly kept secret. **This often motivates "latent plaintiffs" including disgruntled employees and current and even former partners**
- Most fail to contractually assign any **payment stream** *to a protected entity*, so that it is protected from their personal and professional liability

Business owners must remember that in many cases they will no longer have the income stream they previously did from their business to offset any claim-related losses and that they are a much better target (more collectible) than ever before. Why? **Because even people with high incomes have usually not received a lump sum of cash as large as what they get from the sale of a business.**

I also warn every client who is selling a business that asset protection planning is vital at the time of sale to protect the proceeds <u>from the buyers themselves</u>.

I remind clients that if the buyer is not as successful at running the business as the seller was, for any reason (including their own lack of bedside manner, industry knowledge or business and management skills), they and their lawyers will inevitably point to <u>some alleged act or omission on the seller's part</u>, and will want to give the seller back the broken pieces

of their business and get a refund. In many cases they want this refund only after they have destroyed the businesses' credit, inventory, reputation and relationships that in most cases took decades to develop. **Not ok.**

Making sure that the proceeds of sale are well protected from such an exposure with insurance, the right legal structures and the right contractual protections that limit their claims and remedies on the front end is vital to ensure your continued solvency and success.

SELF EVALUATION

Holistic Asset Protection: Identifying and Protecting Against Practice Risks

1. T/F - I may personally have (non-medical malpractice) liability as an owner or executive of a medical practice, even if I have an LLC, Corporation, Etc.

2. T/F - I am not liable for the acts and injures of other people's children at my home if I didn't give them permission to be there.

3. Which of the following could you be liable for?

a. Injury to patient in parking lot
b. Actions of another practice partner towards an employee
c. Representations you have made to investors in a surgical center
d. A partner's unrelated business debts
e. A,B and C only

4. T/F - You can't be held liable for the actions of your adult children

5. You only have liability for which of the following:

a. Hacking and exposure of PII and HIPAA materials by a third party
b. Injuries to employees from workplace violence if predictable in course of duties
c. Injuries to employees from random acts of violence by 3rd parties
d. Hacking and exposure of PII and HIPAA materials by employees
e. All of the above

6. Having your car leased or titled in your business:

a. Can be a legitimate way to get a tax deduction
b. Protects you and your family from liability
c. Puts liability for your personal accidents inside your business
d. A and C only

7. T/F - Once you retire or sell your business you can lower or just drop your professional liability insurance.

8. T/F - Having your liquid investment accounts and home in your revocable trust combined with your medical malpractice insurance is "good enough" protection for most doctors.

Answer Key: 1. T, 2. F, 3. E, 4. F, 5. E, 6. D, 7. F, 8. F

[i] Becker's Hospital Review, More than 50% of physicians have been sued for malpractice, study finds https://www.beckershospitalreview.com/hospital-physician-relationships/more-than-50-of-physicians-have-been-sued-for-malpractice-study-finds.html

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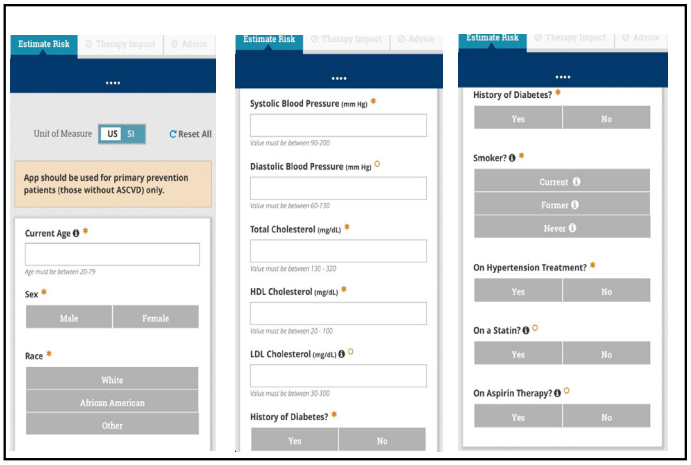
Impacting Cardiovascular Disease through Improved Lipids Management

Updated ASCVD Plus 10 Year Risk Calculator

(Suggested App intended for primary prevention without ASCVD and an LDL <190 mg/dl)
http://static.heart.org/riskcalc/app/index.html#!/baseline-risk

- **Gender: Male/Female**
- **Age (40-79 years)**
- **Race: White/African American/Other**
- **Total Cholesterol (130-320 mg/dl)**
- **LDL Cholesterol (30-300 mg/dl)**
- **HDL Cholesterol (20-100 mg/dl)**
- **Treatment With Statin: Y/N (New)**
- **Systolic Blood Pressure (90-200 mmHg)**
- **Treatment For Hypertension: Y/N**
- **History Of Diabetes: Y/N**
- **Current Smoker: Y/N**
- **Aspirin Therapy: Y/N (New)**

Calculate Baseline Risk



ACC/AHA 4 Statin Benefit Groups

http://dx.doi.org/10.1016/j.jacc.2017.07.745

TABLE 2 Four Statin Benefit Groups and Major Recommendations From the 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults (9)

Patient Group	Major Recommendations
1. Adults aged ≥21 years with clinical ASCVD (including history of or current ACS, MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or PAD presumed to be of atherosclerotic origin)	1. For patients age ≤75 years, high-intensity statin (or moderate-intensity statin if not a candidate for high-intensity statin due to safety concerns) 2. For patients age >75 years, moderate-intensity statin
2. Adults aged ≥21 years with LDL-C ≥190 mg/dL (not due to modifiable secondary causes)	1. High-intensity statin therapy to achieve ≥50% reduction in LDL-C statin (or moderate-intensity statin if not a candidate for high-intensity statin due to safety concerns) 2. May consider combining statin and non-statin therapy to further reduce LDL-C 3. Cascade screening of close biological relatives should be performed to identify others with the disease who would benefit from treatment.
3. Adults aged 40-75 years without ASCVD but with diabetes and with LDL-C 70-189 mg/dL	1. Moderate-intensity statin 2. If 10-year ASCVD risk ≥7.5%, consider high-intensity statin.
4. Adults aged 40-75 years without ASCVD or diabetes, and with LDL-C 70-189 mg/dL and an estimated 10-year risk for ASCVD of ≥7.5%	1. Estimate 10-year ASCVD risk using Pooled Cohort Equations (10): a. If ≥7.5%, moderate- or high-intensity statin; b. If ≥5 to <7.5%, consider moderate-intensity statin. 2. In selected individuals with 10-year ASCVD risk <5%, or age <40 or >75 years, individualize decisions based on presence of other high-risk features.* 3. Before initiation of statin therapy for primary prevention, it is reasonable for clinicians and patients to engage in a discussion that considers the potential for ASCVD risk-reduction benefits and for adverse effects and drug-drug interactions, as well as patient preferences for treatment.

LDL-C and Atherosclerotic CV Disease: Cause or Surrogate Marker?

- Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A **consensus statement from the European Atherosclerosis Society Consensus Panel. 4/25/2017**
- **Conclusion: "Consistent evidence from numerous and multiple different types of clinical and genetic studies unequivocally establishes that LDL causes ASCVD."**
- **LDL-C should no longer be considered a surrogate marker for ASCVD.**
  - European Heart Journal (2017) 0, 1–14 doi:10.1093/eurheartj/ehx144

Low-density lipoprotein (LDL) as a causal factor for atherosclerotic cardiovascular disease: key implications

- **Cumulative LDL arterial burden is a central determinant for the initiation and progression of atherosclerotic cardiovascular disease.**
- **The lower the LDL cholesterol (LDL-C) level attained by agents that primarily target LDL receptors, the greater the clinical benefit accrued.**
- **Both proportional (relative) risk reduction and absolute risk reduction relate to the magnitude of LDL-C reduction.**
- **Lowering LDL-C in individuals at high cardiovascular risk earlier rather than later appears advisable, especially in those with familial hypercholesterolaemia.**
  - European Heart Journal (2017) 0, 1–14 doi:10.1093/eurheartj/ehx144

AACE 2017 Guidelines

Table 6
Atherosclerotic Cardiovascular Disease Risk Categories and LDL-C Treatment Goals

Risk category	Risk factors[a]/10-year risk[b]	Treatment goals		
		LDL-C (mg/dL)	Non-HDL-C (mg/dL)	Apo B (mg/dL)
Extreme risk	– Progressive ASCVD including unstable angina in patients after achieving an LDL-C <70 mg/dL – Established clinical cardiovascular disease in patients with DM, CKD 3/4, or HeFH – History of premature ASCVD (<55 male, <65 female)	<55	<80	<70
Very high risk	– Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease, 10-year risk >20% – Diabetes or CKD 3/4 with 1 or more risk factor(s) – HeFH	<70	<100	<80
High risk	– ≥2 risk factors and 10-year risk 10-20% – Diabetes or CKD 3/4 with no other risk factors	<100	<130	<90
Moderate risk	≤2 risk factors and 10-year risk <10%	<100	<130	<90
Low risk	0 risk factors	<130	<160	NR

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AMERICAN COLLEGE OF ENDOCRINOLOGY ENDOCRINE PRACTICE Vol 23 (Suppl 2) April 2017

LDL-C How Low Should We Go?

- Using the **Cholesterol Treatment Trialists Collaboration** (CTTC) **data, there is a consistent relative risk reduction in major vascular events (a composite of coronary heart death, myocardial infarction, ischemic stroke, or coronary revascularization) per change in LDL-C in patient populations starting as low as a median of 63mg/dL and achieving levels as low as a median of 21mg/dL**, with **no observed offsetting adverse effects.** These data suggest further lowering of LDL-C beyond the lowest current targets would further reduce cardiovascular risk.
  - JAMA Cardiol. doi:10.1001/jamacardio.2018.2258

LDL-C How Low Should We Go?

- **In this meta-analysis, for statins and nonstatins, the risk of major vascular events was significantly reduced by 21% for each 1-mmol/L (38.7-mg/dL) reduction in LDL-C**, which was virtually the same magnitude as seen in the overall Cholesterol Treatment Trialists Collaboration analysis in which the starting LDL-C was nearly twice as high.
  - JAMA Cardiol. doi:10.1001/jamacardio.2018.2258

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA / AGS/APhA/ASPC/NLA/PCNA

Guideline on the Management of Blood Cholesterol: Executive Summary

The full-text guidelines are also available on the following Web sites: ACC (www.acc.org) and AHA (professional.heart.org)

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Top 10 Take Home Messages

1. **In all individuals, emphasize a heart-healthy lifestyle across the life course**.

   A healthy lifestyle reduces atherosclerotic cardiovascular disease (ASCVD) risk at all ages. In younger individuals, healthy lifestyle can reduce development of risk factors and is the foundation of ASCVD risk reduction.

   In young adults 20 to 39 years of age, an assessment of lifetime risk facilitates the clinician–patient risk discussion (see No. 6) and emphasizes intensive lifestyle efforts. In all age groups, lifestyle therapy is the primary intervention for metabolic syndrome.

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Top 10 Take Home Messages

2. **In patients with clinical ASCVD, reduce low-density lipoprotein cholesterol (LDL-C) with high-intensity statin therapy or maximally tolerated statin therapy.**

   The more LDL-C is reduced on statin therapy, the greater will be subsequent risk reduction.

   Use a **maximally tolerated statin to lower LDL-C levels by ≥50%.**

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Top 10 Take Home Messages

3. **In very high-risk ASCVD, use a LDL-C threshold of 70 mg/dL (1.8 mmol/L) to consider addition of nonstatins to statin therapy.**
   - Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions.
   - In very high-risk ASCVD patients, it **is reasonable to add ezetimibe to maximally tolerated statin therapy when the LDL-C level remains ≥70 mg/dL** (≥1.8 mmol/L). **(NNT at 7 years 50 IMPROVE-IT Trial)**
   - **In patients at very high risk whose LDL-C level remains ≥70 mg/dL** (≥1.8 mmol/L) **on maximally tolerated statin and ezetimibe therapy, adding a PCSK9 inhibitor is reasonable, (NNT 30 at 2.8 years LDL >/=100 mg/dl Odyssey Outcomes Trial, NNT 50 at 3 years Fourier Trial)** although the long-term safety (>3 years) is uncertain

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Top 10 Take Home Messages

4. In patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL[≥4.9 mmol/L]) without calculating 10-year ASCVD risk, begin high-intensity statin therapy without calculating 10-year ASCVD risk.

•If the LDL-C level remains ≥100 mg/dL (≥2.6 mmol/L), adding ezetimibe is reasonable

• If the LDL-C level on statin plus ezetimibe remains ≥100 mg/dL (≥2.6 mmol/L) & the patient has multiple factors that increase subsequent risk of ASCVD events, **a PCSK9 inhibitor may be considered**, although the long-term safety (>3 years) is uncertain and economic value is low at mid-2018 list prices.

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Top 10 Take Home Messages

5. In patients 40 to 75 years of age with diabetes mellitus and LDL-C ≥70 mg/dL (≥1.8 mmol/L), start moderate-intensity statin therapy without calculating 10-year ASCVD risk.

In patients with diabetes mellitus at higher risk, especially those with multiple risk factors or those 50 to 75 years of age, it is **reasonable to use a high-intensity statin to reduce the LDL-C level by ≥50%.**

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Top 10 Take Home Messages

6. In adults 40 to 75 years of age evaluated for primary ASCVD prevention, have a clinician–patient risk discussion before starting statin therapy.

Risk discussion should include a review of major risk factors (e.g., cigarette smoking, elevated blood pressure, (LDL-C), hemoglobin A1C [if indicated], and calculated 10-year risk of ASCVD);

- the presence of risk-enhancing factors (see No. 8);
- the potential benefits of lifestyle and statin therapies;
- the potential for adverse effects and drug–drug interactions;
- the consideration of costs of statin therapy; and
- the patient preferences & values in shared decision-making.

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Top 10 Take Home Messages

7. In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL (≥1.8 mmol/L), at a 10-year ASCVD risk of ≥7.5%, start a moderate-intensity statin if a discussion of treatment options favors statin therapy.

Risk-enhancing factors favor statin therapy (see No. 8).

If risk status is uncertain, consider using coronary artery calcium (CAC) to improve specificity (see No. 9). **If statins are indicated, reduce LDL-C levels by ≥30%, and if 10-year risk is ≥20%, reduce LDL-C levels by ≥50%.**

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Top 10 Take Home Messages

8. In adults 40 to 75 years of age without diabetes mellitus and 10-year risk of 7.5% to 19.9% (intermediate risk), risk-enhancing factors favor initiation of statin therapy (see No. 7).

Risk-enhancing factors include
- family history of premature ASCVD;
- persistently elevated LDL-C levels ≥160 mg/dL (≥4.1 mmol/L);
- metabolic syndrome;
- chronic kidney disease;
- history of preeclampsia or premature menopause (age <40 yrs)
- chronic inflammatory disorders (e.g., rheumatoid arthritis, psoriasis, or chronic HIV);
- high-risk ethnic groups (e.g., South Asian);
- persistent elevations of triglycerides ≥ 175 mg/dL (≥1.97 mmol/L);

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Top 10 Take Home Messages

9. In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL- 189 mg/dL (≥1.8-4.9 mmol/L), at a 10-year ASCVD risk of ≥7.5% to 19.9%, if a decision about statin therapy is uncertain, consider measuring CAC.

• If CAC is zero, treatment with statin therapy may be withheld or delayed, except in cigarette smokers, those with diabetes mellitus, and those with a strong family history of premature ASCVD.
• A CAC score of 1 to 99 favors statin therapy, especially in those ≥55 years of age.
• For any patient, if the CAC score is ≥100 Agatston units or ≥75th percentile, statin therapy is indicated unless otherwise deferred by the outcome of clinician–patient risk discussion.

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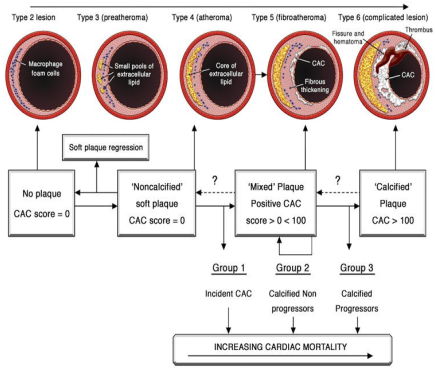
Coronary Calcium Scoring by CT

Arterioscler Thromb Vasc Biol. 2014 Jun; 34(6): 1144–1154



Top 10 Take Home Messages

10. Assess adherence and percentage response to LDL-C–lowering medications and lifestyle changes with repeat lipid measurement 4 to 12 weeks after statin initiation or dose adjustment, repeated every 3 to 12 months as needed.

- Define responses to lifestyle and statin therapy by percentage reductions in LDL-C levels compared with baseline.
- **In ASCVD patients at very high-risk, triggers for adding nonstatin drug therapy are defined by threshold LDL-C levels ≥70 mg/dL** (≥1.8 mmol/L) **on maximal statin therapy** (see No. 3).

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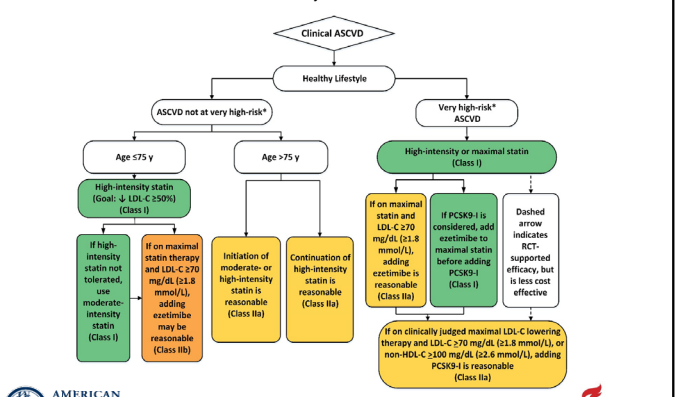
Secondary Prevention



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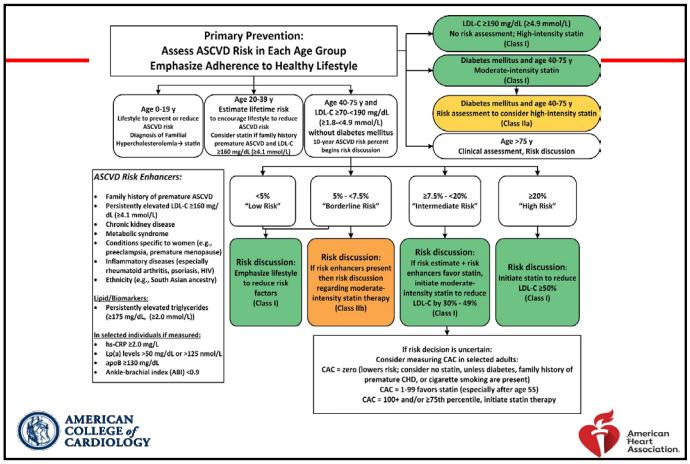

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Table 1. Differences Among 2013 and 2018 ACC/AHA Cholesterol Guidelines.

	2013 Cholesterol Guidelines	2018 Cholesterol Guidelines
Use of LDL-C thresholds	Not supported	Supported
Recommended therapies for LDL-C reduction	Start with guideline-directed statin intensity and increase up to maximally tolerated statin dosing if not achieving expected LDL-C reduction goal (≥50% for high-intensity, 30-50% moderate intensity). Consider adjunctive therapies if not able to achieve percent reduction with maximally tolerated statin alone.	In secondary prevention, maximize lifestyle and statin therapy, and if LDL-C 70 mg/dL or more consider adding ezetimibe and subsequently PCSK9 inhibitors.
Coronary artery calcium scoring	In primary prevention, additional factors may help risk-stratify in those whose risk is uncertain. May consider ***CAC score ≥300 Agatston units or ≥75th percentile*** for age, sex, and ethnicity as evidence of likely to benefit from treatment.	In patients without diabetes and LDL-C 70 mg/dL or above with intermediate risk (ASCVD 7.5-20%); ***CAC score ≥100 Agatston units*** favors treatment with a statin. The absence of CAC indicates that the decision about statin therapy can likely be deferred for at least 5 years.
Other risk enhancing factors for primary prevention treatment candidacy	LDL-C ≥160 mg/dL, hs-CRP ≥2.0 mg/L, ABI <0.9, elevated lifetime ASCVD risk, family history of premature ASCVD.	LDL-C ≥160 mg/dL, apoB ≥130 mg/dL, increased Lp(a), hsCRP ≥ 2.0 mg/L, low ABI (<0.9), metabolic syndrome, chronic kidney disease, chronic inflammatory disorders (e.g. HIV, RA, psoriasis) premature menopause, South Asian ancestry, family history of premature ASCVD.

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Statin management in persons with diabetes age 40-75 with LDL-C 70-189 mg/dL	Use 10-year ASCVD risk calculator to determine if eligible for a clinician patient risk discussion regarding moderate or high intensity statin.	Start moderate intensity statin without need to calculate 10-year ASCVD risk. If multiple risk factors or 50-75 years of age, reasonable to start a high intensity statin.
Heart-healthy lifestyle	Better dietary and exercise habits for all.	Better dietary and exercise habits for all. Assess lifetime risk of ASCVD in young adults and intervene to prevent the metabolic syndrome.
Familial hypercholesterolemia	Patients who have fallen short of treatment goals of 100 mg/dL are not considered "treatment failures," and observational data has shown significant reductions in ASCVD events without achieving specific LDL-C goals.	If LDL-C ≥100 mg/dL in patients with FH, can add ezetimibe and/or PCSK9 inhibitor. Recommend cascade screening of first-degree relatives.

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High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20** *(40)* **mg**	**Atorvastatin 10** *(20)* **mg** **Rosuvastatin** (*5*) **10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40** *(80)* **mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*

Specific statins and doses are noted in bold that were evaluated in RCTs.

Table 11. Statin-Associated Side Effects

Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Statin-associated muscle symptoms (SAMS)			
Myalgias (CK Normal)	Infrequent (1% to 5%) in RCTs; frequent (5% to 10%) in observational studies and clinical setting	Age, female sex, low body mass index, high-risk medications (CYP3A4 inhibitors, OATP1B1 inhibitors), comorbidities (HIV, renal, liver, thyroid, preexisting myopathy), Asian ancestry, excess alcohol, high levels of physical activity, and trauma	RCTs cohorts/observational
Myositis/myopathy (CK > ULN) with concerning symptoms or objective weakness	Rare		RCTs cohorts/observational
Rhabdomyolysis (CK >10 × ULN + renal injury)	Rare		RCTs cohorts/observational
Statin-associated autoimmune myopathy (HMGCR antibodies, incomplete resolution)	Rare		Case reports
New-onset diabetes mellitus	Depends on population; more frequent if diabetes mellitus risk factors are present, such as body mass index ≥30, fasting blood sugar ≥100 mg/dL; metabolic syndrome, or A1c ≥6%.	Diabetes mellitus risk factors/metabolic syndrome High-intensity statin therapy	RCTs/meta-analyses

AMERICAN COLLEGE of CARDIOLOGY

American Heart Association.

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol

- **If mild to moderate muscle symptoms develop during statin therapy:**
  - Discontinue the statin until the symptoms can be evaluated.
  - Evaluate the patient for **other conditions that might increase the risk for muscle symptoms (e.g., hypothyroidism, reduced renal or hepatic function, rheumatologic disorders such as polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, or primary muscle diseases.)**
    - **Additional risk factors: Asian race, F>M, hyperuricemia, alcohol excess, statin dose and drug interactions.**
      - » **Pharmacogenomics 2012;13:579-594**
  - **If muscle symptoms resolve, and if no contraindication exists, give the patient the original or a lower dose of the same statin to establish a causal relationship** between the muscle symptoms and statin therapy.

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol

- If a causal relationship exists, discontinue the original statin.
- **Once muscle symptoms resolve, use a low dose of a different statin.**
- Once a low dose of a statin is tolerated, gradually increase the dose as tolerated.
- If, after 2 months without statin treatment, muscle symptoms or elevated CK levels do not resolve completely, consider other causes of muscle symptoms listed above.
- If persistent muscle symptoms are determined to arise from a condition unrelated to statin therapy, or if the predisposing condition has been treated, resume statin therapy at the original dose.
  - Expert Opinion, Class IIa, Level of evidence B

The Risk of New Onset Type 2 Diabetes with Statins

- **Intensive-dose statin increases risk for diabetes but lowers cardiovascular risk compared to moderate-dose statin (level 1 [likely reliable] evidence)** based on pooled analysis of 5 trials with 32,752 patients without diabetes at baseline assigned to intensive-dose vs. moderate-dose statin with mean follow-up 4.9 years. (JAMA 2011:305:2556)
- **Diabetes developed in 8.4% - comparing intensive-dose statin vs. moderate-dose statin 8.8% vs. 8% odds ratio 1.12** (95% CI 1.04-1.22) **NNH 498 per year**
- **Data from 5 trials in ~137,000 patients found In the first two years of regular statin use, found a significant increase in the risk of new onset diabetes with higher potency statins compared with lower potency agents (rate ratio 1.15,** 95% confidence interval 1.05 to 1.26). **The risk increase seemed to be highest in the first four months of use (rate ratio 1.26, 1.07 to 1.47).** (BMJ 2014;348:g3244 doi: 10.1136/bmj.g3244)
- **CV benefits of statin therapy outweighs the potential risk for diabetes development**

NLA Expert Panel Conclusions

J Clin Lipidol 2014;8:S17-S29

- **Patients at risk for diabetes should be screened with FBS or A1c ideally prior to starting statin therapy, within one year of initiation, and at intervals no longer than 3 years.**
- Statins are associated with an increase in the risk of new on-set type 2 diabetes compared to placebo or usual care and **high intensity statins appear to increase the risk beyond that of moderate intensity statins**
- **Excess risk for diabetes with statin use is most clearly evident in those with major risk factors for type 2 diabetes.**
  - In the JUPITER Trial, the hazard for type 2 diabetes was increased by 28% for those with type 2 diabetes risk factors and by 0% in those without risk factors.
- **CV benefits of statin therapy outweighs the potential risk for diabetes development**

Table 11. Statin-Associated Side Effects

Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Liver			
Transaminase elevation 3 × ULN	Infrequent		RCTs/ cohorts/observational Case reports
Hepatic failure	Rare		
Central nervous system			
Memory/cognition	Rare/unclear		Case reports; no increase in memory/cognition problems in 3 large-scale RCTs
Cancer	No definite association		RCTs/meta-analyses

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Table 11. Statin-Associated Side Effects

Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Other			
Renal function	Unclear/unfounded		
Cataracts	Unclear		
Tendon rupture	Unclear/unfounded		
Hemorrhagic stroke	Unclear		
Interstitial lung disease	Unclear/unfounded		
Low testosterone	Unclear/unfounded		

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American Heart Association.

Primary Prevention Trials

Trial/Drug/Dose	N/Duration	Primary Outcome	RRR/ARR/NNT
WESCOPS Prava 40 mg vs. placebo	6,595 pts Age 45-64 4.9 years	CV death + NF-MI 5.5% 7.9%	31%/2.4%/42
PROSPER Prava 40 mg vs. Placebo	5,804 pts Age 70-82 3.2 years	CV death, NF-MI, CVA 14.1% 16.2%	15%/2.1%/48
ASCOT (LLA) Atorva 10 mg vs. Placebo	10,305 pts Age 40-79 3.3 years	CV death + NF-MI 1.9% 3.0%	36%/1.1%/90
AFCAPS/TexCAPS Lova 20-40 mg vs. Placebo	6605 pts 45-73 M/55-73F 5.2 years	CV death, NF-MI, UA 6.8% 10.9%	37%/4.1%/25
JUPITER (CRP > 2.0) Rosuva 20 mg vs. Placebo	17,802 M>/=55, F>/=65 1.9 years	MI, CVA, UA, Revasc, CV Death 0.77% 1.36%	44%/ 0.59%/84

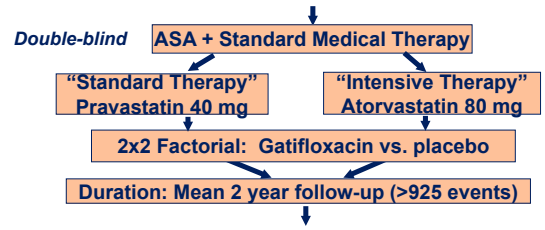
Secondary Prevention Trials

Trial/Drug/Dose	N/Duration	Primary Outcome	RRR/ARR/NNT
4-S Trial Simva 20-40 mg vs. Placebo	4,444 pts (MI/angina) Age 35-69 5.4 years	Total Mortality 8.2% 11.5%	30%/3.3%/31
CARE Trial Prava 40 mg vs. Placebo	4159 pts (s/p MI) Age 21-75 5 years	CV death, NF-MI 10.2% 13.2%	24%/3.0%/33
LIPID Trial Prava 40 mg vs. Placebo	9014 pts (s/p MI) Age 31-75 6.1 years	CV death 6.4% 8.3%	24%/1.9%/53
Heart Protection Simva 40 mg vs. Placebo	20,536 pts (MI,PVD,DM) Age 40-80 5 years	Mort/Vasc events 19.8% 25.2%	24%/5.4%/19
Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Atorva 80 mg vs. Placebo	4731 patients 1-6 months post CVA/TIA and no CHD 60% male, mean age 63 years 4.9 years	Any Nonfatal or Fatal Stroke 11.2% 13.1%	16%/1.9%/53

PROVE IT - TIMI 22: Study Design

N Engl J Med 2004;350:1495-504

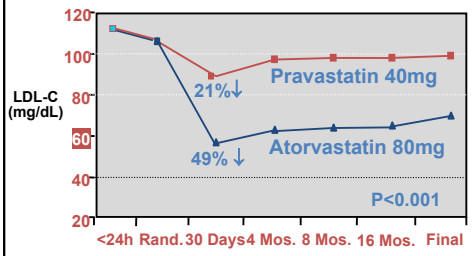
4,162 patients with an Acute Coronary Syndrome < 10 days



Primary Endpoint: Death, MI, Documented UA requiring hospitalization, revascularization (> 30 days after randomization), or Stroke

Changes from (Post-ACS) Baseline in Median LDL-C

N Engl J Med 2004;350:1495-504

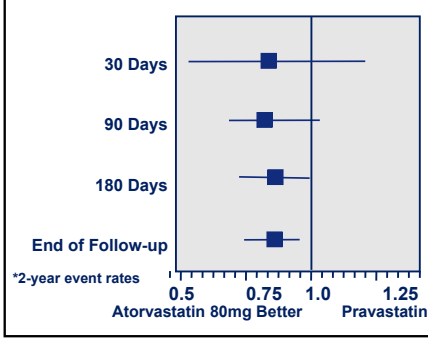


Median LDL-C (Q1, Q3)
95 (79, 113)
62 (50, 79)

Note: Changes in LDL-C may differ from prior trials:
- 25% of patients on statins prior to ACS event
- ACS response lowers LDL-C from true baseline

Primary Endpoint Over Time

N Engl J Med 2004;350:1495-504



	Events Rates	
RR	Atorva 80	Prava 40
17%	1.9%	2.2%
18%	6.3%	7.7%
14%	12.2%	14.1%
16%	22.4%* NNT 26	26.3%*

TNT Trial

10,003 patients with stable coronary heart disease
Age 35-75 years, LDL between 130 and 250 mg/dL, triglyceride ≤ 600 mg/dL
19% female, mean age 60.3 years
All received atorvastatin 10 mg during 8 week open-label run-in period

Atorvastatin 80 mg n=4,995

Atorvastatin 10 mg n=5,006

Primary Endpoint: Major cardiovascular event defined as coronary heart death (CHD) , nonfatal M, resuscitated cardiac arrest, and fatal or nonfatal stroke at a mean follow-up of 4.9 years.

Secondary Endpoint: Major coronary events, cerebrovascular events, hospitalization for congestive heart failure (CHF), all-cause mortality, peripheral artery disease, any cardiovascular event, any coronary event

Presented at ACC 2005

TNT: Primary efficacy outcomes

Outcome	Atorvastatin 10 mg (n=5006)	Atorvastatin 80 mg (n=4995)	Hazard ratio/NNT (95% CI)	p
Total major cardiovascular events (%)	10.9	8.7	0.78/46 (0.69-0.89)	<0.001
▪Death from coronary heart disease (%)	2.5	2.0	0.80 (0.61-1.03)	0.09
▪Nonfatal MI (%)	6.2	4.9	0.78/77 (0.66-0.93)	0.004
▪Resuscitation after cardiac arrest (%)	0.5	0.5	0.96 (0.56-1.67)	0.89
▪Fatal or nonfatal stroke (%)	3.1	2.3	0.75/125 (0.59-0.96)	0.02

LaRosa JC et al. *N Engl J Med* 2005;352:1425-35 http://www.nejm.org.

TNT: Key CV End Points in At-Risk Subpopulations

Patient subpopulation:	Atorvastatin 80 mg (n)	Atorvastatin 10 mg (n)	Outcome measure	Relative risk reduction (RRR)
Diabetes	748	753	Time to first major CV event	- 25% (P= 026) HR=0.75 (CI, 0.58–0.97) ARR=4.1% NNT 25
CKD	1602	1505	Time to first major CV event	- 32% (P= 0003) HR=0.68 (CI, 0.55–0.84) ARR=4.1% NNT 25
Prior HF	377	404	Risk of hospitalization for heart failure	- 41% (P= 008) HR=0.59 (CI, 0.40–0.88) ARR=6.7% NNT 15
≥65 y	1937	1872	Time to first major CV event	-19% (P= 032) HR=0.81 (CI, 0.67-0.98) ARR=2.3% NNT 44

1. Shepherd J et al. *Diabetes Care.* 2006;29(6):1220-1226. **2.** Shepherd J et al. *J Am Coll Cardiol.* 2008;51(15):1448-1454. **3.** Khush KK et al. *Circulation.* 2007;115(5):576-583. **4.** LaRosa JC et al. *N Engl J Med.* 2005;352(14):1425-1435. **5.** Wenger NK et al. *Ann Intern Med.* 2007;147(1):1-9.

What about adding a second lipid altering agent to a statin?

FDA Drug Safety Communication Trilipix (fenofibric acid)

11/9/2011 Trilipix (fenofibric acid) may not lower a patient's risk of having a heart attack or stroke.

- **RECOMMENDATION: Fenofibrate at a dose equivalent to 135 mg of Trilipix was not shown to reduce coronary heart disease morbidity and mortality in patients in two large randomized controlled trials of patients with type 2 diabetes mellitus (FIELD and ACCORD); healthcare professionals should consider the benefits and risks of Trilipix when deciding to prescribe the drug to patients, and counsel patients about those benefits and risks.**

Cardiovascular outcomes during extended follow-up of the AIM-HIGH trial cohort

J Clin Lipidology 2018; 12:1413-19

- AIM-HIGH was a placebo-controlled **trial of 3414 patients with established CV disease, low baseline HDL-C, and elevated triglycerides levels randomized to ERN 1500–2000 mg/d vs placebo. Participants also received simvastatin with or without ezetimibe to attain on-treatment low-density lipoprotein cholesterol levels of 40–80 mg/dL.** The trial was **halted after a mean 3-year follow-up because of futility.**
- Among 3236 participants alive at the end of blinded study, 2613 **(81%; ERN = 1,312, placebo = 1301) were followed a mean 1.1 additional years. Ninety-five percent of subjects remained on statin, but only 4% on ERN. At a mean total follow-up of 4.1 years,** there were 343 primary CV endpoints in the ERN arm and 305 CV endpoints in placebo participants **(HR 1.11, 95% CI 0.96, 1.30).**
- **An additional year of follow-up off assigned treatment did not alter these findings.**

IMPROVE-IT: Results

- The results of IMPROVE-IT (AHA 11/17/2014 Scientific Sessions). **The study included more than 18 000 patients from 39 countries who were stable following ACS (<10 days).** Patients were randomized to one of two treatment strategies**: simvastatin 40 mg alone or simvastatin 40 mg plus ezetimibe 10 mg.** They were followed for a minimum of 2.5 years or until the study investigators accrued 5250 clinical events.
- At baseline, the mean LDL-cholesterol level among the ACS patients was 95 mg/dL in both treatment arms. With **simvastatin 40 mg, LDL-cholesterol levels were reduced to 69.9 mg/dL at 1 year. The addition of ezetimibe 10 mg to simvastatin further lowered LDL-cholesterol levels, to 53.2 mg/dL at 1 year**. Over 7 years, there remained a significant difference between the two treatments in the achieved LDL-cholesterol levels.
  - N Engl J Med 2015;372:2387-97

IMPROVE-IT

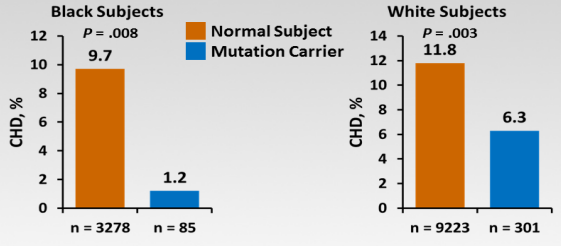
Primary End Point and Individual Components (7-Year Event Rates)

Clinical Outcomes	Simvastatin, n=9077 (%)	Ezetimibe/Simvastatin, n=9067 (%)	*P*
Primary end point (Cardiovascular death, MI, unstable angina, coronary revascularization, or stroke)	34.7	32.7	0.016
All-cause death	15.3	15.4	0.782
MI	14.8	13.1	0.002
Stroke	4.8	4.2	0.052
Ischemic stroke	4.1	3.4	0.008
Unstable angina	1.9	2.1	0.618
Coronary revascularization	23.4	21.8	0.107

Primary combined endpoint at 7 years: RRR 6.4%; ARR 2.0%; NNT 50
MI at 7 years: ARR 1.7%; NNT 59
Ischemic stroke at 7 years: 0.7%; NNT 142

'Modest' Benefit When Adding Ezetimibe to Statins in Post-ACS Patients. *Medscape*. Nov 17, 2014.

PCSK9 Loss-of-Function Mutations Resulted in Low LDL-C Levels and Reduced CHD Rates[a]



- Wild-type PCSK9 degrades LDL receptors[b-c]
- Loss-of-function mutations increase hepatic *LDLR* expression, reducing LDL-C levels by 15%-40%[a,c]
- CHD was reduced 47%-88% in *PCSK9* loss-of-function mutation carriers compared with normal individuals[a]

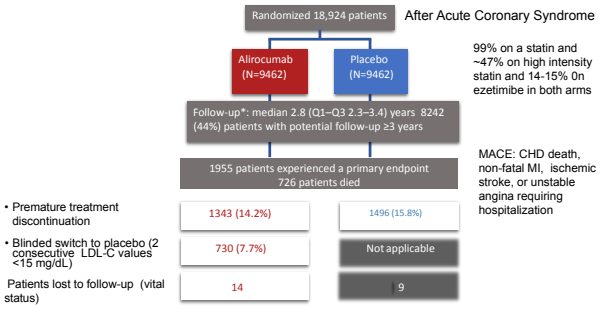
a. Cohen JC, et al. *N Engl J Med*. 2006;354:1264-1272.
b. Peterson AS, et al. *J Lipid Res*. 2008;49:1595-1599.
c. Cohen J, et al. *Nat Genet*. 2005;37:161-165.

METABOLIC

Alirocumab-Praluent

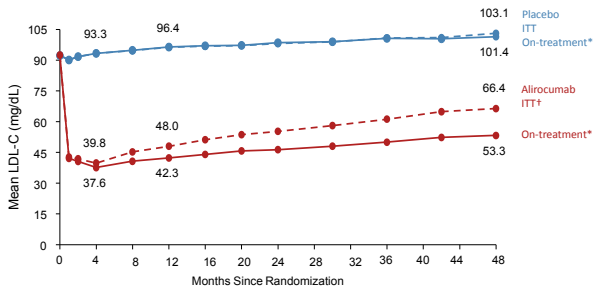
- Supplied in single-dose pre-filled pens and single-dose pre-filled glass syringes. Each pre-filled pen or pre-filled syringe is designed to deliver 1 mL of **75 mg/mL or 150 mg/mL solution. (available in cartons containing 1 or 2, pre-filled pens and 1 or 2, pre-filled syringes).**
- **Dose 75-150 mg SC every 2 weeks or 300 mg every 4 weeks**
- **Cost: $14,600.00/year**
- **Now $5,850.00/year**

ODYSSEY OUTCOMES Trial Patient Disposition



*Ascertainment was complete for 99.1% and 99.8% of potential patient-years of follow-up for the primary endpoint and all-cause death, respectively

LDL-C: ITT and On-Treatment Analyses

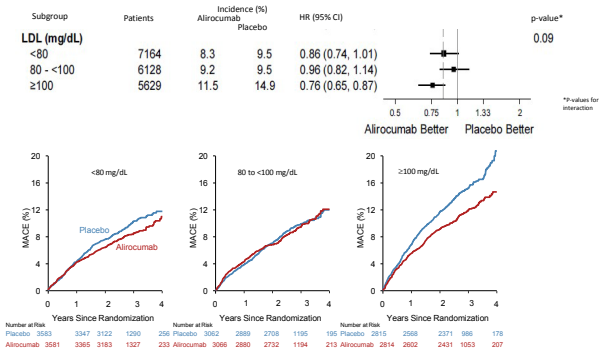


*Excludes LDL-C values after premature treatment discontinuation or blinded switch to placebo
†All LDL-C values, including those after premature treatment discontinuation, blinded down titration, or blinded switch to placebo

Primary Efficacy and Components

Endpoint, n (%)	Alirocumab (N=9462)	Placebo (N=9462)	HR (95% CI)	Log-rank P-value
MACE	**903 (9.5)**	**1052 (11.1)**	**0.85 (0.78, 0.93) NNT 59**	**0.0003**
CHD death	**205 (2.2)**	**222 (2.3)**	0.92 (0.76, 1.11)	0.38
Non-fatal MI	**626 (6.6)**	**722 (7.6)**	0.86 (0.77, 0.96) **NNT 100**	**0.006**
Ischemic stroke	**111 (1.2)**	**152 (1.6)**	0.73 (0.57, 0.93) **NNT 250**	**0.01**
Unstable angina	**37 (0.4)**	**60 (0.6)**	0.61 (0.41, 0.92)	0.02

Primary Efficacy in Main Prespecified Subgroups



Efficacy: Subgroup with Baseline LDL-C ≥100 mg/dL (Median Baseline LDL-C 118 mg/dL)

Endpoint, n (%)	Alirocumab (N=2814)	Placebo (N=2815)	Absolute risk reduction (%)/NNT	HR (95% CI)
MACE	324 (11.5)	420 (14.9)	**3.4/30**	**0.76** (0.65, 0.87)
CHD death	69 (2.5)	96 (3.4)	**1.0/100**	**0.72** (0.53, 0.98)
CV death	81 (2.9)	117 (4.2)	**1.3/77**	**0.69** (0.52, 0.92)
All-cause death	114 (4.1)	161 (5.7)	**1.7/59**	**0.71** (0.56, 0.90)

Alirocumab-Praluent

INDICATIONS AND USAGE (FDA label 4-26-2019)

- **Prevention of Cardiovascular Events - PRALUENT is indicated to reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease.**
- **Primary Hyperlipidemia (including heterozygous familial hypercholesterolemia) - PRALUENT® is indicated as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia to reduce low-density lipoprotein cholesterol (LDL-C).**

Evolocumab – Repatha

by Amgen

- **FDA approved 8-27-2015 a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody indicated as an adjunct to diet and: for the treatment of patients with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol(LDL-C).**
- **Patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C when other LDL-C lowering therapies are not adequate (e.g., statins, ezetimibe, LDL apheresis).**

Evolocumab – Repatha

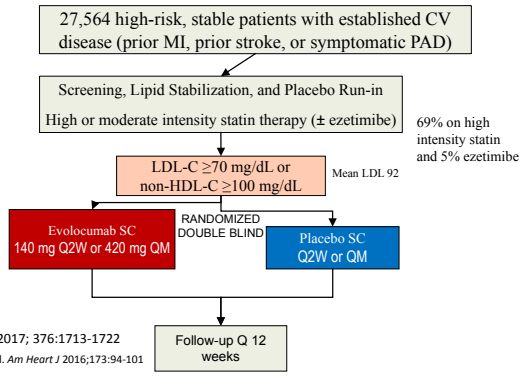
- **Available as:**
  - **Injection: 140 mg/mL in a single –use prefilled syringe**
  - **Injection: 140 mg /mL in a single –use prefilled SureClick ® autoinjector**
  - **Cartridge 420 mg/3.5 ml for Pushtronex System**
  - **Cost: $542.31/140 mg dose WAC or about $14,100.00/year for the every other week dosage. Now $5850.00/year**

Storage:
Keep in the refrigerator. Prior to use, allow to warm to room temperature for at least 30 minutes. Alternatively, for patients and caregivers, the drug can be kept at room temperature (up to 25°C (77°F)) in the original carton. However, under these conditions , the medication must be used within 30 days.

Evolocumab – Repatha

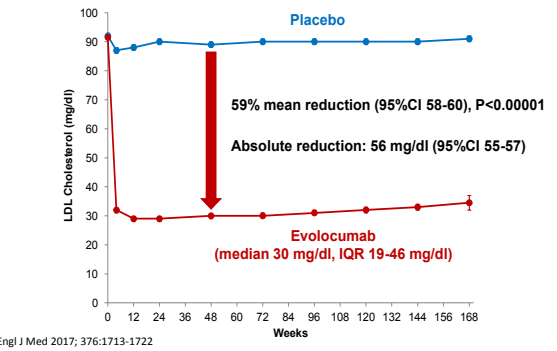
- Administer by **subcutaneous injection**
- Primary hyperlipidemia with established **clinical atherosclerotic CVD or HeFH:**
  - **140 mg every 2 weeks or 420 mg* once monthly in abdomen, thigh, or upper arm**
- **HoFH:**
  - **420 mg* once monthly**
  - ***To administer 420 mg, give 3 x 140 mg injections consecutively within 30 minutes or use 420 mg Pushtronex System**

Fourier Trial Design



N Engl J Med 2017; 376:1713-1722
Sabatine MS et al. *Am Heart J* 2016;173:94-101

LDL Cholesterol



N Engl J Med 2017; 376:1713-1722

Types of CV Outcomes

Endpoint	Evolocumab (N=13,784)	Placebo (N=13,780)	HR (95% CI)
	3-yr Kaplan-Meier rate		
CVD, MI, stroke, UA, or revasc	**12.6**	**14.6**	**0.85 (0.79-0.92) NNT 50**
CV death, MI, or stroke	**7.9**	**9.9**	**0.80 (0.73-0.88) NNT 50**
Cardiovascular death	**2.5**	**2.4**	**1.05 (0.88-1.25)**
MI	**4.4**	**6.3**	**0.73 (0.65-0.82) NNT 53**
Stroke	**2.2**	**2.6**	**0.79 (0.66-0.95) NNT 250**
Hosp for unstable angina	**2.2**	**2.3**	**0.99 (0.82-1.18)**
Coronary revasc	**7.0**	**9.2**	**0.78 (0.71-0.86) NNT 46**
Urgent	3.7	5.4	0.73 (0.64-0.83)
Elective	3.9	4.6	0.83 (0.73-0.95)
Death from any cause	**4.8**	**4.3**	**1.04 (0.91-1.19)**

N Engl J Med 2017; 376:1713-1722

Summary for Evolocumab

- ↓ LDL-C by 59%
  - Consistent throughout duration of trial
  - Median achieved LDL-C of 30 mg/dl (IQR 19-46 mg/dl)
- ↓ CV outcomes in patients already on statin therapy
  - 15% ↓ broad primary endpoint; 20% ↓ CV death, MI, or stroke
  - Consistent benefit, incl. in those on high-intensity statin, low LDL-C
  - 25% reduction in CV death, MI, or stroke after 1st year
  - Long-term benefits consistent w/ statins per mmol/L ↓ LDL-C
- Safe and well-tolerated
  - Similar rates of AEs, including DM & neurocog events w/ Evolocumab & placebo
  - Rates of Evolocumab discontinuation low and no greater than placebo
  - No neutralizing antibodies developed

N Engl J Med 2017; 376:1713-1722

Evolocumab - Praluent

Indications: (FDA label 2-2017)

- **to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.**
- **as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol (LDL-C).**
- **as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C**

PCSK9 Inhibitor Price Update

- Reuters (**2/11/2019**) reports **Regeneron and Sanofi announced that they would reduce the list price of cholesterol drug alirocumab (Praluent) by 60% to $5,850.00/year.** The price reduction follow a similar move by rival Amgen Inc which cut evolocumab (Repatha) by 60% to $5,850.00 per year in Oct 2018 in hopes of increasing use of the drug.

REDUCE-IT Trial with Icosapent ethyl (EPA, Vascepa)

- September 2018 Amarin/Kowa announced the topline results of the **Reduce-It Trial a cardiovascular (CV) outcomes study of icosapent ethyl (VASCEPA) capsules met its pre-specified primary composite endpoint (4 point MACE of CV death, nonfatal myocardial infarction (MI, including silent MI), nonfatal stroke, coronary revascularization, and unstable angina requiring hospitalization) in the intent – to - treat population:**
- Randomized **8,179 patients on a 1:1 basis to statin plus VASCEPA 4g/day or statin plus placebo and compared the incidence of MACE between treatment arms over a median period of 4.9 years.**
- **Baseline LDL-C controlled to between 41-100 mg/dL (median baseline 75 mg/dL) by statin therapy and with various cardiovascular risk factors including persistent elevated TGs between 150-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention) or diabetes mellitus and at least one other CV risk factor (primary prevention)**
- **Showed reduction in a composite of major adverse cardiovascular events (MACE) of approximately 25% – P value <0.001** (highly statistically significant)
  - N Engl J Med 2019; 380:11-22

FDA - Approved Indication and Limitations of Use for VASCEPA

- Icosapent ethyl (VASCEPA) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (>500 mg/dL) hypertriglyceridemia.
- In patients with severe hypertriglyceridemia, the effect of icosapent ethyl on cardiovascular mortality or morbidity or on the risk of pancreatitis has not been determined.
- The daily dose of icosapent ethyl is 4 grams per day taken as four 0.5-gram capsules or two 1-gram capsules twice daily with food.
- Cost 1 Gm caps x 120 ~ $242.00, 500 mg caps x 240 ~$282.00 GoodRx.com 9/26/18

Primary End Point:

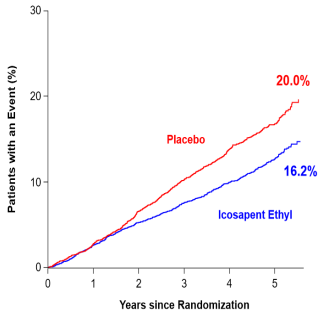
CV Death, MI, Stroke, Coronary Revasc, Unstable Angina

reduce-it

Hazard Ratio, 0.75
(95% CI, 0.68–0.83)
RRR = 24.8%
ARR = 4.8%
NNT = 21 (95% CI, 15–33)

Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med.* 2018. Bhatt DL. AHA 2018, Chicago.

Key Secondary End Point:
CV Death, MI, Stroke



Hazard Ratio, 0.74
(95% CI, 0.65–0.83)
RRR = 26.5%
ARR = 3.6%
NNT = 28 (95% CI, 20–47)
P=0.0000006

Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med.* 2018. Bhatt DL. AHA 2018, Chicago.

Prespecified Hierarchical Testing

Endpoint	Hazard Ratio (95% CI)	Icosapent Ethyl n/N (%)	Placebo n/N (%)	Hazard Ratio (95% CI)	RRR	P-value
Primary Composite (ITT)		705/4089 (17.2%)	901/4090 (22.0%)	0.75 (0.68–0.83)	25%▼	<0.001
Key Secondary Composite (ITT)		459/4089 (11.2%)	606/4090 (14.8%)	0.74 (0.65–0.83)	26%▼	<0.001
Cardiovascular Death or Nonfatal Myocardial Infarction		392/4089 (9.6%)	507/4090 (12.4%)	0.75 (0.66–0.86)	25%▼	<0.001
Fatal or Nonfatal Myocardial Infarction		250/4089 (6.1%)	355/4090 (8.7%)	0.69 (0.58–0.81)	31%▼	<0.001
Urgent or Emergent Revascularization		216/4089 (5.3%)	321/4090 (7.8%)	0.65 (0.55–0.78)	35%▼	<0.001
Cardiovascular Death		174/4089 (4.3%)	213/4090 (5.2%)	0.80 (0.66–0.98)	20%▼	0.03
Hospitalization for Unstable Angina		108/4089 (2.6%)	157/4090 (3.8%)	0.68 (0.53–0.87)	32%▼	0.002
Fatal or Nonfatal Stroke		98/4089 (2.4%)	134/4090 (3.3%)	0.72 (0.55–0.93)	28%▼	0.01
Total Mortality, Nonfatal Myocardial Infarction, or Nonfatal Stroke		549/4089 (13.4%)	690/4090 (16.9%)	0.77 (0.69–0.86)	23%▼	<0.001
Total Mortality		274/4089 (6.7%)	310/4090 (7.6%)	0.87 (0.74–1.02)	13%▼	0.09

0.4 1.0 1.4
Icosapent Ethyl Better | Placebo Better
RRR denotes relative risk reduction

Bhatt DL. AHA 2018, Chicago. Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med.* 2018.

ADA 2019 Standards of Medical Care in Diabetes Update 3/28/2019

- Section 10, on cardiovascular disease and risk management, was revised to include a recommendation **based on the outcomes from the Reduction of Cardiovascular Events with Icosapent Ethyl Intervention Trial (REDUCE-IT) advising that icosapent ethyl be considered to reduce cardiovascular risk in patients with diabetes and atherosclerotic cardiovascular disease, or other cardiac risk factors, who are taking a statin and have controlled low-density lipoprotein cholesterol (LDL-C) but elevated triglycerides.**

The Bottom Line

- **Why do we treat patients?**
  - **I hope we treat to reduce events not just to get selected biomarkers or surrogate endpoints to goal.**
  - **POEMs (Patient oriented evidence that matters) not DOEs (Disease oriented evidence)**
  - **We all need to do what is best for the patient based upon the best evidence that we currently have.**

Costs

- Atorvastatin (Lipitor) $6-20.00/30 tabs 10-80 mg generic
  Brand $320-475.00/30 tabs 10-80 mg
- Rosuvastatin (Crestor) $12-85.00/30 tabs 5-40 mg generic
  Brand $175-280.00/30 tabs 5-40 mg tabs
- Pravastatin (Pravacol) $12-40.00/30 tabs 10-80 mg generic
  Brand $125-280.00/30 tabs 10-80 mg
- Simvastatin (Zocor) $6-27.00/30 tabs 10-80 mg generic
  Brand $150-265.00/30 tabs 10-80 mg
- Lovastatin (Mevacor) $6-27.00/30 tabs 10-40 mg (Brand no longer available)
- Pitavastatin (Livalo) $320.00/30 tabs 1-4 mg (Brand only)

Costs

- Ezetimibe (Zetia) $15-40.00/30 tabs 10 mg generic
  Brand $365-375.00/30 tabs 10 mg
- Simvastatin/Ezetimibe (Vytorin) $65-243.00/30 tabs 10/10 -10/80 mg tabs generic
  Brand $365.00/30 tabs 10/10-10/80 mg tabs
- Alirocumab (Praluent) $487.50/mo 75-150 mg pens
- Evolocumab (Repatha) $487.50/mo 140 mg autoinjector

SELF EVALUATION

Impacting Cardiovascular Disease through Improved Lipids Management

1. T/F - The Updated ASCVD Plus 10 Year Risk Calculator for Primary Prevention from the AHA/ACC was modified to include the benefits of a patient being on a statin or low dose aspirin.

2. T/F - The new 2018 AHA/ACC Guideline on the Management of Blood Cholesterol have been modified to include not only targeting a statin dose but now also have added a secondary LDL cholesterol goal of less than 70 mg/dl for patients with ASCVD disease (secondary prevention patients).

3. T/F - The new 2018 AHA/ACC Guideline on the Management of Blood Cholesterol have been modified to include In patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL, begin moderate-intensity statin therapy without calculating 10-year ASCVD risk.

4. Which of the following is **Not** considered a risk enhancing factor?

a. metabolic syndrome;
b. chronic kidney disease;
c. history of preeclampsia or premature menopause (age <40 yrs)
d. chronic inflammatory disorders (e.g., rheumatoid arthritis, psoriasis, or chronic HIV);
e. None of the above, all are risk enhancing factors

5. T/F - The American Diabetes Association has updated their 2019 Standards of Medical Care based on the outcomes from the Reduction of Cardiovascular Events with Icosapent Ethyl Intervention Trial (REDUCE-IT) advising that icosapent ethyl (EPA) be considered to reduce cardiovascular risk in patients with diabetes and atherosclerotic cardiovascular disease, or other cardiac risk factors, who are taking a statin and have controlled low-density lipoprotein cholesterol (LDL-C) but elevated triglycerides.

Answer Key: 1. T, 2. T, 3. F, 4. E, 5. T

Kathy Gaughan

Kathy Gaughan of Irvine, California is Senior Marketing Strategist at Healthcare Success Strategies, a data driven healthcare marketing company. She has over 25 years experience in healthcare marketing having personally consulted with over 7,000 clients and created thousands of strategic plans for clients in myriad medical and institutional clients. Kathy has authored numerous articles in her field and has spoken to hundreds of audiences across the country.

You may contact Ms. Gaughran with your questions of comments by phone at (714) 328-2865, or email at kathy@healthcaresuccess.com.

HEALTHCARE SUCCESS®
Scientific Marketing That Delivers Patients

Patient Experience and Brand Management - Parts 1 & 2

Kathy Gaughan

WHY DOES PX MATTER?

- Rise in patient experience
- It shapes your brand – If you don't control it, your patients will
- Builds referrals
- Retains patients
- Creates advocates
- Staff – When was the last time you had them trained?
- Low cost way to differentiate your brand
- Reimbursement

FACTORS WHEN CHOOSING A PROVIDER

	Very Important	Somewhat Important	Not Important
Accepts my health insurance	89%	6%	5%
Convenient office location	59%	36%	5%
Physician's years of experience	46%	46%	8%
Part of a trusted group practice	44%	37%	19%
Word of mouth (family and friends)	38%	47%	15%
Referral from another physician	34%	46%	19%
Physician's rating on websites	19%	40%	41%

Source: JAMA, Public Awareness, Perception, and Use of Online Physician Rating Sites 2014

AFTER APPOINTMENTS, PATIENTS ARE SPREADING THE WORD ABOUT THEIR EXPERIENCES

50% recommended family, friends, and colleagues contact the same facility

12% posted review on social network site

6% posted a review on a website

SIGNS OF TROUBLE IN CONSUMER/PHYSICIAN RELATIONSHIPS

51% of consumers described their physician's value as limited to "routine care"

43% of consumers visited a new physician in the past year

45% of consumers feel only "somewhat loyal" to their current physician

22% of consumers need a physician right now

When consumers don't feel a connection with their physician, satisfaction suffers and the desire to select a new provider increases. The consumer/physician carousel is already spinning quickly and as better information and understanding of options emerge for consumers, it seems unlikely to slow.

Healthcare Consumer Trends, National Research Corporation

IMPROVE PATIENT EXPERIENCE

The Moments That Patients Remember Most

Patient experience is more than customer service and satisfaction ratings. True patient experience reflects the total perceived value from interacting with a doctor, practice or health system. It encompasses clinical innovation and operating standards that have a positive ripple effect throughout the entire patient health delivery system. The best experience is a seamless, compassionate healthcare journey — from the first impression to the last.

- Healthcare practices and organizations that want to drive lasting loyalty and growth can no longer afford to focus exclusively on checklists and process changes.
- They must also persistently focus on enhancing the human experience.

EFFICIENCY PLUS EMPATHY

Differentiating on the Human Experience: Efficiency Plus Empathy

Quality, Safety, Flow | Emotion, Communication, Relationships | Loyalty and Growth

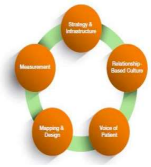
2860 Michelle Drive, Suite 230 • Irvine, CA 92606 • (800) 656-0907 • www.HealthcareSuccess.com

BUILDING A TRIAD LEADERSHIP MODEL

IMPROVE PATIENT EXPERIENCE

Practices and organizations that commit to delivering the optimal human experience follow five core imperatives to drive differentiation and results

- Develop strategy and infrastructure that align experience and outcomes.
- Build a relationship-based culture.
- Infuse the voice of the patients and families into decision making.
- Map the gaps in efficiency plus empathy and design solutions to humanize care.
- Put science behind the patient experience.



PATIENT SERVICE EXCELLENCE

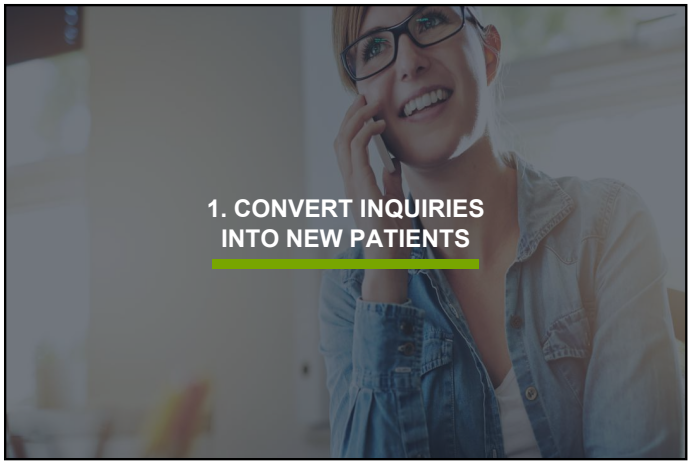
- Excellent patient experience applies to all team members - phone, front desk, those who respond to billing concerns, mid-levels and Provider. Basically anyone who engages with patients.
- Create a streamlined approach to patient communication services, capabilities and general insurance questions that can be handled on routine phone calls with the ultimate goal to book the initial appointment. Document all, script, and then train your teams.
- Provide consistency in message points that market your Providers and vast array of services as a team, i.e., *"You've called the right place. We proudly offer our unparalleled pain management evaluation and treatment and our care team is among the best."* Know your brand and ensure your team members do as well.
- Develop a "concierge" approach to patient greeting, patient flow and patient exiting. Ensure that the team at the front desk consider the patient in the reception area to be their key focus, consider having phones answered not at the reception desk
- Enhance each team member's ability to show confidence that the patient has called or come to the right place.

PATIENT SERVICE EXCELLENCE

- Perception is reality in healthcare—"You're always on show!"
- Think like a patient—How do Patients Judge?
- Track source of awareness to better use your marketing dollars
- Deal well with different patient personalities—Effectively communicating to different personalities is part of the job
- Allow each team member to incorporate his/her own voice, style and delivery to project "best in class" patient care?
- Conduct mystery patient calls to judge effectiveness
- Train your team and include role playing to ensure they are comfortable
- Include patient satisfaction scores in teams' objectives. Incent to success measures. Embed in Human Resources guidelines, performance reviews, etc.
- Discuss patient satisfaction in routine staff meetings, so that the behaviors continue consistently
- Create listening opportunities to determine if there are obstacles to your staff's success here. Are there team members who are thwarting success? Is EMR or another operational issue in the way of success?

5 PRIMARY INTERNAL STRATEGIES

1. Convert phone inquiries into first visits
2. Turn visitors into loyal patients
3. Generate patient referrals
4. Promote key services to patients
5. Case presentation



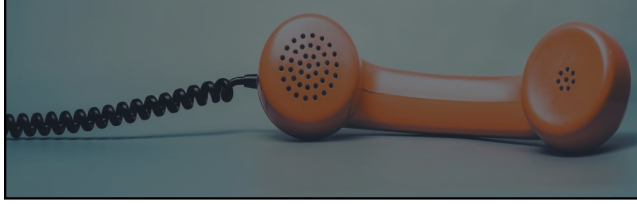
IT STARTS WITH THE PHONE

Your practice is like an upside down pyramid, sitting on the end of the finger, of the person answering your phone.

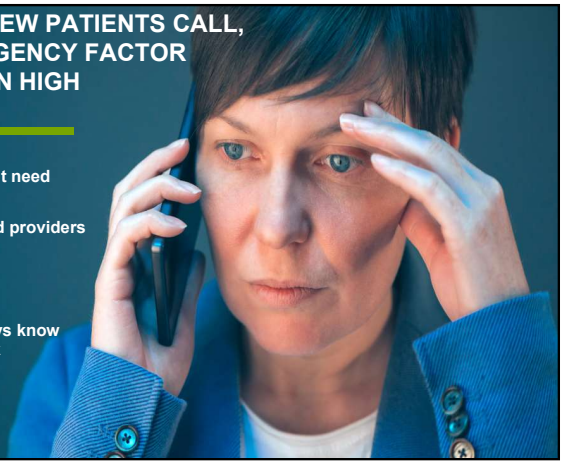
ANALYTICS FROM AUDIT CALL DATABASE (OVER 1,000 CALLS)

MYSTERY CALLS AND CALL MONITORING REVEAL

- Long holds
- Forgotten Callers
- Busy Signals
- No Answer
- Polite but confused
- Rudeness
- Stressed environment

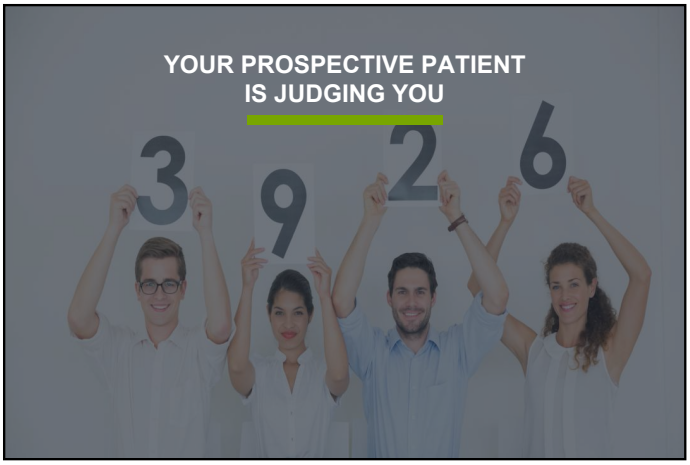


WHEN NEW PATIENTS CALL, THE URGENCY FACTOR IS OFTEN HIGH



- Have urgent need
- Researched providers
- Called YOU
- Don't always know what to ask

YOUR PROSPECTIVE PATIENT IS JUDGING YOU



ECONOMICALLY SPEAKING, WHY YOU SHOULD CARE…

- **Ex: If you spend $10,000 per month on Marketing (Acquisition Cost)**
- **Failing to convert 50% of callers will result in …**
- **$5,000/month ($60,000/yr) of wasted marketing dollars on the front end.**
- **Those are not even the *BIG* $$ you are losing**

OPPORTUNITY COST

- Average revenue per new patient = $3,000
- One patient per day x 250 business days per year
- **$750,000 lost every year!**

WHY YOUR STAFF STRUGGLES WITH PHONE INQUIRIES

Front office staff are faced with:

- Try to educate patients over the phone
- Complicated insurance and pricing questions
- Too many competing tasks
- No system of accountability
- Insufficient training
- Wrong person

ONLINE & ADVERTISING CALLS ARE EVEN MORE DIFFICULT

- Different from referred patients! (less trust, more skepticism)
- New patient/client appointments from the internet or external marketing must be scheduled quickly (1-3 days)

MAJOR AH-HA!

- The best way to educate the public is to get them off the phone and into your office
- A Team Member's job is NOT simply to answer questions with a smile, it is to sell appointment times
- Just because a Team member is friendly over the phone does NOT mean that they are fully successful in their job

CRITICAL PHONE SKILLS SOLUTIONS

1. New patient inquiry is a top priority
2. Set them up to succeed
3. Get the call off the front desk
4. Objective is a first visit
5. Nominate your best phone people
6. Hire right - pay right
7. Train them
8. Consider incentives
9. Track

5 CRITICAL COMPONENTS OF ANY EFFECTIVE PHONE CONVERSATION

1. **Establish rapport with a perfect greeting**
2. **Discover the need**
3. **Establish value**
4. **Dual alternative close**
5. **Answer objections**

GREAT FIRST IMPRESSIONS

- Make sure offices look warm, clean and inviting
- Greet patients and establish rapport
- Build trust
- Beware of long wait times
- Empathize with their emotional state

IN SERVICE BUSINESSES, THE CUSTOMER EXPERIENCE IS EVERYTHING.

- Doctors and staff create the lasting impression– good or bad
- You ARE the "product"
- Customer service and people skills training can really help
- How would you feel in their shoes?

INTERNAL SIGNAGE

REMEMBER: CURRENT PATIENTS ARE ALWAYS YOUR BEST PROSPECTS

- **Patients have a *relationship* with you**
- **They can buy additional services from you**
- **They can refer friends, loved ones and co-workers to you**

QUICK QUIZ

Which internal marketing strategy works incredibly well and costs *nothing* to implement, yet few do it even though most have heard they should?

Answer:

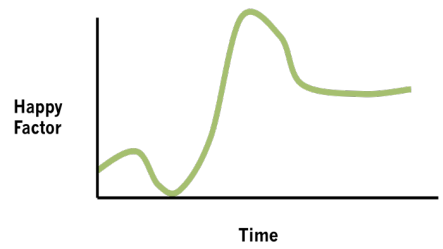
Ask patients for referrals

ASKING PATIENTS FOR REFERRALS

Things to remember:

- No cost = infinite ROI
- It works
- Doctors and staff can all participate
- Mark the patient chart with "AFR" code after they have been asked to refer
- Ask at the peak of their experience

ASK FOR REFERRALS AT THE PEAK OF THE PATIENT EXPERIENCE



ASK FOR REFERRAL SAMPLE SCRIPT

"Mrs. Smith, we think you are just terrific.

We would love to treat more patients like you in our practice.

If you know of anyone who can benefit from our care, please let them know about us and we promise to take good care of them"

CREATING PATIENT AMBASSADORS

Acknowledge all referrals with positive reinforcement

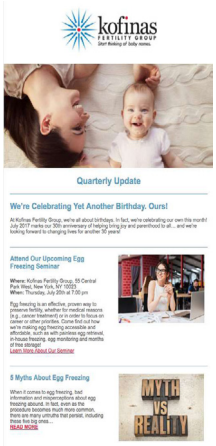
- Warm phone call
- Thank you note

Encourage frequent referrers to become "Health Ambassadors"

- Arm them with your marketing materials
- Make them feel special

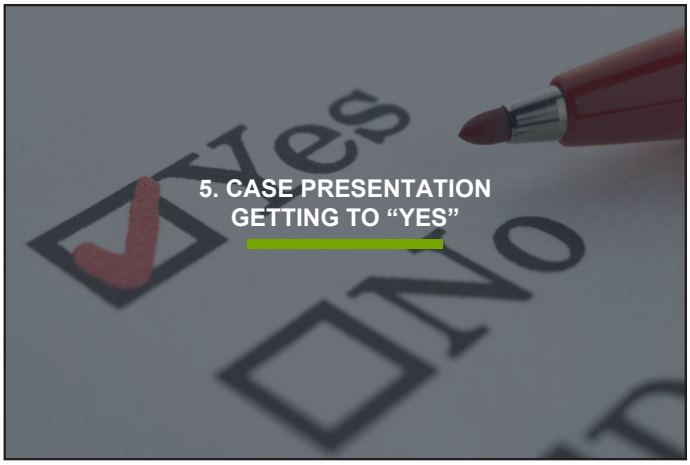
PATIENT EMAILS

- Build opt-in email list
  - -Intake forms
  - -Incentives at front desk
- Promote specific services and ask for referrals
- Special offers
- Frequency varies
- Postal mail too for special cases



PROMOTE KEY SERVICES IN BROCHURES

INTERNAL SIGNAGE



THE ROLE OF THE TREATMENT COORDINATOR

- Especially important for elective care
- Primary new patient advocate and liaison
- Commission-based sales experience
- Confident and success driven
- Part of a larger sales system
- Can hire or train existing staff

ADAPT TO THEIR PERSONALITY

- **Friendly**
- **Expressive**
- **Analytical**
- **Controlling**

MAGIC QUESTIONS – *NEEDS*

- What were you hoping we could do for you?
- Why are you interested?
- How long have you considered this?
- What would you like to change?
- What's most important to you?

MAGIC QUESTIONS – *OBJECTIONS*

- What concerns do you have?
- What research have you done?
- Why haven't you done this in the past?
- If there is one thing that would hold you back, what would it be?

COMMON PITFALLS AND THEIR SOLUTIONS

Pitfall #1: Treating experience as an initiative

While 84% of healthcare executives claim patient experience is one of their top 3 strategic priorities, few have appointed executives to lead the work or allocated financial resources to driving improvement. As a result, solutions are often seen by frontline staff as a series of initiatives with no broader strategy. Employees either fail to embrace these "flavor of the month" initiatives, or run out of energy chasing each new opportunity with no cohesive framework and value.

Solution: Appoint a C-level executive to lead experience, or the like. The experience leader needs organizational authority, budget and staff, and medical credibility to succeed.

COMMON PITFALLS AND THEIR SOLUTIONS

Pitfall #2: Failure to obtain physician and staff buy-in

The most common reasons cited by organizations that feel they are not making progress toward an optimal human experience are competing priorities and lack of physician buy-in. Traditionally, experience improvement work has not been viewed as part of a complete clinical excellence strategy. As such, physicians have not been at the table as leaders in shaping experience strategy or gauging its clinical value. As a result, experience work is often tabled due to the perception that it competes with the more pressing demands of quality and safety improvement.

Solution: Town hall meetings and dyad leadership. Use town hall meetings to gather the physician and staff perspective on what works and what's broken. Appoint dyad (nurse-physician) leaders for each clinic, department, or unit to drive ownership of mapping the gaps and designing solutions to the front lines.

COMMON PITFALLS AND THEIR SOLUTIONS

Pitfall #3: Lack of alignment with quality and safety

Faced with the need to improve care quality and reduce costs, many health systems have implemented efficiency methodologies, and quality and safety checklists. When used effectively, these practices improve patient flow and can address quality and safety risks. However, they neglect to address some of the greatest barriers to patient care including fragmented communication, broken relationships, failure to address emotional needs and concerns, and physical barriers to receiving care. These gaps in the human experience are key drivers of sentinel events, low patient engagement, and poor clinical quality.

Solution: Create a central project management team. Create a single project management hub that builds alignment across experience and process improvement, HR practices, and quality and safety initiatives.

REPUTATION MANAGEMENT

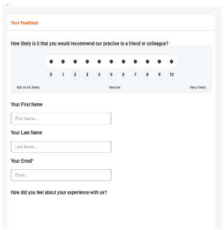
If reputation management isn't at the top of your marketing priority, it should be.

You've spent years building your practice, invested sweat, tears and time. It's too easy to let it all go to waste.

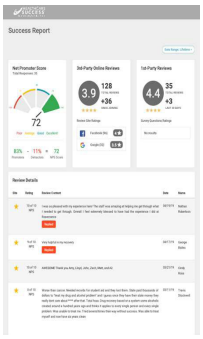
In a recent Nielsen study for Global Trust in Advertising, 66% of consumers indicated that they trust online reviews from strangers.

Sample Reputation Management Platform

EMAIL



REPORTING



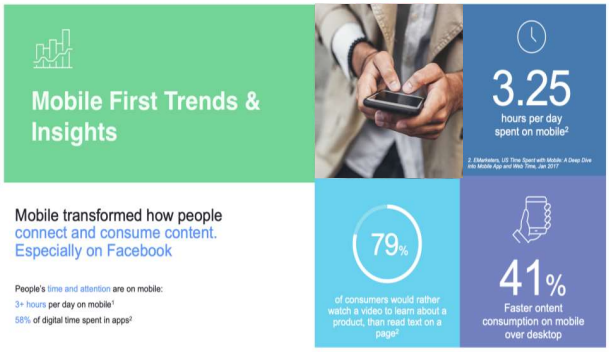
WHY IS SOCIAL MEDIA IMPORTANT?

- Allows for ongoing communication
- Boosts SEO performance
- Facebook in particular ranks well in top 10 search results.
- Leads to relationship and trust building with potential patients and their influencers.
- Publicly advocates for your practice.
- Manage expectations between organic and paid

FACEBOOK RETARGETING

- Patient visits your site and is later "retargeted" on Facebook in a boosted post
- Can re-engage an otherwise missed opportunity
- This adds another branding layer to help to build awareness and drive new patient conversions

Video Recommendations



WARNING

- Do NOT write your own reviews
- Do NOT have family members review you
- Do NOT buy reviews
- You can't opt out of reputation management

FACT

- Businesses with mostly 1 and 2 star reviews fail to convert roughly 90% of prospective customers.
- If someone does research on your company, chances are they will search for your reviews before coming to see you.

Source: https://blog.reputationx.com/online-reputation-management-statistics

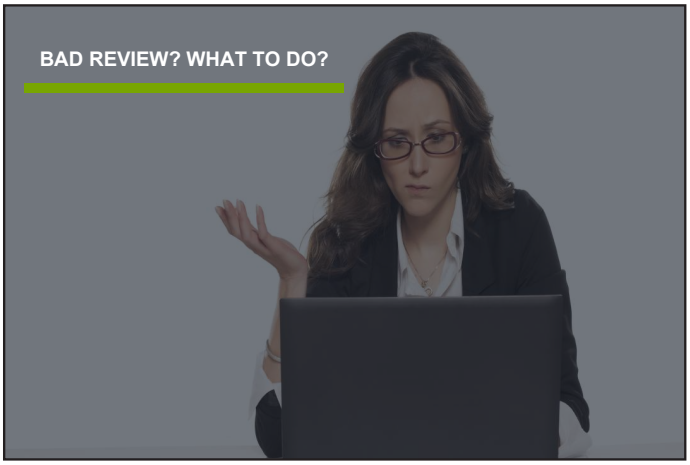
IMPORTANCE OF CLAIMING SOCIAL MEDIA PROFILES & DIRECTORIES

A big mistake many companies make is forgetting to register their social profiles and local directories. It's hard to control your reputation online when you don't own your profiles.

WEBSITES YOU SHOULD CLAIM

- Facebook
- Twitter
- LinkedIn
- YouTube
- Yelp
- GoogleMyBusiness
- Bing Places
- Yahoo Local

BAD REVIEW? WHAT TO DO?



BAD REVIEW: WHAT TO DO

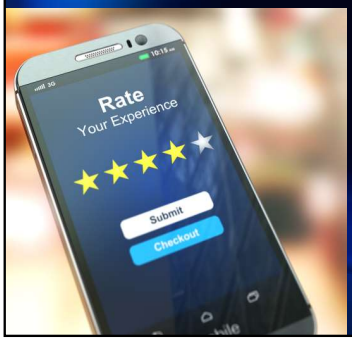
1. Respond politely to patients and take conversation offline. Never get into a battle online or disclose HIPAA protected info.
2. Ask review sites to take down libelous or slanderous reviews
3. Create properties online so that you dominate searches for your name and push review sites down (e.g., Facebook, Youtube, DrYourName.com, etc)
4. Ask happy patients to post positive reviews

The Importance of Communication

Communication: There are several approaches to acknowledging the client's feelings and de-escalating the situation as much as possible.

- **C**onnecting: saying the patients' name, introducing yourself, shaking hands, making good eye contact;
- **A**ppreciating: apologizing, acknowledging their feelings, appreciating that they let us know;
- **R**esponding: giving choices to the patients, assuring them you will help, fixing what you can.
- **E**mpathizing: Giving the tools out when you yourself, if you were in the patient's shoes, would feel bad, ignored, disappointed, inconvenienced or irritable due to the clinic's system.

HOW TO GENERATE REVIEWS



- Simply ask for them from patients you believe are happy
- Hang a sticker on your window
- Ask for reviews on a post card
- Automate the review process
- Kiosk in office and at check-out
- Email requests
- Also ask your referral sources and their staff!!
- Reach back to past happy patients as well.

REPUTATION MANAGEMENT USING NET PROMOTER SCORE (NPS)

The NPS is an index ranging from 10-100 that measures the willingness of customers to recommend your company's services to others.

By asking on a scale of 1-10, you can find out who are the Detractors (1-6), Passives (7-8), and Promoters (9-10).

The Promoters are the patients willing to build your brand.

SELF EVALUATION

Patient Experience and Brand Management - Parts 1 & 2

1. Why does patient experience matter?

a. build referrals
b. retains patients
c. differentiates your practice
d. all of the above

2. T/F - It is important to track the source of all new patients from first phone call

3. Identify which of the following is NOT a critical component of an effective phone call for new prospects?

a. establish rapport with a perfect greeting
b. dominate the call
c. discover the need

4. Why is social media important?

a. allows for ongoing communication
b. adds traffic to your website
c. provides a forum for patients to vent their complaints

5. T/F - You should send a gift or call a patient after they have referred you a new patient?

6. T/F - It is important to have a reputation management strategy in your practice?

7. T/F - You should delete a negative review from Facebook?

8. T/F - Video testimonials are effective?

9. What is retargeting?

a. identifying your best prospects
b. redirecting your staff during a conversation
c. following patients who have previously visited your website

10. In a recent Nielsen study for Global Trust in Advertising, what percentage of consumers indicated that they trust online reviews from strangers?

a. 66%
b. 57%
c. 38%

Answer Key: 1. D, 2. T, 3. C, 4. A, 5. T, 6. T, 7. F, 8. T, 9. C, 10. A

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Practical Aspects of Depression Management

Off-Label Content

- Thyroid hormone supplementation for augmentation therapy of MDD
- Initial dual antidepressant therapy of MDD

My (and maybe your?) 4 Main Errors in MDD Management

- Acceptance of "Better" instead of "Well"
- Insufficient Monitoring
- Failure to employ augmentation
- Failure to stratify Rx intensity to severity

Error #1 Acceptance of BETTER rather than WELL

- Better vs Well = Responder vs Remission
  - Responder = 50% ↓ Sx Score
  - Remission = Sx score < MDD threshold
- When Better may *not* be acceptable
  - INR close to therapeutic
  - Incontinence
  - Myopia
  - ED

Error #2 Insufficient Concrete Monitoring

- Global subjective vs validated Sx score

Error #3 Failure to Employ Augmentation: Missteps

- Hung on too long hoping for effect
- Switched thru too many multiple classes
- Despite credible evidence of efficacy, infrequently employed augmentation
  - Thyroid hormone
  - Atypical antipsychotics (esp aripiprazole)

Error #4 Failure to Stratify Rx Intensity to Severity

- HTN:
  - Polypharmacy routine
  - Stage 2 HTN initiate 2 drugs
- DM
  - Polypharmacy routine
  - A1c > 7.6 initiate 2 drugs (AACE Guideline)
- Exceptional to *initiate* 2 agents for MDD Sx

So I'm Going to Try to Convince You To…

- Revise your Rx goal to REMISSION
- Perform routine Sx score MONITORING (like BP for HTN, A1c for DM)
- Consider AUGMENTION more often
- Consider INITIAL POLYPHARMACY more often

Why Bother?

Consequences
Epidemiology

Top Causes of Death: U.S.A. 1994

1) Heart Disease
2) CA
3) CVA
4) Accidents
5) COPD
6) Pneumonia/Influenza
7) Diabetes
8) Suicide
9) Liver Disease
10) HIV

US Business & Health 1994 (March): 15

Top Causes of Death: U.S.A. 2000

1) Heart Disease	710,000
2) CA	553,000
3) CVA	167,000
4) COPD	122,009
5) Accidents	97,900
6) Diabetes	69,301
7) Pneumonia/Influenza	65,313
8) Alzheimer Disease	49,558
9) Nephritis, Nephrotic Syndrome	37.251
10) Septicemia	31,224
11) Suicide	29,350

US Mortality Public Use Data Tape, National Center for Health Statistics,CDCP 2002

Top 10 Causes of Death, USA 2012

Heart Disease	595,444	Alzheimer's	83,308
CA	573,855	Diabetes	68,905
COPD	137,789	Renal Disease	50,472
CVA	129,180	Flu/pneumonia	50,003
Accidents	118,043	Suicide	37,793

Murphy SL, Xu J, Kochanek KD National Vital Statistics Report 2012;60(4):1-69

Top 10 Causes of Death, USA 2013

Heart Disease	611,105	Alzheimer's	84,757
CA	584,861	Diabetes	75,578
COPD	149,205	Flu/pneumonia	56,979
Accidents	130,557	Renal	47,112
CVA	129,978	Suicide	41,149

http://www.cdc.gov/nchs/fastats/leading-causes-of-death accessed 2/1/2016

Top 10 Causes of Death, USA 2016

Heart Disease	633,842	Alzheimer's	110,561
CA	595,930	Diabetes	79,535
COPD	155,041	Flu/pneumonia	57,062
Accidents	146,071	Renal	49,959
CVA	140,323	Suicide	44,193

Heron M *National Vital Statistics Reports* 2018;67(6):1-77

MI: Impact of Depression on Mortality

- OBECTIVE: Determine impact of depression upon acute MI
- METHOD: Interview day 5-15 post admit (n=222)
- FOLLOWUP: 6 months
- OUTCOME: mortality H.R. = 5.76 (p=0.0006)

Frasure-Smith et al, JAMA 1993;270:1819-1825

Depression in Elderly HTN May ↑ CVD

- SHEP Trial (n=4,736) adults >60 yrs
- Method: Rx ISH X 5 years (tenormin, HCTZ)
- Measured: Center for Epidemiology Studies Depression Scale (CES-D), depressive Sx, clinical psych eval
- Outcomes: Depression → 60% ↑ stroke, MI
  80% ↑ mortality
- Any depressive Sx score > WNL → 2X ↑ RR death

Smoller S. Medical Tribune 1994(April 7):p 7

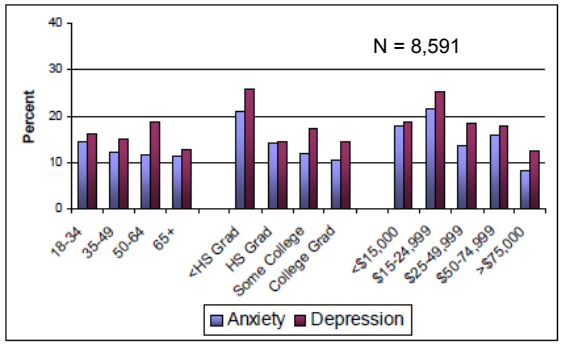
Maryland BRFSS 2010 Report
What Was the Telephone Interviewers Question?

"Has a doctor or other healthcare provider ever told you that you had an anxiety disorder or depressive disorder?"

N =8,591

Maryland BRFSS State of the State Report November 2010
www.marylandbrfss.org

Maryland BRFSS 2010 Report



Maryland BRFSS State of the State Report November 2010
www.marylandbrfss.org

Maryland 2010 BRFSS Report
Bottom Lines

- Anxiety: 12%
- Depression: 16%
- Men < Women
  - Anxiety: 10.5% vs 14.3%
  - Depression: 14.2% vs 17.3%
- ↑income (>$75K) → less anxiety or depression
- Less education → more anxiety or depression
- No impact of age

Maryland BRFSS State of the State Report November 2010
www.marylandbrfss.org

Why Don't We Make the Dx of MDD More Often?

- 'Oblique' presentation
  - Fatigue
  - Insomnia
  - Weight
- Concern to 'R/O Important Organic First'
  - Anemia
  - Hypothyroidism
  - Systemic Disease
- Stigma

DSM-5 Dx Criteria: Major Depression

- ≥5 Sx including depressed mood &/or anhedonia for ≥ 2 weeks representing a change from prior function
- Others symptoms may include:
  - Significant unintentional weight change (↑or↓)
  - Insomnia or hypersomnia nearly every day
  - Psychomotor agitation/retardation
  - Pervasive loss of energy/fatigue
  - Feelings of worthlessness/XS or inappropriate guilt
  - Difficulty concentrating
  - Recurrent thoughts of death/suicide

Am Psych Assoc DSM-5 2013

The FDA-mandated Language for BPD Screening

"**Screening patients for BPD**— A major depressive episode may be the initial presentation of BPD. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for BPD. Whether any of the Sx described above represent such a conversion is unknown. However, prior to initiating Rx with an antidepressant, patients with depressive Sx should be adequately screened to determine if they are at risk for BPD; such screening should include a detailed psychiatric history, including a FHx of suicide, BPD, and depression. It should be noted that _____ is not approved for use in treating BPD.

Duloxetine and Mirtazapine Prescribing Information

Risk of Transition from MDD to Bipolar NESARC

- NESARC: National Epidemiologic Survey on Alcohol and Related Conditions
- Study: nationally representative household survey conducted by National Institute on Alcohol Abuse and Alcoholism
- Wave 1 (2000-2001): n=43,093
- Wave 2 (2004-2005): n=34,653

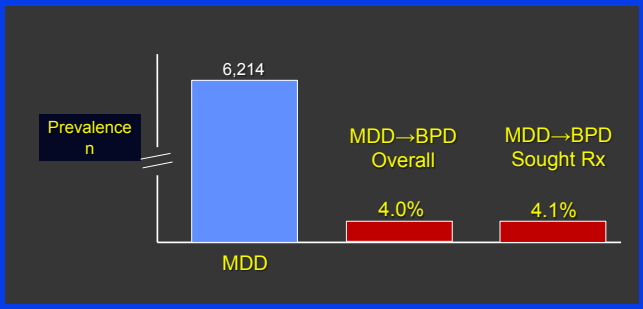
Gilman SE, et al RH J Clin Psychiatry 2012;73(6):829-836

NESARC:Transition MDD → Bipolar

- Wave 1: AUDADIS structured interview for MDD and BPD as per DSM-IV criteria
- Clinical characteristics survey
  - Age at onset
  - Atypical features
  - Family History
  - # Episodes
  - Anxiety
  - Panic
  - Substance Use
  - Childhood abuse
- Wave 2: Interview of MDD pts (N=6,214) for mania Sx over prior 3 years

Gilman SE, et al RH J Clin Psychiatry 2012;73(6):829-836

NESARC: Results at 4 years

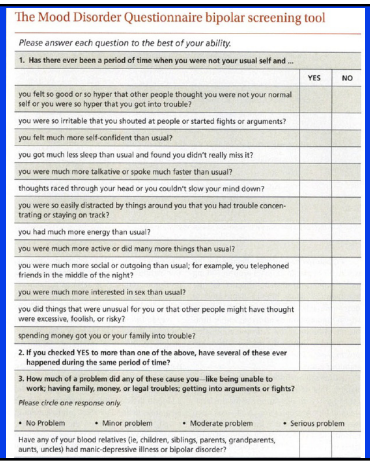


Gilman SE, et al RH J Clin Psychiatry 2012;73(6):829-836

Preventing BPD Dx Delay

Positive Screen
Q1: 7+
Q2: +
Q3 ≥ Moderate

Hirschfeld RM et al Am J Psychiatry 2000;157;1873-1875



The Mood Disorder Questionnaire bipolar screening tool

Please answer each question to the best of your ability.

1. Has there ever been a period of time when you were not your usual self and ...

	YES	NO
you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?		
you were so irritable that you shouted at people or started fights or arguments?		
you felt much more self-confident than usual?		
you got much less sleep than usual and found you didn't really miss it?		
you were much more talkative or spoke much faster than usual?		
thoughts raced through your head or you couldn't slow your mind down?		
you were so easily distracted by things around you that you had trouble concentrating or staying on track?		
you had much more energy than usual?		
you were much more active or did many more things than usual?		
you were much more social or outgoing than usual; for example, you telephoned friends in the middle of the night?		
you were much more interested in sex than usual?		
you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?		
spending money got you or your family into trouble?		
2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time?		
3. How much of a problem did any of these cause you—like being unable to work; having family, money, or legal troubles; getting into arguments or fights? *Please circle one response only.* • No Problem • Minor problem • Moderate problem • Serious problem		
Have any of your blood relatives (ie, children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?		

Rx Goal: REMISSION Why?

"Remission is the aim of Rx because patients whose depression has remitted have better functioning and a better prognosis than those without remission."

Rush AJ, et al *Am J Psych* 2011;168(7):689-701

Goal Attainment: How are we Doing?

"Antidepressant meds, when used as monotherapy in placebo-controlled registration trials, typically results in 30-35% remission rates."

Rush AJ, et al *Am J Psych* 2011;168(7):689-701

Goal Attainment: How are we Doing?

"Lower remission rates (25%-30%) are reported for patients with more chronic depressions."

Rush AJ, et al *Am J Psych* 2011;168(7):689-701

Is There a BEST Antidepressant?

Rx: Example Primary Care Choices

- Heterocyclics
  - Tricyclics: amitriptyline, imipramine
  - Tetracyclics: mirtazapine, maprotiline
- SSRIs: paroxetine, fluoxetine, citalopram
- SNRIs: venlafaxine, duloxetine
- Aminoketone: bupropion

EFFICACY: A BEST Antidepressant?

"According to the APA Guidelines for MDD in adults…the data indicate

SIMILAR RATES OF RESPONSE TO ALL ANTIDEPRESSANT DRUGS;

therefore, the choice must be predicated on other factors."

American Psychiatric Association. Am J Psychiatry 1993;150

Best Antidepressant?

" A series of pivotal effectiveness studies in psychiatry….showed that virtually all antidepressant strategies had …similar efficacy in major depression."

Parikh SV "Antidepressants are not all created equal" Lancet 2009;373:700-701

BEST Antidepressant?

- Study: metaanalysis 117 RCT (H:H)
  - n=26,000
  - 12 antidepressants studied
- No industry involvement
- Analyses:
  - Efficacy = ≥50% ↓ Sx at week 8
  - Acceptability = D-C by week 8 (any reason)

Cipriani A, Furukawa TA, Salanti G, et al "Comparative efficacy and acceptability of 12 new-generation antidepressants" Lancet 2009:373:746-758

Best Antidepressant: Winners

Superior Efficacy	Superior Tolerability
escitalopram (Lexapro)	bupropion (Wellbutrin)
mirtazapine (Remeron)	citalopram (Celexa)
sertraline (Zoloft)	escitalopram (Lexapro)
venlafaxine (Effexor)	sertraline (Zoloft)

Cipriani A, Furukawa TA, Salanti G, et al "Comparative efficacy and acceptability of 12 new-generation antidepressants" Lancet 2009:373:746-758

And the BIG WINNER Is……

"Balancing efficacy and acceptability and lower drug costs, the researches concluded that SERTRALINE might be particularly appropriate as a first-choice Rx."

Cipriani A, Furukawa TA, Salanti G, et al "Comparative efficacy and acceptability of 12 new-generation antidepressants" Lancet 2009:373:746-758

TCAs : Side Effect Profile

- Dry mouth
- Weight Gain
- Urinary Retention
- Hypotension
- Constipation
- Sedation

TCAs & Seniors:? NOT?

"…TCAs are included in the Beers Criteria list of potentially inappropriate medications associated with high rates of adverse drug events among older adults."

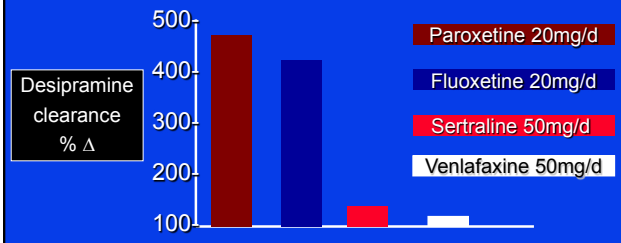
Taylor WD "Depression in the Elderly"
NEJM 2014;371:13:1228-36

TCAs & Seniors: HOWEVER

"If SSRIs or SNRIs are ineffective, TCAs may be considered (either as monotherapy or as augmentation)."

Taylor WD "Depression in the Elderly"
NEJM 2014;371:13:1228-36

Antidepressants: P450 IID6 System



Results are NOT from head-to-head comparison

Preskorn S. Am J Med 1993;94(Suppl 5A)

Some Commonly Used Drugs Metabolized by P450 IID6

- Chlorpromazine
- Clomipramine
- Codeine
- Desipramine
- Dextromethorphan
- Imipramine
- Metoprolol
- Nortriptyline
- Perphenazine
- Propranolol
- Thioridazine
- Timolol

Mendoza R. Psychopharmacology Bulletin #27; 1991:453

Another Safe Path For Maximizing Rx?

- Study: DBRPCT Adults with MDD (n=124)
- Rx: Sertraline + Liothyronine (T_3) or Sertraline + Placebo X 8 wks
  - Week 1: Sertraline 50 mg/d, T_3 20-25 mcg/d
  - Weeks 2-8: Sertraline 100 mg/d, T_3 40-50 mcg/d
- Outcomes:
  - Primary: HAMD responder rate (= ↓50%)
  - Secondary: Remission rate (HAMD score ≤6)

Cooper-Kazaz R, Apter JT, et al Arch Gen Psych 2007;64:679-688

Another Safe Path For Maximizing Rx?

	S + T3	S + Pl	p
Responder Rate	70%	50%	0.02
Remission Rate	58%	38%	0.02
Pre-Rx TSH	1.7 mIU/L	1.61 mIU/L	NS
Post-Rx TSH	0.41 mIU/L	1.59 mIU/L	<0.001
AEs	No Between-Group Adverse Event Signal		

Cooper-Kazaz R, Apter JT, et al Arch Gen Psych 2007;64:679-688

JAMA | Original Investigation JAMA 2017;318(2):132-145

Effect of Antidepressant Switching vs Augmentation on Remission Among Patients With Major Depressive Disorder Unresponsive to Antidepressant Treatment

The VAST-D Randomized Clinical Trial

Somaia Mohamed, MD, PhD; Gary R. Johnson, MS; Peijun Chen, MD, PhD, MPH; Paul B. Hicks, MD, PhD; Lori L. Davis, MD; Jean Yoon, PhD; Theresa C. Gleason, PhD; Julia E. Vertrees, PharmD, BCPP; Kimberly Weingart, PhD; Ilanit Tal, PhD; Alexandra Scrymgeour, PharmD; David D. Lawrence, MS; Beata Planeta, MS; Michael E. Thase, MD; Grant D. Huang, MPH, PhD; Sidney Zisook, MD; and the VAST-D Investigators

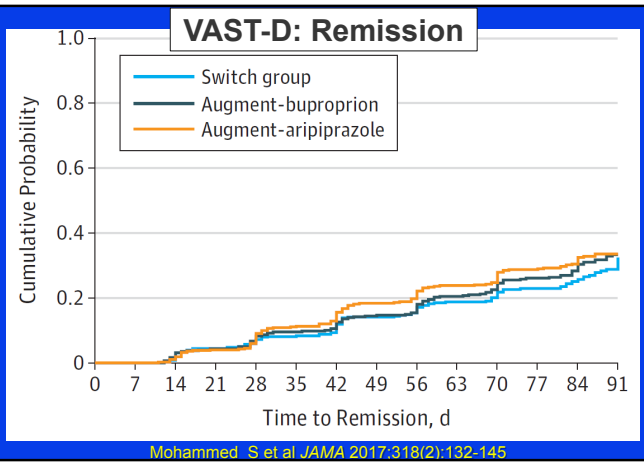
VAST-D
VA **A**ugmentation and **S**witching **T**reatment for Improving **D**epression Outcomes

MDD: Switch vs Augment VAST-D

- Study: RSBT MDD adults (n=1,522)
- Inclusion:
  - failed SSRI, SNRI, or mirtazapine
  - QUIDS-C_{16} score ≥11 (= moderate MDD)
- Rx:
  - Switch: current Rx to bupropion (≤300 mg/d)
  - Augment A: add aripiprazole (≤15 mg/d)
  - Augment B: add bupropion (≤ 300 mg/d)
- 1^0 Outcome: Remission

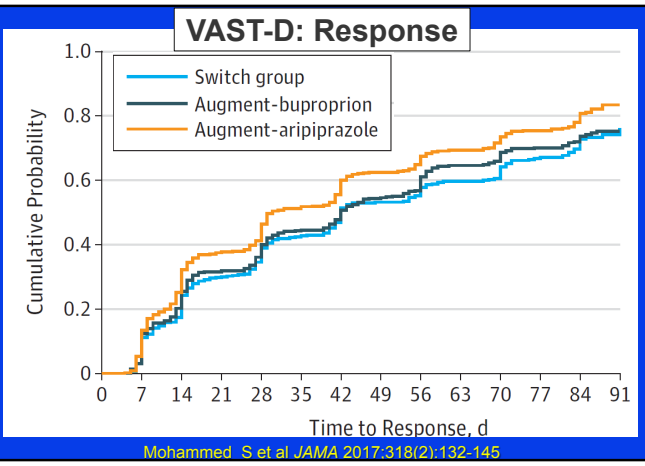
Mohammed S et al *JAMA* 2017;318(2):132-145

VAST-D: Remission



Mohammed S et al *JAMA* 2017;318(2):132-145

VAST-D: Response



Mohammed S et al *JAMA* 2017;318(2):132-145

VAST-D: Outcomes

Group	Remission	Response
Switch to bupropion	22.3%	62.4%
Augment with Aripiprazole	28.9%*	74.3%*
Augment with Bupropion	26.9%	65.6%

*p < 0.05 vs Switch
*p < 0.05 vs Switch or Bupropion Augmentation

Mohammed S et al *JAMA* 2017;318(2):132-145

VAST-D: Tolerability

- Lowest D-C rate: aripiprazole augmentation

HOWEVER

Weight Gain ≥7%

Group	Week #12	Week #36
Switch to bupropion	2.3%	5.2%
Augment with Aripiprazole	9.5%	25.2%
Augment with Bupropion	1.9%	5.2%

Mohammed S et al *JAMA* 2017;318(2):132-145

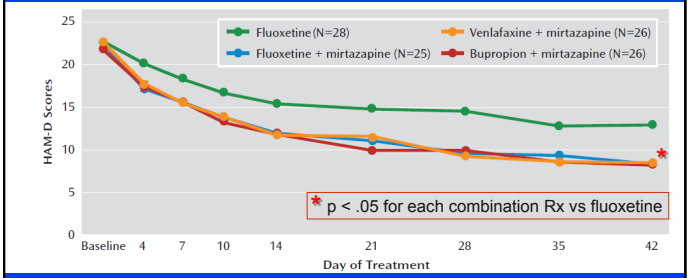
Could INITIAL DUAL ANTIDEPRESSANT Rx (≠Augmentation) Out-perform Monotherapy?

Initial DUAL Antidepressant Rx

- Study: DBRCT Adults MDD (n= 105)
- Inclusion: Baseline HAM-D ≥18
- Rx (6weeks):
  - fluoxetine 20 mg/d
  - mirtazapine 30 mg/d + fluoxetine 20 mg/d
  - mirtazapine 30 mg/d + venlafaxine 225 mg/d
  - mirtazapine 30 mg/d + bupropion 150 mg/d
- 1^0 Outcome: HAM-D Score

Blier P et al *Am J Psych* 2010;167(3):281-288

Initial DUAL Antidepressant Rx vs Monotherapy



Blier P et al *Am J Psych* 2010;167(3):281-288

DUAL Antidepressant Rx vs Monotherapy: Remission (= HAM-D ≤7)

Rx	Remission Rate	*p
Fluoxetine	25%	
Fluoxetine + mirtazapine	52%	<0.05
Mirtazapine + venlafaxine	58%	<0.05
Mirtazapine + bupropion	46%	NS

*p versus fluoxetine monotherapy

Blier P et al *Am J Psych* 2010;167(3):281-288

DUAL Antidepressant Rx vs Monotherapy: Conclusions

- Combo Rx
  - 'as well tolerated' as mono
  - → greater ↓ HAM-D scores
  - substantially improved remission rates

Blier P et al *Am J Psych* 2010;167(3):281-288

DUAL Antidepressant Rx vs Monotherapy: Conclusions

"The results of this study, taken together with those of 3 prior DB studies, provide mounting evidence that combination therapy from Rx initiation provides superior clinical effectiveness in the Rx of major depression."

Blier P et al *Am J Psych* 2010;167(3):281-288

Evolving Rx

JAMA Psychiatry | Original Investigation

Efficacy and Safety of Intranasal Esketamine Adjunctive to Oral Antidepressant Therapy in Treatment-Resistant Depression

A Randomized Clinical Trial

JAMA Psychiatry 2018;75(2):139-148

Ella J. Daly, MD; Jaskaran B. Singh, MD; Maggie Fedgchin, PharmD; Kimberly Cooper, MS; Pilar Lim, PhD; Richard C. Shelton, MD; Michael E. Thase, MD; Andrew Winokur, MD, PhD; Luc Van Nueten, MD; Husseini Manji, MD, FRCPC; Wayne C. Drevets, MD

MDD Eskatamine Nasal Spray

- Premise: "Approximately 1/3 of patients with MDD do not respond to available antidepressants."
- Objective: Assess esketamine efficacy, safety and dose-response in Tx-resistant depression

Daly EJ et al *JAMA Psychiatry* 2018;75(2):139-148

What is ESKETAMINE?

- NMDA (N methyl-D-aspartate) receptor antagonist
- S-enantiomer Ketamine (↑ NMDA receptor affinity)
- Ketamine
  - Rapid onset of antidepressant activity
  - Requires IV formulation

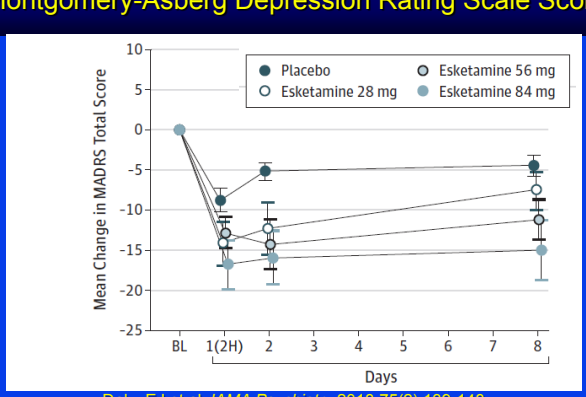
Daly EJ et al *JAMA Psychiatry* 2018;75(2):139-148

Esketamine for Treatment-Resistant Depression (TRD)

- Study: DBRPCT Adults with TRD (n=67)
- Inclusion: non-response to ≥2 meds (as per MGH Antidepressant Rx Response Questionnaire)
- Rx (*added* to current Rx regimen):
  - Phase 1: esketamine Nasal 28, 56, 84 mg twice weekly X two one-week intervals
  - Phase 2: open-label dose frequency taper 8 wks
  - (2x/wk x 2 weeks, 1x/wk x 3 weeks, 1x/2wks x 2)

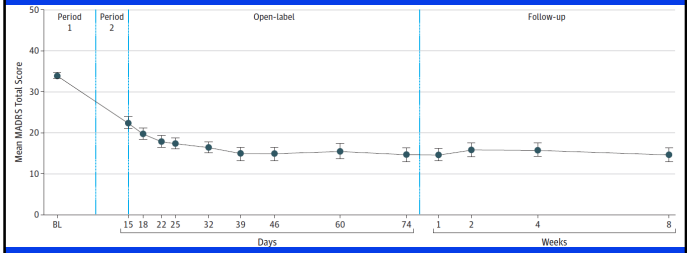
Daly EJ et al *JAMA Psychiatry* 2018;75(2):139-148

Montgomery-Asberg Depression Rating Scale Score



Daly EJ et al *JAMA Psychiatry* 2018;75(2):139-148

Montgomery-Asberg Depression Rating Scale Score



Daly EJ et al *JAMA Psychiatry* 2018;75(2):139-148

Non-Traditional Pharmacologic Rx

St. John's Wort vs. Imipramine

- STUDY: DB Dx MDD, n=135
- Rx: hypericum 300 mg tid vs imipramine 25mg tid
- Measured: CGI, HAMD, side effects
- Results
  - clinical efficacy : hypericum = imipramine
  - side effect profile : hypericum < imipramine

Vorbach EU, Hubner WD, Arnoldt KH J Geriatr Psychiatry Neurol 1994;7(suppl 1):S19-S23

St. John's Wort Efficacy : Metaanalysis

- Randomized Trials X 23 (n=1757), mod-severe MDD
- Results: "Hypericum extracts were significantly superior to placebo and similarly effective as standard antidepressants"
- Side effects: hypericum = 19.8%, drugs = 52.8%
- Dropouts : hypericum = 0.8%, meds = 3.0%

Linde K, Ramirez G, Mulrow CD et al BMJ 1996; 313 : 253-8

CAM: My Story Line

- Sample Size?
- Published?
- Site?
- Product Consistency?
- Surveillance

Essential Tools: Carl Rogers

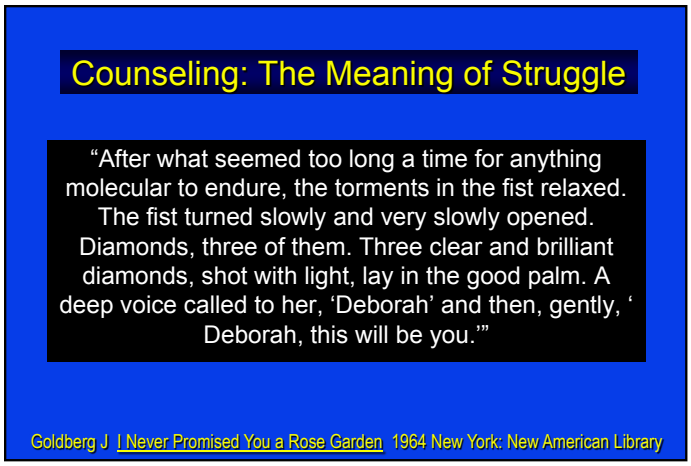
- Genuinity
- Empathy
- Unconditional positive regard

Kaplan HI, Sadock BJ (1985), Comprehensive Textbook of Psychiatry. Baltimore: Lippincott Williams & Wilkins

Counseling: The Meaning of Struggle

"Her dream began with winter darkness. Out of this darkness came a great hand, fisted. It was a man's hand, powerful and hollowed….The fist opened and in the long plain of the palm lay three small pieces of coal. Slowly the hand closed, causing within the fist a tremendous pressure. The pressure began to generate a white heat and still it increased. There was a sense of weighing, crushing time. She seemed to feel the suffering of the coal with her own body, almost beyond the point of being borne. At last she cried out to the hand, 'Stop it! Will you never end it! Even a stone cannot bear to this limit…even a stone…' "

Goldberg J I Never Promised You a Rose Garden 1964 New York: New American Library



SELF EVALUATION

Practical Aspects of Depression Management

1. Clinicians commonly focus upon affective consequences of depression, like mood and sleep alterations. Over the last 30 years, where has suicide ranked as a cause of death in the USA?

a. #1
b. Consistently in the top 10
c. Consistently in the bottom 1/3

2. Patients frequently seek help from primary care clinicians in reference to anxiety and/or depression. Which is more common?

a. MDD > anxiety disorder
b. Anxiety disorder > MDD
c. Anxiety disorder = MDD
d. MDD > anxiety disorder, but only in men

3. Traditional medical dogma advocates screening for bipolar disorder prior to initiating antidepressants, lest a mania episode be induced. Which statement below is correct?

a. Increased risk of mania induced by MDD Rx has never been confirmed in a RCT
b. Numerous trials show substantial ↑ risk
c. Observational data does shows ↑ risk
d. Observational data shows ↓risk

4. The preferred treatment goal of MDD should be

a. ≥10% Sx Score reduction
b. ≥30% Sx Score reduction
c. ≥50% Sx Score reduction
d. Remission

5. As far as therapeutic efficacy, is there a 'best' antidepressant?

a. SSRIs are most efficacious
b. SNRIs are most efficacious
c. Heterocyclics are most efficacious
d. All antidepressants are similarly effective

6. Adding liothyronine (T3) to sertraline (vs sertraline alone) for MDD might be anticipated to result in

a. No efficacy benefit over sertraline alone
b. A substantial increase in anxiety
c. Significantly more HTN
d. >50% RR ↑ of attaining remission

7. Remission is attained in only 25%-35% of MDD patients treated with monotherapy. How does dual antidepressant Rx (adding mirtazapine) compare to fluoxetine monotherapy?

a. Adding mirtazapine doubles remission rates
b. Adding mirtazapine has no effect
c. Adding mirtazapine reduces remission rates
d. Minimally improved remission rates are counterbalanced by adverse effects

Answer Key: 1. B, 2. A, 3. A, 4. D, 5. D, 6. D, 7. A

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Practice Risk Assessment - Part 2: Patients, Partners & Staff

Top Liability Risk

- Government Enforcement
- Patients
- Partners
- Employees

Top Liability Risk – Part I

- **Government Enforcement**
  - Anti-Referral Laws
  - Anti-Kickback Laws
  - Board Jurisdiction

Top Liability Risk – Part II

- Patients
- Partners
- Employees

Malpractice Lawsuits

1. Surgery (General): 85%
2. Urology: 84%
3. Otolaryngology: 83%
4. OB/GYN & Women's Health: 83%
5. Surgery (Specialized): 80%
6. Radiology: 76%
7. Emergency Medicine: 76%
8. Cardiology: 65%
9. Gastroenterology: 63%
10. Anesthesiology: 62%

*Medscape's Malpractice Report 2019

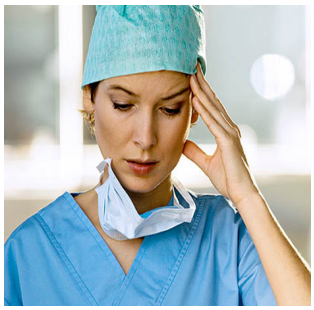
What does an angry patient do?

- **Post Negative Review**
- File Complaint with Medical Board
- File Malpractice Claim

Reputation Management

Reduction of Exposure

1. Patient Communication!
2. Have positive reviews.
   - Incorporate strategies to ask happy patients to make a review.
3. Patient Rebate Strategy
4. Work with your partners on their website and community presence
5. Respond to investigations timely and efficiently



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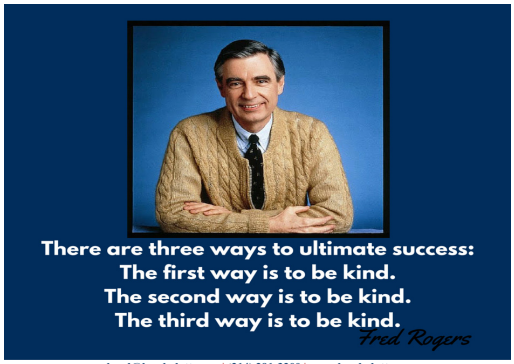
Reduction of Exposure



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What do angry patients do?

- Post Negative Review
- **File Complaint with Medical Board**
- File Malpractice Claim

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Pandora's Box

- Investigators Powers
  - Interview witnesses
  - Demand medical, court, police records, personnel information, and business records
  - Conduct site visits
  - Consider standards of care

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Are You Compliant?

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What do angry patients do?

- Post Negative Review
- File Complaint with Medical Board
- **File Malpractice Claim**

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Malpractice

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- Insurance - First Line of Defense
- Risk varies greatly by state

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Professional Liability Insurance

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- Claims Made Policies
  - Coverage
    - Claims Made During Policy
    - Extended Reporting Endorsement ("Tail")
- Occurrence Policies
  - Coverage
    - Protects From Incidents Occurring While Policy is In Force
    - Covers Incidents Forever
    - No Tail Coverage Required

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Asset Protection Planning

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- Second Line of Defense
- Varies state by state

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Strategies –Partner Disputes

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- Why
  - Personality
  - Unmet Expectations
- 4Cs

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4Cs

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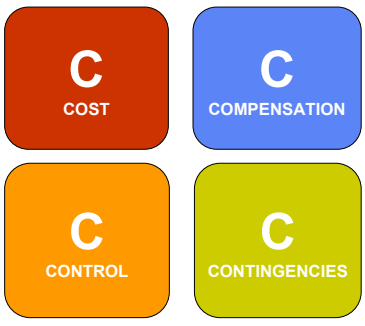

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Cost

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What are you paying?

What are you receiving?

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Compensation

Three Basic Partnership Compensation Models:

1. Eat What You Kill
2. Enterprise Model
3. Communist Model

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Control

Decision making
- Day-to-day
- Big decisions
- Founder protections?

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Contingencies

Dreaded D's:
1. Death
2. Disability
3. Divorce (business/personal)

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Hiring

1. Scope of Practice
2. Qualifications
3. Engage in Process
4. Hire Slow

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Managing

1. Supervision & Delegation
2. SOPs
3. Patient Privacy
4. Employee Handbook
5. Training

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Firing

1. Employee File
2. Performance Improvement Plan
3. Contract?
4. Two people in room

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Supplemental Material

To receive a copy of our supplemental material, visit our website:

https://www.byrdadatto.com/landing/aeiwebinar/

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SELF EVALUATION

Practice Risk Assessment - Part 2: Patients, Partners & Staff

True or False

1.___ Angry patients do not pose a threat to your practice, unless they file a lawsuit alleging malpractice.

2.___ Patient communication is the best way to mitigate the inherent risks of a patient to a medical practice.

3.___ You do not need to purchase a tail policy if you leave a practice and have an occurrence policy.

4.___ The biggest risk to a partner relationship are issues that fall into the 4Cs: (1) character, (2) clout, (3) cunning, and (4) charisma.

5.___ The contingencies to plan for with a partner are death, disability and divorce (business and personal).

6.___ As long as you have an employee handbook and other practice policies in place, you will be protected from liability.

7.___ The risks to a medical are practice are so complicated that the big idea from this presentation is to not be a lone wolf.

Answer Key: 1. F, 2. T, 3. T, 4. F, 5. T, 6. F, 7. T

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Treating the Highly Non-Compliant Patient

Non-compliance or resistance is defined as conscious or unconscious opposition to the treatment intervention. Most patients resist treatment to a lesser or greater degree because they fear change. While it is normal to be afraid of change, change is often necessary to survive.

This program focuses on how to conceptualize and address formidable non-compliance. Through lecture and discussion, Dr. Shannon will delineate specific sources of non-compliance as well as a strategic model for "re-framing" non-compliance as "positive" and therefore treatable.

As a result of completing this training, participants will be able to:

1. Define non-compliance;
2. List and describe examples of non-compliance;
3. Delineate the underlying causes for non-compliance; and
4. List and describe strategic principles for addressing non-compliance.

I. Introduction:

A. Definition – Non-compliance (resistance) is conscious (i.e., deliberate) or unconscious opposition to a therapeutic intervention.

B. Examples:
   1. Not showing for appointments
   2. Being chronically late for appointments
   3. Multiple appointment cancellations
   4. Disrespectful behavior toward the practitioner or support staff, e.g., rudeness, overt hostility, etc.
   5. Not following through with treatment recommendations
   6. "Yes, butting…"
   7. Medication non-compliance
   8. Not completing "homework," e.g., not keeping a journal of food eaten; not practicing physical therapy exercises, etc.
   9. Unusual dependency on practitioner/support staff, e.g., endless, novel-length emails or voicemails
   10. Not paying co-payments in a timely way
   11. Complaints, threats, lawsuits

C. Non-compliance is typically defined as a "patient problem." In truth, practitioners can significantly contribute to it or minimize it depending on how they interact with the patient.

D. Non-compliance will occur to a lesser or greater degree with most patients. It is typically fueled by the patient's fear of change.

E. Some patients are so non-compliant that they can not be helped.

F. The ways in which the patient demonstrates non-compliance with you the practitioner will mirror how they sabotage their life outside your office.

II. Why Do Patients Resist Treatment?

A. They do not want to see themselves as having a problem; they can rationalize, minimalize or deny a problem. Being "in treatment" is a threat to their denial.

B. They benefit in some way from keeping their symptoms:
   1. Special attention or sympathy
   2. Medication, e.g., pain medication
   3. Their symptoms give them a feeling of being special or unique

4. Their current symptoms distract them from something that they fear more.
5. Being a "patient" has become their identity.
6. They get to stay on disability and avoid going back to a stressful work situation.
7. They can use their symptoms to manipulate others.
8. They can see themselves as a "victim"; this means they won't be able to do anything themselves to get well.
9. They don't have to risk failure.
10. They can hang onto what is familiar and "safe" and avoid change and the "unknown".

C. They are engaging in a repetition compulsion that mirrors "baggage" from their past. For example, the patient may see their doctor as a "critical parent" and themselves as the "rebellious child." They are repeating an old pattern and hoping for a different outcome.

D. They simply don't have the necessary skills/resources to be successful at treatment:
1. They have cognitive deficits.
2. They have poor impulse control.
3. They have poor judgment.
4. They are profoundly disorganized and undisciplined in the way that they approach life.
5. They have motivational barriers, e.g., they are getting rewarded for bad behaviors and punished for being resourceful.
6. They are profoundly mentally-ill.
7. They are substance abusers and cannot or will not sustain their sobriety.
8. They have little or no family/community support.
9. They have little or no experience working collaboratively with another person.

III. How Practitioners Contribute to Non-Compliance

A. Lack of practitioner skills to develop a collaborative/working alliance with the patient.

B. An appalling lack of empathy/compassion for the patient's pain

C. Lack of clarity regarding roles, rules, boundaries, expectations and mutual responsibility for treatment outcome

D. The diagnosis or goals of treatment have not been clearly formulated or stated and agreed upon.

E. Practitioner may be excellent but is hampered by a poorly trained, inadequate, toxic or otherwise dysfunctional support staff.

F. Practitioner does not clearly state how his/her diagnostic formulation will translate into the treatment protocol.

G. Practitioner does not properly socialize the patient to the treatment model and address reasonable concerns the patient may have.

H. *Practitioner mismanages transference and counter-transference throughout the process of treatment.

I. *Practitioner is unclear about billing practices and/or does not address billing concerns on the part of the patient.

* These are the top two reasons patients will file a complaint with a licensing board and/or file a malpractice suit in civil court.

IV. How to Reduce/Minimize Non-Compliance

A. Develop and use active, empathic listening skills to forge a therapeutic alliance with the patient. See Appendix A.

B. Do not take the patient's non-compliance personally. See their resistance as a type of energy that can be harnessed for their success at treatment. "It takes energy to resist…"

C. Empathize with the patient's struggle to change and ask if there is anything that YOU can do to help.

e.g., "I can see that you are having difficulty following through with our treatment plan. Let's look at what may be getting in your way…"

D. Reframe any "failure" as a "success" in repeating a familiar pattern that yields predictable results; if the patient want different results, they have to be willing to approach the problem differently.

e.g., "It makes perfect sense to me that you would have binged on sugar last night. You had gone all day without eating. That's what set you up to binge. So let's look at what's getting in the way of your eating at least two meals during your day…"

E. Transform problems (what the patient doesn't want) into solutions (what they do want):
1. "Can't" transformed to "won't do" or "haven't done yet";
2. When exploring the problem and its history, always place the problem in the past:

"When you fought with your husband in the past, what happened and how was this a problem for you?"

3. Make solutions as specific as possible; you can start with the following questions:

"How would you know if the problem were gone; what would be different?"
"What would you be doing or thinking differently such that you would feel better?"
"Regarding the current problem:
Where do you have control?
Where could you gain control?
Over what do you not have control (but are "obsessing?").

4. Always put solutions in the present or future.

"What would you like to do in the future such that you will feel our time together has been valuable?"
"What would you like to work on changing today?"

F. All of the above steps should minimize resistance; if resistance does manifest itself, explore the meaning of it with the patient and address accordingly.

G. Be aware of transference and counter-transference and address as necessary; what both have in common is the past, i.e., both involve a use (sometimes rigid) of information from the past to address a current problem; the goal is flexibility.

H. Always remember: Treatment is about change and change is scary.

I. The level or degree of resistance is directly proportional to the level of pain/fear; strive to empathize with this.

J. If your empathy and compassion are consistently overshadowed by feelings of anger and frustration with the patient, something is wrong; seek advice, support from a colleague and refer on, if necessary. Moreover, if the feelings have to do with counter-transference, be aware of it but say nothing to the patient.

V. Legitimate Reasons To Terminate Treatment

A. The patient is not a good candidate for your approach to treatment, e.g., they have certain cognitive/skill deficits that would undermine treatment success.

B. The patient is clearly not benefiting from your treatment even though they are compliant.

C. Continued treatment may prove harmful to the patient.

D. The patient is being overtly disrespectful to you or your support staff.

E. The patient is threatening your or your support staff.

F. The patient is severely emotionally unstable and refuses to seek mental health treatment. The emotional instability leads to disruptive or dangerous behavior in your office.

G. In spite of your patience and compassion, the patient continues to miss appointments, not follow through with treatment recommendations or otherwise resist treatment.

H. The patient refuses to honor his/her financial obligation/agreement.

I. The patient is holding you or your staff hostage with threats of self-harm/suicide.

VI. Additional Recommendations

A. Peer consultation/supervision
B. Meticulous documentation

VII. Recommended Readings:

Eddy, W. (2006). High Conflict People in Legal Disputes. Canada: Janis Publications.
Leutenberg, E.A. and Liptak, J.J. (2012). Coping with difficult people work book. Duluth, MN: Whole Person Press.
Masterson, J.F. (1983). Countertransference and psychotherapeutic technique. New York: Wiley.
Young, J.E. (1990). Cognitive therapy for personality disorders: A schema-focused approach. Sarasota, FL: Professional Resource Exchange.
Yudofsky, S.C. (2005). Fatal flaws: Navigating destructive relationships with people with disorders of personality and character. Washington, D.C.: American Psychiatric Publishing, Inc.

SELF EVALUATION

Treating the Highly Non-Compliant Patient

1. Non-compliance or resistance is:

a. Conscious or unconscious opposition to treatment.
b. Related to the patient's fear of change.
c. Oftentimes related to the degree of physical or psychological pain the patient is experiencing.
d. ALL of the above are true.

2. Which of the following is NOT an example of non-compliance/resistance?

a. Not showing for appointments
b. Being chronically late for appointments
c. Paying the bill in a timely fashion
d. "Yes, butting…"

3. Which of the following is an example of non-compliance/resistance?

a. Not taking medication as prescribed
b. Unusual dependency on the practitioner or support staff
c. Complaints, threats, lawsuits
d. ALL of the above are examples of resistance/non-compliance.

4. Which of the following statements is true above non-compliance/resistance?

a. Practitioners rarely contribute to it.
b. It occurs only with severely mentally-ill patients.
c. It can be either conscious (deliberate) or unconscious.
d. It occurs only with highly-litigious patients.

5. Primary causes for non-compliance/resistance include which of the following?

a. Patients don't want to see themselves as having a problem; it's a threat to their denial.
b. Patients may benefit from keeping their symptoms.
c. Patients can use their symptoms to manipulate others.
d. ALL of the above are true.

6. Which of the following factors is NOT linked to patient non-compliance/resistance?

a. The patient's age
b. The patient's gender
c. A previous history of non-compliance
d. ALL of the above factors can influence the degree of non-compliance/resistance.

7. Which of the following skill deficits potentially influence non-compliance/resistance?

a. Cognitive deficits
b. Poor impulse control
c. Poor judgment
d. Lack of self-discipline/organizational skills
e. ALL of the above skill deficits could potentially influence treatment compliance.

8. Which of the following is NOT recommended when dealing with a non-compliant patient?

a. Err in the direction of being overtly confrontational.
b. Develop active, empathic listening skills.
c. Do NOT take non-compliance personally.
d. ALL of the above are recommended.

9. Which of the following is a recommended strategy for reducing patient non-compliance/resistance?

a. Reframe any "failure" as a "success" in repeating a familiar pattern of behavior.
b. Empathize with the patient's struggle to change maladaptive behavior.
c. Transform problems into solutions.
d. ALL of the above are recommended.

10. Which of the following is NOT a legitimate reason to terminate treatment?

a. The patient is annoying-as-hell.
b. The patient is clearly NOT benefiting from your treatment.
c. The patient is being overtly disrespectful to you or your support staff.
d. The patient is holding you or your staff hostage with threats of self-harm/suicide.

ANSWER KEY: 1. D, 2. C, 3. D, 4. C, 5. D, 6. B, 7. E, 8. A, 9. D, 10. A

Susan Childs, FACMPE

Susan Childs, FACMPE, of Raleigh, North Carolina, is principal of Evolution Healthcare Consulting. She has over 30 years of experience in hospital and public accounting in healthcare administration and in her consulting and public speaking focuses on the physician-patient relationship and optimal management of the medical practice in areas including revenue cycle management, financial checks and balances, operations and workflow and many others. Ms. Childs is a contributor to numerous medical publications and a frequent speaker to healthcare audiences across the country.

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High Deductible Patients: Optimizing Care and Collections

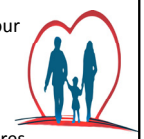
The High Deductible Patient Challenges and Solutions

Helping Patients Make Independent Healthcare Decisions …Including Financial Ones!

- High deductible policies have substantially placed the financial burden directly in many of our patient's laps.
- These deductibles effectively shift patients into a self-pay model, which require medical groups to be more savvy, assertive and transparent regarding financial policies and patient compliance issues. Prompt pay laws and legal discounts.
- We assess how your revenue cycle management processes can meet the needs of your patients.
- …And strategies that help create a more predictable income where the patient is able to separate the money from the visit.

Susan Childs, FACMPE
Evolution Healthcare Consulting

WELCOME



- Introduction to health savings accounts and understanding your "consumer driven patient"
- Improve revenue cycle processes and collections strategies that meet distinctive needs of your patient
- Physician/patient rapport – education and compliance measures
- With a plethora of options, there are some great win-win payment plans for helping high deductible patients meet his or her financial responsibilities
- We will distinguish financial policies, access issues and daily "check and balance" procedures that can protect your practice and tighten up controls and reduce the opportunity to embezzle
- I feel very confident that you will find the one that fits your practice best!

GOALS

- How physicians can communicate with and track managers' performance that ensure secure internal checks and balances.
- Establish provider active involvement in the practice's revenue cycle processes and defining financial policies.
- Proven examples and successful collections approaches that improve overall financial performance, fair to the patient, and get your bill paid!
- Tips, steps and actions that you can use as soon as you return to your office

HIGH DEDUCTIBLE PATIENT CHARACTERISTICS AND CONSUMER SELF – CARE/EDUCATION

- **Researches before making healthcare decisions**
- Has already been engaged and involved in self-care since we've had to do it for so long already
- Reacts to direct ads and convenience factors!
- Checks out your competition, from urgent care to the pharmacist.

- **"Typical behavior?" Higher educated - higher income? Not anymore!**
- Most practices have anywhere from 35% - 50% of patients with this kind of plan

- According to a 2017 kaiser family foundation survey, 46% of HDHP enrollees report difficulty affording deductibles
- Approximately 1/3 with chronic conditions report delaying or avoiding care due to the high cost
- And nearly half of HDHP enrollees with a family member with a chronic condition report problems paying medical bills or other bills because of healthcare costs.

Introduction to HSA's and "Consumer" Health

Current Monetary Allowances and Averages

PLEASE REFERENCE IRS PUBLICATION 929

	2015	2019	Variance
HSA CONTRIBUTION	IND: $ 3,350 FAM: $ 6,650	3,500 7,000	+150 +350
HSA CATCH UP 55+	$ 1,000	1,000	0
HDHP MIN DED TO QUALIFY	IND: $1,300 FAM: $2,600	1,350 2,700	+50 +100
HDHP MAX OUT OF POCKET (NOT INCL. PREMIUMS)	IND: $6,450 FAM: $12,900	6,750 13,500	+300 +600

TOP THREE "YES'S" YOU WANT TO PROVIDE FOR YOUR PATIENTS!

- CAN I BE SEEN TODAY?
- DO I HAVE 24/7 ACCESS TO MY PHYSICIAN?
- DO I KNOW WHAT I *HAVE* TO PAY TODAY?

ONE THING YOU CAN DO AS SOON AS YOU RETURN TO THE OFFICE?
- Ask your vendors about features that engage and help establish patient payment plans.
- Most systems include updated patient education as part of your maintenance and can be built in and required part of your every day operations.

ITS OFTEN UP TO US TO INFORM PATIENTS ABOUT BENEFITS, SUCH AS ABOUT SAFE HARBOR
- These are preventive and screening benefits that are covered with 0 deductible dollars paid – for example, wellness exam, mammograms, colonoscopies…
- Global periods too! But our patients are often not aware of this.
- This is what staff members should be informing patients about.

AS A PATIENT, AND I AM TERRIFIED OF MY NEW HIGH DEDUCTIBLE PLAN...
- I must believe in the value of your services. Please keep me engaged.
- I may be your millionth patient, but you are my first rheumatologist.
- When needed for financial discussions, this is where you refer your patient to your accessible staff.
- It completes the circle of care, and as a result each person supports each other's part of the care.

WHEN DO YOU HAVE A CAPTIVE AUDIENCE?

- When is your office like an airport ?

Think about it. The average hold is 32 seconds
- You can get a lot of information in that time.
- Such as: we have some new payment options available. Please phone our business office today to discuss your specific benefits.
- Also, waiting at the lab? In the lobby? X-ray?
- **If more privacy is needed,** it is not hard to section off an already semi private area, such as the check-out to discuss payments.
- There are all sorts of opportunities other than exam rooms where you can display financial information respectful to the patient or they may take some written information home.

BUILD IN FINANCIAL INFORMATION INTO YOUR WEBSITE WITH LANGUAGE SPECIFIC TO HIGH DEDUCTIBLE PATIENTS WITH A WELCOMING MESSAGE TO CALL YOUR BUSINESS OFFICE… SUCH AN AS:

"IF YOU HAVE A HIGH DEDUCTIBLE OR ARE UNDERINSURED, PLEASE CALL OUR OFFICE TODAY TO DISCUSS YOUR SPECIFIC BENEFITS AND PLAN"

PLEASE DON'T FORGET TO POST *ALL* FINANCIAL POLICIES

THE PORTAL
- A marvelous way to introduce patients to electronic accessibility to physicians
- You don't have to be present for your patients to feel your presence.
- The portal offers patient services that allow your staff to focus on other things and address issues in a more predictable manner – great for patient flow.
- This can also enhances a patient's perception of your care…which can make a substantial difference in when your bill is paid.
- The key is to have patients very comfortable with using your portal as ambassador of care, so to speak.

FINANCIAL TRANSPARENCY IS A MUST IF WE WANT PATIENTS TO TRUST OUR PAYMENT PLANS RECOMMENDATIONS!
- Systems enhancements, such as an estimator tool is an excellent idea on many levels.
- It allows for specificity to the patient's plan which can later be referenced by another employee without having to redo the quote or eligibility.
- It's very easy for your staff members to reference, utilize and remain current.
- **For the best estimators**
- Make sure that information such as diagnoses and specific cpt codes can be used to generate accurate fee estimates as well as coverage and benefits
- **E-billing!**
- Electronic billing is just that - online statements and patient payments-
- Patient billings and payments are transacted via their insurance portal
- The best thing since buttered popcorn- e-statements!
- They are less expensive you can be paid in as little as 30 minutes!!
- Remember - we tend to retain an email address more than a physical one.

FOREWARNED IS FOREARMED
- Have your billing managers and other staff that work with patient payment plans

To review the schedule two weeks ahead of time so they may call specific patients and ask them to either come in earlier or make payment arrangements over the phone before being seen.

- This will help the patient concentrate on their care instead of a bill that may not have been paid otherwise
- **Also reduces your no-shows** as some patients will opt not to be seen in order to avoid making some kind of payment.
- **If the patient is approached in an accepting and manageable manner by your staff, you will get much better results!**

HELP THEM PAY THEIR BILL!

- ✓ SHORTEN BILLING CYCLE – SEND STATEMENTS SOONER AND TURN OVER TO COLLECTIONS AT 60 DAYS
- ✓ SAMPLES ANYONE? IF YOU ARE ABLE TO OFFER SAMPLES AT NO CHARGE, PATIENTS ARE GRATEFUL AND MORE APT TO REMIT FOR YOUR SERVICES.
- ✓ STAMPED RETURN ENVELOPE – SOMETIMES SIMPLEST IS BEST - SUPPLYING PATIENTS WITH ONE OF THESE COULD HELP AS WELL
- ✓ STATEMENTS IN OTHER LANGUAGE

- **Credit card on hold is a wonderful thing** that is totally secure in your office as payments are made automatically on a monthly basis or whatever is decided for your office and patients.
- **Lesson?** Credit card on hold is excellent for checks and balances because information is encrypted, tokenized and processed on your practice management system.
- **One of the best things** about credit card on hold as it can literally separate the money from the care as a patient has automatic payments and hopefully paid off within just a few months.
- **One thing to be cautious about** with credit card on hold is to not have a charge on the initial eob unless the patient has already agreed to it.

A sample of this would be a surgery where the patient knows their liability before the procedure.

- As we know sometimes insurance has denied an error and it is our job to work on behalf of the patient.
- Therefore we have to allow enough time for the patient to become involved and appeal as necessary.

STAFF TRAINING IS AMAZING! HAVE AN IN-HOUSE TRAINER COME IN AND WORK WITH YOUR COLLECTION STAFF AND FRONT DESK STAFF AND YOU WILL SEE COLLECTIONS SOAR!

For example: emotional intelligence defined is: "the capacity to be aware of, control, and express one's emotions, and to handle interpersonal relationships judiciously and empathetically."

- It is managing your relationships and awareness in a positive and empathetic direction
- …Tapping into your instincts - being aware of your actions and managing relationships in a positive direction .
- This is a "win win" training for you and your staff
- Those trained in EI collect substantially more than those who are not.
- Whether it be an inhouse or conference setting pays for itself.
- This also shows your staff you believe in them enough to invest in them.
- Training allows each staff member to be conveying the same message to patients - a unified approach.
- Average collectors collect 83% of their goal.
- Well trained collectors collect 163% of their goal!

Standard practice policies

Although the last thing you ever want to tell a patient is *that it is our policy*, each staff member needs to be completely informed about policies as well is easily referenced when needed.

One thing that physicians can do now is to allow your collections and front desk staff to handle payment agreements. In other words, if a patient comes to you please refer them to the staff that you rely upon and support their policies to collect.

It is also most important for you to have an active part in defining those policies.

SEE "FINANCIAL TRANSPARENCY" AS A PATIENT WOULD

LOOKING AT FINANCIAL TRANSPARENCY FROM YOUR PATIENTS POINT OF VIEW, YOUR WEBSITE IS AN EXCELLENT PLACE TO START

- Perception is everything and 75% of your patients view your website before walking in your door.
- The goal for those in between the visit times, or at 3am; a marvelous way to introduce payment options for the patient that is tired of their bill and just wants to take care of it.
- Give them more power in decision-making

PROMPT PAY AND PAYER DISCLOSURE POLICIES

THIS DEPENDS OF COURSE UPON YOUR SPECIFIC CONTRACT WITH EACH INSURANCE COMPANY.

- Please check with your manager or other professional that may be handling your insurance contracts.
- Most contracts include these references…that you are only to collect certain amounts depending upon their policy,
- …And the second being that you are legally obliged to collect whatever you believe to be your portion at the time of the visit.
- Each payer has language similar to that reflecting how you may collect from patients.
- Most (99%) of your patients receive an explanation of benefits that lists your charge and what is allowed according to their specific plan.
- Because the patient sees this information, there should be no issue in your staff/ insurance office sharing numbers with them as it is inecitibly their portion to be remitted

PROMPT PAY DISCOUNTS AND THE OIG

THE OIG CONCLUDED THAT THE PROMPT PAY DISCOUNT IS UNLIKELY TO BE USED TO ENCOURAGE REFERRALS BUT RATHER IMPLEMENTED FOR THE PURPOSE OF IMPROVING BILLING COLLECTIONS.

- **FOR SELF PAY OR INSURANCES YOU ARE NOT ON CONTRACT WITH AND DISCOUNTS**
  - Should you? Yes, very carefully. Speak with your manager and healthcare professional about this.
- You can arrive at very comfortable amount that is a discount for the patient, you can you still cover a cost with administrative cost to build into your fee

PROMPT PAY DISCOUNTS AND THE OIG - WHAT IS LEGAL?

- Central to the analysis were the following elements of the prompt pay discount include:
- Patients were notified of the prompt pay discount during the course of the actual billing process.

- Please understand the billing process begins as you make that appointment and the receptionist says "I see that you have this insurance and your co-pay of this amount will be due at the time of check-in". That's the first time.
- This is clearly explained during/as a part of the billing process
- Third-party payors would be notified of the prompt pay discount.
- All costs associated with the arrangement would be borne by the health system.
- The prompt pay discount would be reasonably related to the amount of collection cost that would be avoided

Think about what you can do at your office considering the cost of collections. Offering a discounted range is a very attainable goal that is calculated according to your specific practice and population

WORKING WITH ADMINISTRATORS, MANAGERS AND STAFF USE SEVERAL CHANNELS OF COMMUNICATION

As you review your schedule to allow more time for working directly with managers and other staff

Members, what does your staff want? You! Just like your patients.

Give them 5 minutes and watch the confidence and pride rise!

- To consider? - How often will you meet with managers? At least monthly
- Have static meetings to keep each other informed about goals and objectives.
- Confirm standardized benchmarking measurements

Conversations and interaction that count quickly build relationships, credibility and comfort.

You can be in charge and be open

One tip? Communicate with asking open-ended questions in a non-threatening manner.

- A closed-ended question - "how much time do you spend reconciling daily cash flow?"
- Or…an open-ended question - not assuming anything - "tell me about how you reconcile cash flow?"
- "Help me understand" is a great phrase – inquires with acceptance
- These vital communications contribute to their performance and the practice's success

CLARIFY YOUR RCM PROCESS AND CONTINUALLY UPDATE PRACTICE WIDE POLICIES

Determine and confirm most important reports and favorites:

- Accounts receivables analysis – insurance & patient - insurers and patients AR with the aging of the debt.
- Time of service reports - reflects the front desk 100% collections potential compared to the amount actually collected
- Denial report - let the staff see most common claims issues and errors so they may correct!
- Provider productivity - offers the entire scope of types of visits, patient make up, cost, revenue etc.

Standard month end options

- Speak with your manager, accountant and vendors
- Always - charges, payments, new patients, provider productivity, time of service cost per patient, to start.
- There is such a thing as too much information- no one has time for all of those reports.
- Have a system that offers great reporting and a manager that is trained on and knows how to dig deep!
- Ask how you may personalize your reporting just as you can with EMR templates. Each product has options.
- At your office, speak with your manager and see which reports can be combined to give you more information and save time – a personalized dashboard so to speak!

Clarify Your RCM Process and Continually Update Practice Wide Policies

Benchmarking – gauge, measure and share

- Tracking success and points to improve
- Identify high deductible patients in PMS- to begin – all patients with HDHP to have HD at the end of the insurance code – then easy to track.

Refine A/R staff interaction policies

- Managers and staff to update physician to approve and finalize policy
- Physician always approves outside collections turnover
- Measure and reward success- bring out initiative and you

Collections

- Internal? Yes, at 30 or 45 days
- 30, 45 day letters and/or calls, then turn over? When? At 60 days
- Another option - send a letter at 45 days notifying patient. Give two weeks to respond to letter within two weeks.
- If uncollectable - place alert on patient

IDENTIFY YOUR OUTCOMES CONTINUALLY! CLARIFY, COMMUNICATE, CONFIRM, CONNECT CREATE A CULTURE THAT INSPIRES ENGAGEMENT AND PRIDE IN ADMINISTRATORS AND MANAGERS

If you want results, then offer staff the power to move forward and the tools they need…such as an additional screen at the front desk to help with patients as they would like to know more about their account.

- Poor communication creates or exacerbates problems.

Listen to and implement "small ideas"

- The 30 day rule
- Implementing these small ideas shows you are listening!
- "My way or the highway" causes two things: a decrease in productivity and an increase in useless activity.
- And your staff stops talking to you!
- For better communication, we become better listeners by hearing out and filtering ideas that can be easily implemented and have an impact..
- Your manager should make efforts to "communicate up," sharing what is on their minds and requesting help when needed.
- Identify your outcomes - establish clear goals and expectations with deadlines
- A team gathering at any point of the day is a good way to discuss the goals and challenges for the day.

PHYSICIAN/PRACTICE CHECKS AND BALANCES

Secure general practice internal checks and balances as you review internal controls

A major rule in business is to "protect your investments".
That means you, and of course, your practice.

ELIMINATE OPPORTUNITY

Who should receive what?

- Bank statements sent to someone other than the check writers.

What can be changed later in your system?

- E.G. Payee? Random audit of refunds
- Accounting software - can you change payee after check is written?

PHYSICIAN/PRACTICE CHECKS AND BALANCES

MEETING WITH YOUR MANAGER
SECURE GENERAL PRACTICE INTERNAL CHECKS AND BALANCES

- Physician and manager to review monthly numbers and activity together at least monthly
- Accounts payable weekly
- Sign off on daily reports too!
- Imperative to recognize patterns
- You can be your manager's check and balance.

PHYSICIAN/PRACTICE CHECKS AND BALANCES

SECURE GENERAL PRACTICE INTERNAL CHECKS AND BALANCES

Presence and communication at your front desk

- **Some start small – to the penny!**
- Think of how much $ your accounting staff handles every day!
- Only one person should have access to the receipts drawer where patient payments are placed.
- This drawer should to be locked at all times and money balanced upon every shift or employee change.

How physicians can keep abreast of practice finances

- **To audit - which reports?**
- One thing you can do is do random deposit audits of one days transactions. That would be totaling all of the payments received at the front desk and comparing them to what is applied to the account and the actual deposits. They should match.
- **One warning sign?** Patients begin to call stating that they pay their bill but they continue to get statements…they could be paying in cash and someone is not entering the payments.

WHAT CAN I DO NOW?

Proven suggestions and successes that can be immediately put to action.

- **EXPAND COMMUNICATION AND TRANSPARENCY**
  - Request time to meet with managers and staff
- **IMPROVE OPERATIONAL EFFICIENCIES**
  - Review job descriptions to reduce redundancies and increase your ROI
  - Make sure your website has your financial policies and language regarding high deductible plans
- **SHARE REPORTS WITH YOUR STAFF**
  - Let them feel the value of their role in the success of your practice!

WHAT CAN I DO NOW?

Proven suggestions and successes that can be immediately put to action.

NEVER DISCOUNT THE LOYALTY FACTOR

- If your staff and patients believe in you, then it will happen.
- Possibly in the end, this can help support the true patient physician relationship including financial health care decision-making so that all may concentrate on the care and healing.

I HOPE YOU ENJOYED THIS PRESENTATION AND FOUND THE INFORMATION USEFUL

We Covered

Introduction to health savings accounts and understanding your "consumer driven patient."

- 35 To 50% of your patient base typically have high deductible plans. They are savvy, they check out your website and many are already used to making their own healthcare decisions.

Improve revenue cycle processes and collections strategies that meet the distinctive needs of the high deductible patient.

- There are a plethora of plans out there for patients to work with. Credit card on hold, receiving electronic statements and other options make it approachable and predictable for both patients and the practice.

Physician/patient rapport – education and compliance measures

- Ask your vendors about what they may offer on patient education, compliance efforts and also offering statements in other languages.
- The doctor's approach to the patient should be not include financial agreements with patients.
- Please refer any financial conversations to the business office or manager for assistance.
- The staff to be aware of and educate your patients on safe harbor preventive screenings that declare zero dollars deductible…in other words no charge.

Cited examples of approaches that improve overall RCM performance, are fair and get your bill paid!

- Train your staff on collections especially from patients at the front desk with high deductible plans.
- Create scripts for staff to relay the same message
- Consider credit card on hold and other payment options.

How you can expand communication with managers and ensure secure financial checks and balances.

- Establish and maintain static meetings with your manager and staff.
- Review financial reports such as accounts receivable aging with a focus on patient balances and collections efforts.

RESOURCES

- CPA PROFESSIONAL ASSOCIATIONS
- MEDICAL SPECIALTY GROUPS AND SOCIETIES
- MEDICAL GROUP MEDICAL MANAGERS ASSOCIATION (MGMA)
- YOUR PEERS

SELF EVALUATION

High Deductible Patients: Optimizing Care and Collections

1. One characteristic of a high deductible patient is:

a. May seek other resources for care depending upon expense
b. He or she never worries about cost until receiving the bill
c. Patients with high deductible policies tend to have higher incomes.

2. T/F - In 2019, those age 55 and older can make an additional HSA contribution of $1,000 per year

3. With patients and benefits, the term “Safe Harbor” refers to:

a. The patient is not billed for services for 6 months
b. Zero dollars deductible for wellness checks and screenings
c. No deductible for the year.

4. Emotional Intelligence is:

a. To be aware of and control your actions, and being aware of other’s emotions around you.
b. Managing your relationships and awareness in a positive empathetic direction
c. Both A and B

5. According to a 2017 Kaiser Family Foundation survey, this % of high deductible enrollees report difficulty affording deductibles.

a. 20%
b. 46%
c. 70%

6. Approximately what % of patients with chronic conditions report delaying or avoiding care due to the high cost of care?

a. 33%
b. 20%
c. 15%

7. A most useful end of month report to reflect payer and patient amounts due is:

a. Insurance denials that are transferred to the patient
b. Accounts Receivable sorted by patient and payer categories, with aging of balances due
c. Month end net charges and payments

8. What percentage of high deductible health plan enrollees have a family member with a chronic condition and have real problems paying medical bills or other bills because of other healthcare costs?

a. 50%
b. 75%
c. 35%

9. The best way to introduce a new financial policy is:

a. The front desk introduces verbally to each patient as they check in.
b. The policy is introduced in writing and on your website so patients may approach the office staff with questions, and prepared for the next appointment/visit.
c. Patients are mailed information.

Answer Key: 1. A, 2. T, 3. B, 4. C, 5. B, 6. A, 7. B, 8. A, 9. B

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Barry A. Franklin, PhD
Director of Preventive Cardiology and Cardiac Rehabilitation

Interpreting the Conventional Exercise Stress Test

Mining Exercise Test Responses: Beyond Ischemic ST-Segment Depression…

"Variables with demonstrated prognostic value beyond ST-segment depression, include: anginal symptoms, functional capacity (peak METs, VE/VCO2 slope) chronotropic response, exertional hypotension, heart rate recovery, bundle branch block, dyspnea, frequent ventricular ectopy during exercise and in recovery, and treadmill scores."

Objectives of Exercise Testing

- To aid in the diagnosis of hidden or latent coronary artery disease;
- To evaluate cardiopulmonary fitness;
- To establish the safety of vigorous exercise;
- To formulate an effective exercise prescription; and,
- To assess work-related capabilities.

Identifying the Person "At Risk"

Symptomatic Coronary Artery Disease in a Marathon Runner

LCDR Jeffrey B. Handler, MC, USNR; LCDR Ronald W. Asay, MC, USNR; LCDR Sanford E. Warren, MC, USNR; LCDR Peder M. Shea, MC, USNR

• **A highly trained marathon runner had progressive angina pectoris. His exercise stress test showed ischemia, and selective coronary angiography demonstrated a 99% obstruction of the left anterior descending coronary artery. A lipid analysis revealed normal total serum cholesterol levels with elevated high-density lipoprotein and markedly decreased low-density lipoprotein fractions. The remaining risk factors for coronary artery atherosclerosis were also absent. Unlike previous reports of ischemic heart disease in runners, in which the level of conditioning has been low, the duration of running brief, the risk factors operative, or the documentation weak, this patient represents unequivocal evidence that a long-distance marathon runner's life-style is not necessarily protective against the progression of coronary atherosclerosis.**
(*JAMA* 1982;248:717-719)

RUNNING is believed by some to protect against the development of coronary artery disease and its ischemic consequences.[1] This has been termed the "exercise hypothesis."[2] Others claim that exercise is not protective and may even be injurious.[3] Subjects who have been highly trained over a long period are scarce, and few data regarding the prevalence of coronary artery disease in this population exist. We report a case of severe coronary disease in a superbly trained athlete with no known risk factors for development of cardiovascular disease.

Report of a Case

A 48-year-old man had a one-month history of exertional chest pain. The pain was reproducible by moderate exertion and rapidly relieved by rest. On evaluation, his chest pain syndrome was thought to be consistent with stable exertional angina, and treatment with propranolol hydrochloride and isorbide dinitrate was begun. His exercise tolerance was only mildly improved, and he continued to have exertional angina.

The patient had been active in competitive athletics since childhood and had begun a vigorous running program approximately eight years previously. During this time he averaged 50 to 60 miles per week of running at an eight-minute-per-mile pace, increasing his distance to more than 70 miles per week during periods when he was in training for marathon competitions. He had successfully completed seven marathons and had competed frequently at other distances ranging from 10 km to a 52-mile ultramarathon. He usually finished in the top 10% in his age group. He had never previously experienced chest pain, shortness of breath, or any cardiorespiratory symptoms. Review of cardiac risk factors di

JAMA 1982;248[6]:717

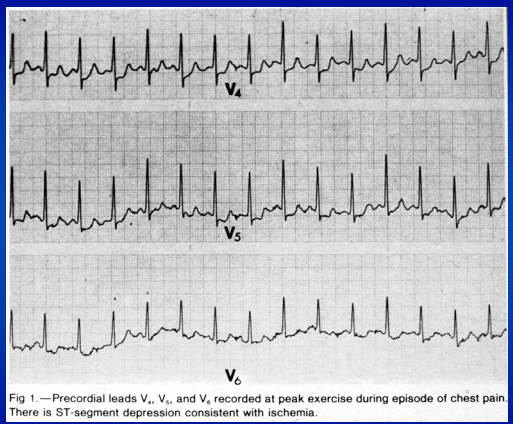


Fig 1.—Precordial leads V_4, V_5, and V_6 recorded at peak exercise during episode of chest pain. There is ST-segment depression consistent with ischemia.

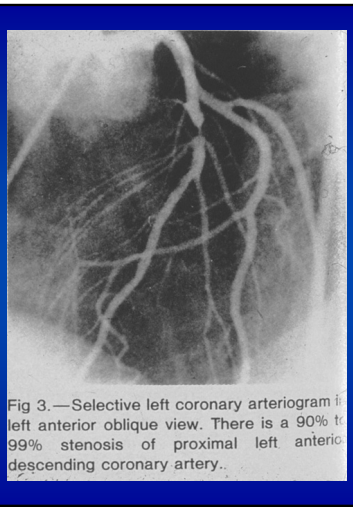


Fig 3.—Selective left coronary arteriogram i left anterior oblique view. There is a 90% t 99% stenosis of proximal left anteric descending coronary artery..

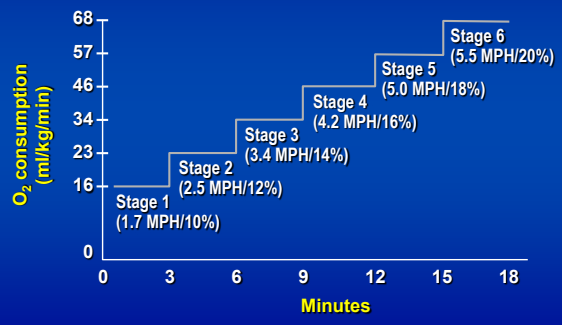
Selection of the Appropriate Exercise Test Protocol

The exercise component of symptom-limited exercise tests should ideally last 9-12 minutes. Protocols that increase by 1 MET/stage (e.g., Balke, Naughton) are appropriate for high risk patients with functional capacities of < 7 METs; metabolic demands of ≥ 2 METs/stage (e.g., Bruce) may be appropriate for low - intermediate risk patients with functional capacities > 7 METs.

The Rule of 2 and 3 mph: At 0% grade (on the level), these speeds correspond to 2 and 3 METs, respectively

At a 2-mph walking speed, each 3.5% increase in treadmill grade adds approximately 1 MET to the gross energy cost. For patients who can negotiate a faster walking speed (3-mph), recognize that each 2.5% increase in treadmill grade adds an additional MET to the gross energy expenditure.

Bruce Treadmill Protocol: For Some Patients, an 'Uphill Climb'



Symptom-Sign Limited Testing Endpoints – When to stop ?

- Dyspnea, fatigue, chest pain (>2/4; moderate+)
- Systolic blood pressure drop (>10 mmHg)
- ECG--ST changes (> 2mm), arrhythmias
- Volitional fatigue (patient request)
- Borg Scale (17 or greater) and/or >100% age-predicted HRmax using the formula (220-age)

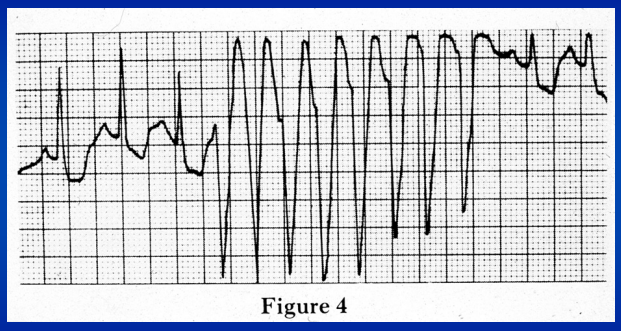
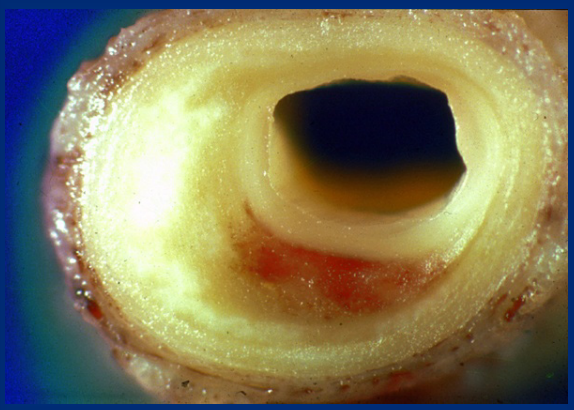
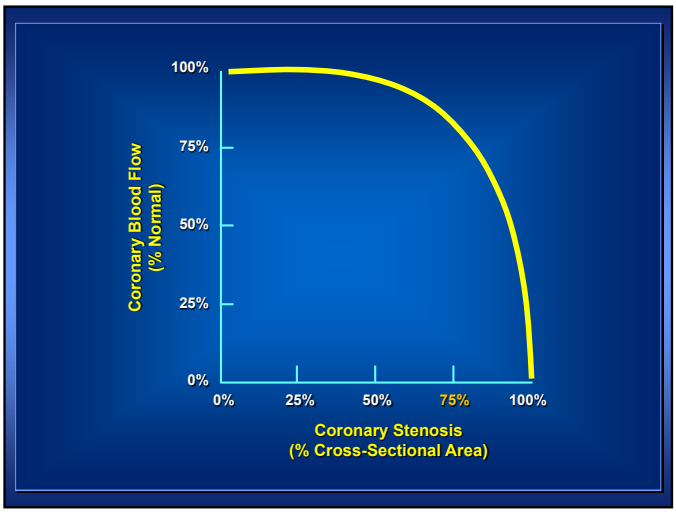


Figure 4

ECG INTERPRETATION



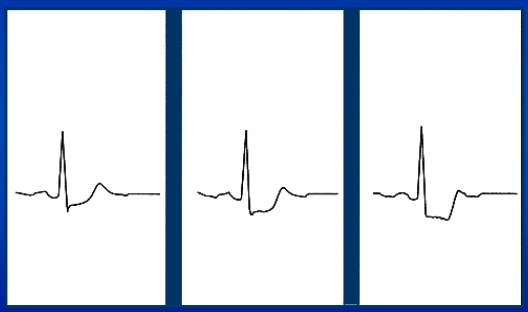


Atherosclerosis

CAD: Ischemic Cascade

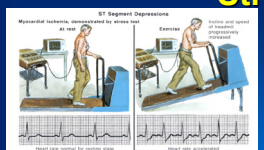
- **Myocardial Ischemia - temporary lack of oxygen to the myocardium**
- **Ischemia (oxygen imbalance) leads to:**
  - **→ cellular membrane and electrolyte flux abnormalities**
  - **→ relaxation failure**
  - **→ wall contraction abnormalities**
  - **→ increased LV filling pressures**
  - **→ ST segment shifts (not always)**
  - **→ [hypotension (if severe, global)]**
  - **→ with or without (35% of the time) angina (lies at the end of the ischemic cascade)**

Traditional: ST Response

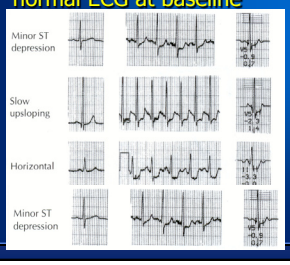


Stress Test

ECG

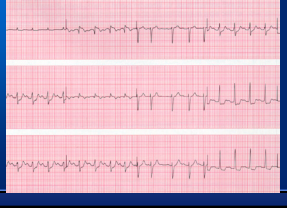


Use when intermediate risk and normal ECG at baseline



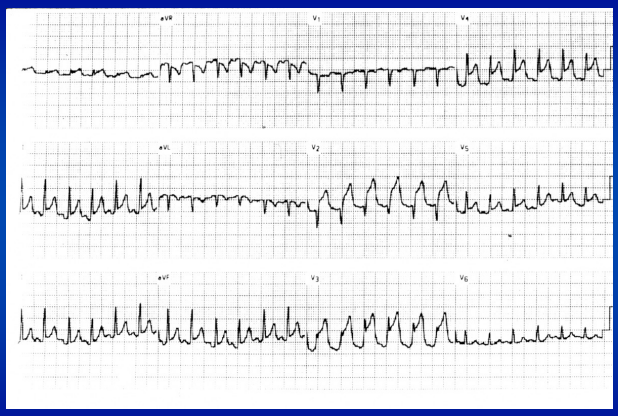
Positive test more likely if:

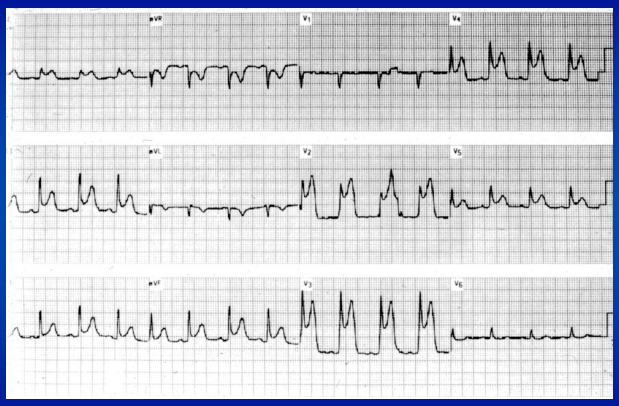
- More ST depression
- Shorter test duration or ischemia indicator(s) occur at low HR or work rate
- Longer recovery to baseline*
- Angina is associated
- All of these are associated with poor prognosis



ST-Segment Elevation

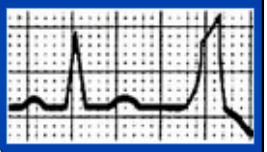
Exercise-induced ST-segment elevation in leads displaying a previous Q-wave infarction almost always reflects an aneurysm or a wall motion abnormality. In the absence of significant Q-waves, exercise-induced ST-segment elevation is often associated with a fixed, high-grade coronary stenosis.





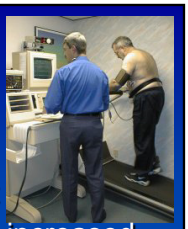
Exercise-Induced PVCs: The Paris Prospective Study

- 6,101 French men (42 to 53 years) without known or suspected CVD underwent GXT.
- After a 23-year follow-up, exercise-induced myocardial ischemia and frequent PVCs during /after exercise were independently associated with an increased cardiovascular mortality with similar relative risks (2.6 and 2.5, respectively).



Jouven X et al. NEJM 2000;343:862
Jouven X et al. NEJM 2003;348:2357

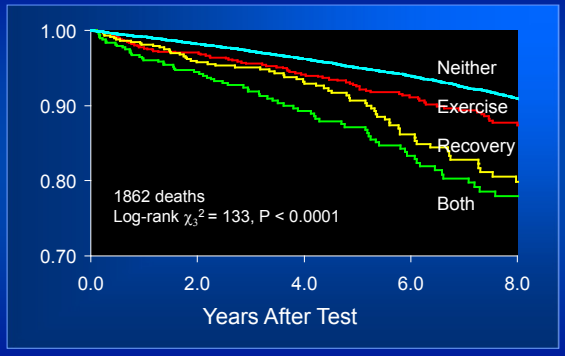
Frequent Ventricular Ectopy After Exercise Testing*



During a 5-year follow-up, frequent PVCs during exercise predicted an increased risk of death (9% vs 5% among patients without frequent ventricular ectopy during exercise), but frequent ventricular ectopy during recovery was a stronger predictor (11% vs 5%)

**Frolkis JP et al. NEJM 2003;348:781*

Ventricular Ectopic Activity



Frolkis JP, Lauer MS, N Engl J Med 2003;781-90.

CLINICAL STUDIES

Complete Bundle Branch Block as an Independent Predictor of All-Cause Mortality: Report of 7,073 Patients Referred for Nuclear Exercise Testing

Barbara Hesse, MD, Lazaro A. Diaz, MD, Claire E. Snader, MA, Eugene H. Blackstone, MD, Michael S. Lauer, MD

PURPOSE: Complete left bundle branch block is a well-established independent risk factor for mortality, but the prognostic importance of right bundle branch block is unclear. We determined whether left and right bundle branch block was associated with all-cause mortality risk after adjustment for potential confounders, including clinical, exercise, and nuclear scintigraphic variables.

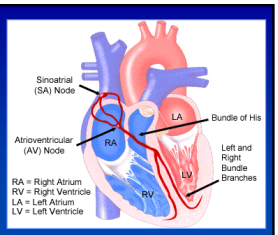
SUBJECTS AND METHODS: We studied 7,073 adults who were referred for symptom-limited nuclear exercise testing. Patients with heart failure or pacemakers were excluded. The presence or absence of bundle branch block was determined from resting electrocardiograms. The main outcome measure was all-cause mortality during a mean of 6.7 years of follow-up.

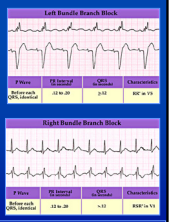
RESULTS: One hundred ninety patients (3%) had complete right bundle branch block, and 150 (2%) had complete left bundle branch block. There were 825 deaths (12%). Mortality was greater in patients with complete right bundle branch block (24% [46 of 190]) or left bundle branch block (24% [36 of 150]) than in those without these findings (11% [779 of 6,883 and 789 of 6,923, respectively]; both $P < 0.0001$). After adjustment for potential confounders, right bundle branch block was as strong an independent predictor of mortality (hazard ratio [HR] 1.5; 95% confidence interval [CI]: 1.1 to 2.1; $P = 0.007$) as left bundle branch block (HR 1.5; 95% CI: 1.0 to 2.0; $P = 0.017$). Incomplete right bundle branch block was not associated with mortality.

CONCLUSION: Complete right and left bundle branch block are independent predictors of all-cause mortality risk even after adjustment for exercise capacity, nuclear perfusion defects, and other risk factors. Am J Med. 2001;110:253–259.

Bundle Branch Block

- 7,073 adults with suspected CAD who were referred for nuclear exercise testing and followed for ~ 7 years.
- After adjustment for potential confounders, complete bundle branch block (right or left) remained associated with a 50% greater risk of death.





* Determined from the resting ECG
** Hesse B et al. Am J Med 2001;110:253

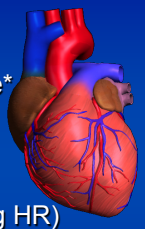
Chronotropic Incompetence: History of the Concept*

In the early 1970's, Ellestad tested a 50-year-old man who had a good exercise tolerance and no ST ↓ or angina but was only able to reach a maximum heart rate of 110 bpm. The patient attributed his blunted heart rate response to his athletic background. Shortly thereafter he died suddenly, and the autopsy revealed severe CAD.

*Ellestad MH. Circ 1996;93:1485

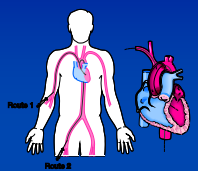
Chronotropic Incompetence

- Achievement of target HR based on age* < 85% of (220 – age)
- Proportion of HR reserve used**
  (Peak HR-resting HR) / (220-age-resting HR)
  Value of ≤ 0.80 indicates higher risk (severe CAD)
  Value of ≤ 0.62 indicates higher risk for patients on beta blockers



* Balady GJ et al. Circ 2004;110:1920
** Lauer MS et al. Circ 1996;93:1520

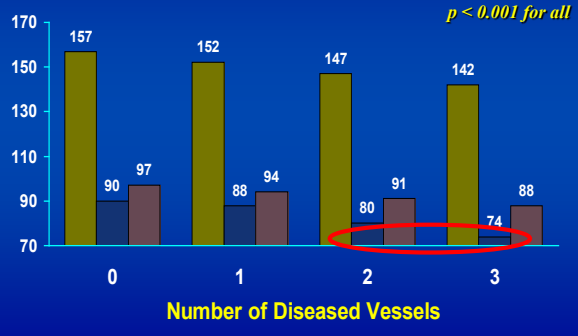
Chronotropic Response to Exercise Predicts Angiographic Severity of CAD*



475 consecutive patients ≥ 30 years old with suspected or stable CAD who underwent coronary angiography within 180 days of symptom-limited exercise testing

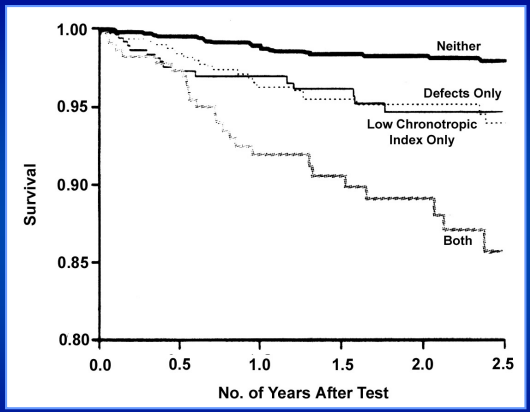
*Brener SJ et al. AJC 1995;76:1228

CHRONOTROPIC RESPONSE TO EXERCISE



The chronotropic response to exercise predicts the presence and angiographic severity of coronary disease. This association is likely related to the proportion of left ventricular myocardium rendered ischemic during stress.

Brener SJ et al. AJC 1995;76:1228



Lauer MS et al. JAMA 1999;281:524

BLOOD PRESSURE RESPONSES

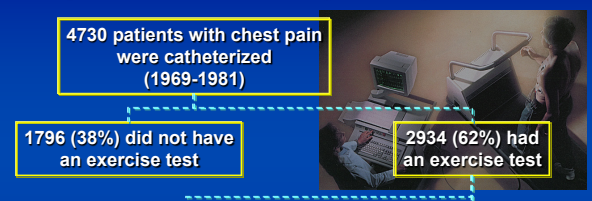
Relation Between Maximal Exercise Systolic Pressure and Annual Rate of Sudden Cardiac Death*

Maximal Systolic Pressure, mmHg	Annual Rate of Sudden Death, Per 1,000
< 140	97.0
140 - 199	25.3
> 200	6.6

** Irving JB et al. AJC 1977;39:841*

TREADMILL SCORES

Exercise Treadmill Score for Predicting Prognosis in Coronary Artery Disease*



4730 patients with chest pain were catheterized (1969-1981)

1796 (38%) did not have an exercise test

2934 (62%) had an exercise test

2842 patients (final study population)

70% Male
Mean age = 49 yrs

92 excluded for un-interpretable ECGs

Follow-up (5 yr. median)

**Mark DB et al. Ann Intern Med 1987;106:793*

Prognostic Variables → Treadmill Exercise Score*

The largest net ST-segment displacement (↓ or ↑) recorded during exercise in the 12-lead ECGs proved to be the single most important variable for predicting prognosis.

After adjusting for this using the Cox model, only 2 other variables contained additional prognostic information: the treadmill angina index and treadmill exercise time (Bruce protocol).

** Of the 2842 pts, 1422 were used to develop the score and 1420 provided an independent validation sample.*

Duke Treadmill Exercise Score

(Exercise Duration) - (5 x ST_{max}) - (4 x Angina Index)

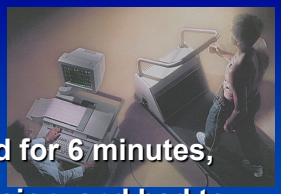
Angina Index:
0 = no angina during exercise
1 = non-limiting angina
2 = limiting angina

Low risk score: ≥ +5
Intermediate risk score: -10 to +4
High risk score: < -11

Mark DB, et al. Ann Intern Med. 1987;106:793-800

A patient who exercised for 9 minutes, without ST depression or angina would have a treadmill score of + 9:

+ 9 - [5 x 0] - [4 x 0] = + 9



A patient who exercised for 6 minutes, had 2 mm of ST depression, and had to stop exercising because of angina, would have a treadmill score of - 12:

+ 6 - [5 x 2] - [4 x 2] = - 12

Relationship of the Treadmill Score to Survival Rates*

Risk	(n)	Treadmill Score	5-Year Survival Rate (%)
High	377	- 11 or lower	72
Moderate	1497	- 10 to + 4	91
Low	968	+ 5 or greater	97

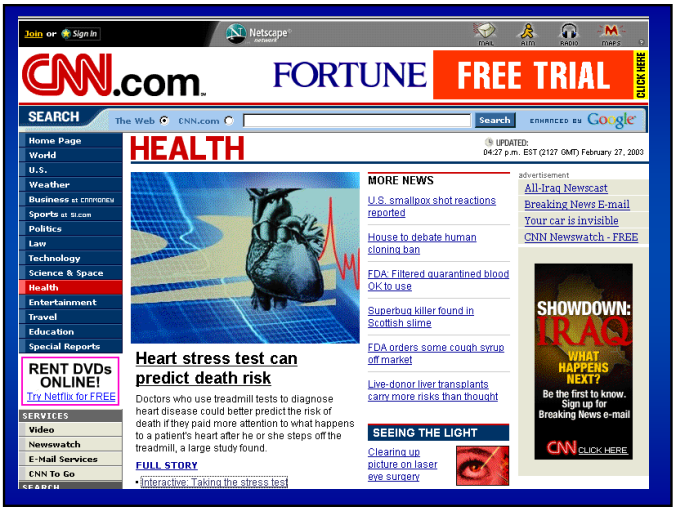
** Mark DM et al. Ann Intern Med 1987;106:793*

Risk Stratification: Implications Using the Duke Treadmill Score

"Treadmill scores can help to determine the type and advisability of further testing. For example, low-risk patients could be spared from additional studies, high-risk patients would undergo coronary angiography, and intermediate-risk patients would have additional diagnostic tests. Thus, for patients identified as either low- or high-risk, treadmill scores render additional noninvasive testing unnecessary."

Victor F. Froelicher, MD

HEART RATE RECOVERY



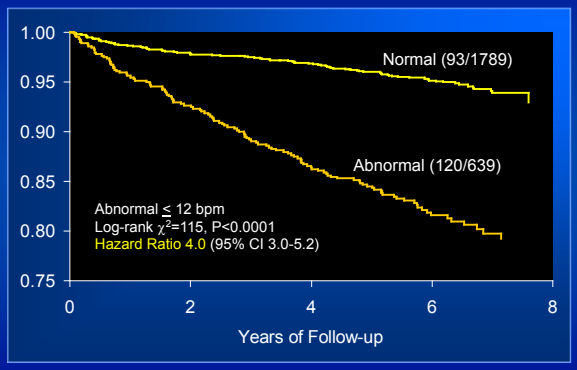
Heart-Rate Recovery Immediately After Exercise As A Predictor of Mortality*

- 2428 adults (57 ± 12 yrs, 63% men)
- Symptom-limited GXT + thallium MPI
- 6-year follow-up → 213 deaths
- An abnormal 1-min value for the recovery heart rate was defined as a reduction of:

12 beats/min or less from the peak heart rate

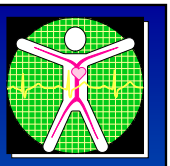
**Cole CR et al. NEJM 1999;341:1351*

Heart Rate Recovery and Mortality



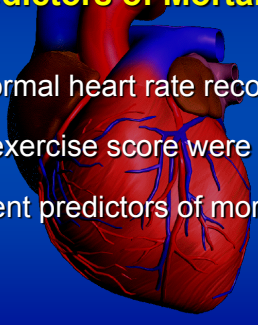
Cole, Lauer. N Engl J Med 1999;341:1351

Conclusion



A delayed decrease in the heart rate during the first minute after graded exercise, which may be a reflection of decreased vagal activity, is a powerful predictor of overall mortality, independent of workload, the presence or absence of myocardial perfusion defects, and changes in heart rate during exercise.

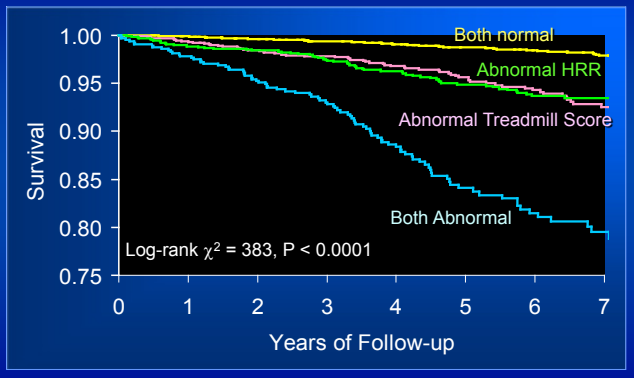
Heart Rate Recovery and Treadmill Exercise Score as Predictors of Mortality*



Both abnormal heart rate recovery and treadmill exercise score were independent predictors of mortality.

**Nishime EO et al. JAMA 2000;284:1392*

HRR and Duke Exercise Score



Nishime, Lauer, JAMA 2000;284:1392-1398

MET Capacity: An Underutilized Prognostic Indicator

Exercise capacity is a stronger predictor of mortality than established risk factors of hypertension, smoking, and diabetes, and stress testing parameters of ST-segment depression, peak HR, or arrhythmias during exercise

Myers, J. Circulation 2003;107:e2-e5

Clinical Investigation and Reports

Exercise Capacity and the Risk of Death in Women
The St James Women Take Heart Project

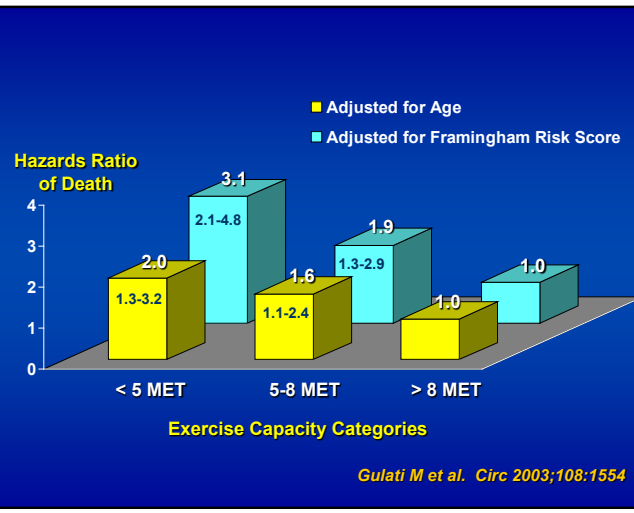
Martha Gulati, MD, MS; Dilip K. Pandey, PhD; Morton F. Arnsdorf, MD; Diane S. Lauderdale, PhD; Ronald A. Thisted, PhD; Roxanne H. Wicklund, RN; Arfan J. Al-Hani, MD†; Henry R. Black, MD

Background—Cardiovascular disease is the leading cause of death among women and accounts for more than half of their deaths. Women have been underrepresented in most studies of cardiovascular disease. Reduced physical fitness has been shown to increase the risk of death in men. Exercise capacity measured by exercise stress test is an objective measure of physical fitness. The hypothesis that reduced exercise capacity is associated with an increased risk of death was investigated in a cohort of 5721 asymptomatic women who underwent baseline examinations in 1992.

Methods and Results—Information collected at baseline included medical and family history, demographic characteristics, physical examination, and symptom-limited stress ECG, using the Bruce protocol. Exercise capacity was measured in metabolic equivalents (MET). Nonfasting blood was analyzed at baseline. A National Death Index search was performed to identify all-cause death and date of death up to the end of 2000. The mean age of participants at baseline was 52±11 years. Framingham Risk Score–adjusted hazards ratios (with 95% CI) of death associated with MET levels of <5, 5 to 8, and >8 were 3.1 (2.0 to 4.7), 1.9 (1.3 to 2.9), and 1.00, respectively. The Framingham Risk Score–adjusted mortality risk decreased by 17% for every 1-MET increase.

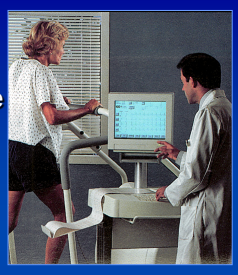
Conclusions—This is the largest cohort of asymptomatic women studied in this context over the longest period of follow-up. This study confirms that exercise capacity is an independent predictor of death in asymptomatic women, greater than what has been previously established among men. The implications for clinical practice and health care policy are far reaching. **(*Circulation*. 2003;108:1554-1559.)**

Key Words: exercise ■ epidemiology ■ mortality ■ women



Gulati M et al. Circ 2003;108:1554

Exercise capacity is a strong independent predictor of all-cause death in asymptomatic women, after adjusting for traditional cardiac risk factors.



For each 1-MET increase in exercise capacity, there was a 17% reduction in mortality rate.

Gulati M et al. Circ 2003;108:1554

Exercise Physiology

Importance of Treadmill Exercise Time as an Initial Prognostic Screening Tool in Patients With Systolic Left Ventricular Dysfunction

Eileen Hsich, MD; Eiran Z. Gorodeski, MD, MPH; Randall C. Starling, MD, MPH; Eugene H. Blackstone, MD; Hemant Ishwaran, PhD; Michael S. Lauer, MD

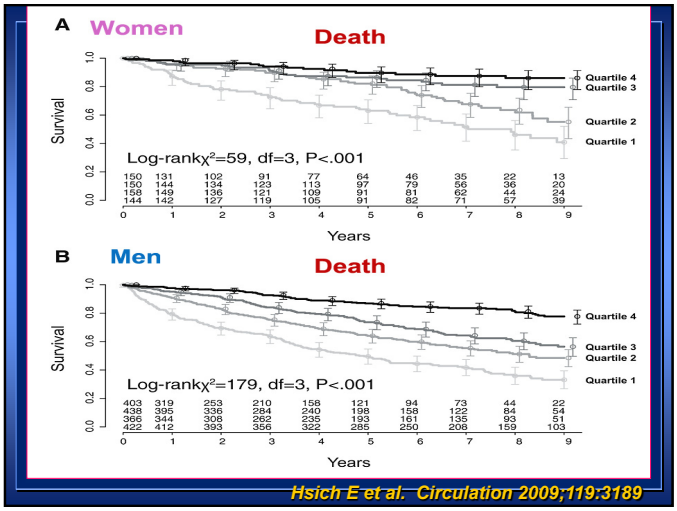
For a 1-minute decrease in exercise time, there was a 7% increased hazard of death (eg, comparing 480 to 540 seconds, hazard ratio = 1.07, 95% confidence interval 1.02 to 1.12, P=0.004)

2.75, $P=0.03$; for prediction of the composite outcome, 1.75, 95% confidence interval 1.15 to 2.66, $P=0.009$). For a 1-minute change in exercise time, there was a 7% increased hazard of death (eg, comparing 480 to 540 seconds, hazard ratio =1.07, 95% confidence interval 1.02 to 1.12, $P=0.004$).

Conclusions—Because cardiopulmonary stress testing is not available in every hospital, treadmill exercise time with a modified Naughton protocol may be of value as an initial prognostic screening tool. **(*Circulation*. 2009;119:3189-3197.)**

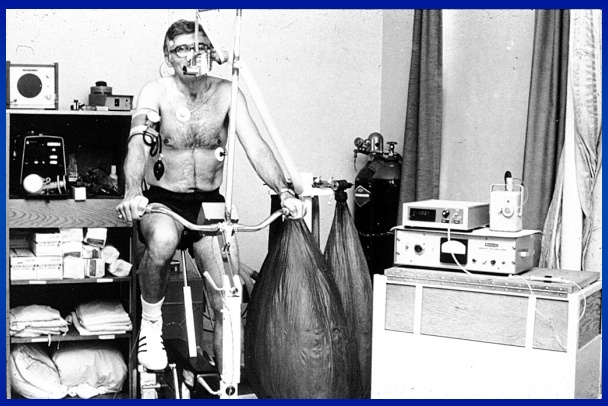
Key Words: heart failure ■ exercise ■ sex ■ prognosis

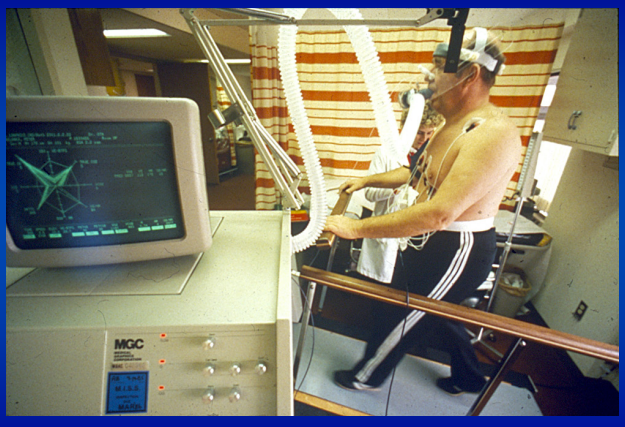
Circulation 2009;119:3189-3197



Hsich E et al. Circulation 2009;119:3189

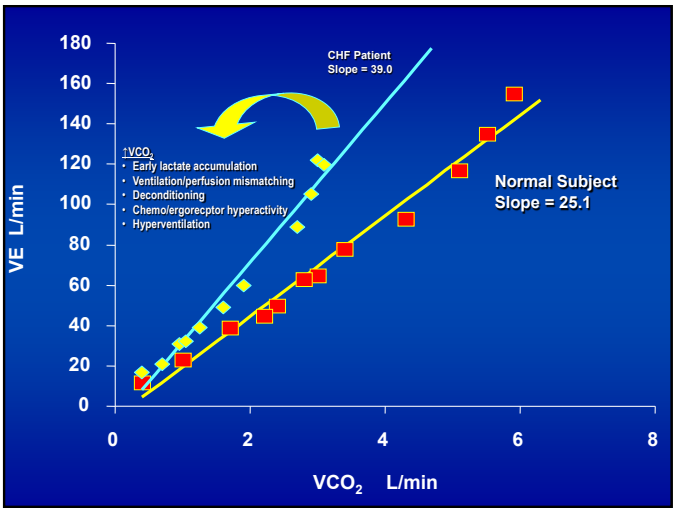
CARDIOPULMONARY EXERCISE TESTING

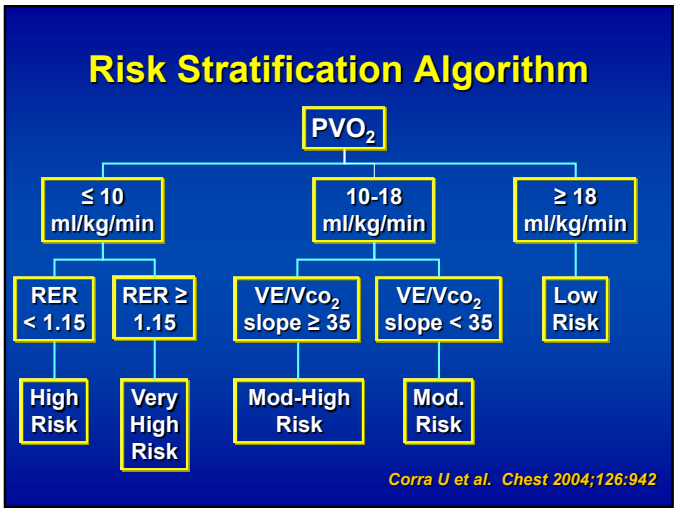




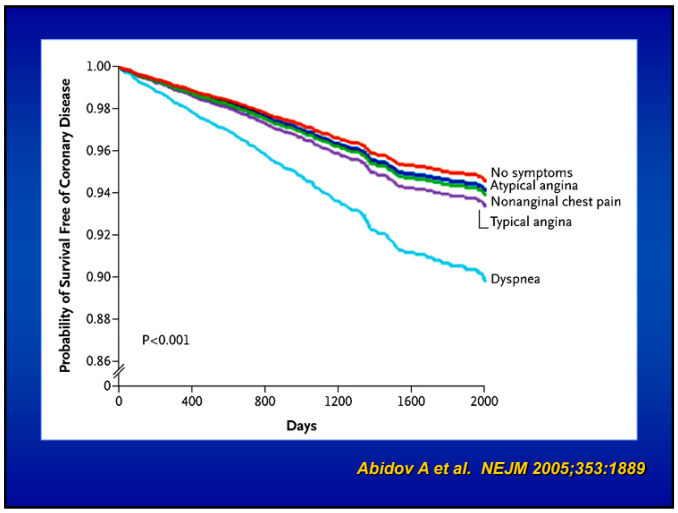
Cardiopulmonary Exercise Testing Predictors of Risk Other Than Peak VO_2

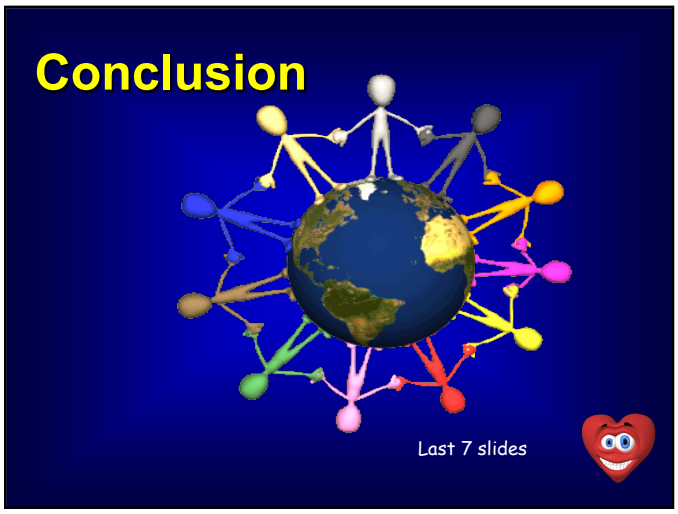
- VE/VCO_2 slope (> or = 35)
- Oxygen uptake efficiency slope (OUES)
- VO_2 kinetics
- Anaerobic or ventilatory threshold
- End-tidal CO_2 pressure at rest and exercise
- VO_2 in recovery
- Exercise periodic (oscillatory) breathing during exercise
- Multivariate scores – including historical, pre-test, cardiopulmonary, and hemodynamic data (including heart rate recovery and chronotropic incompetence)

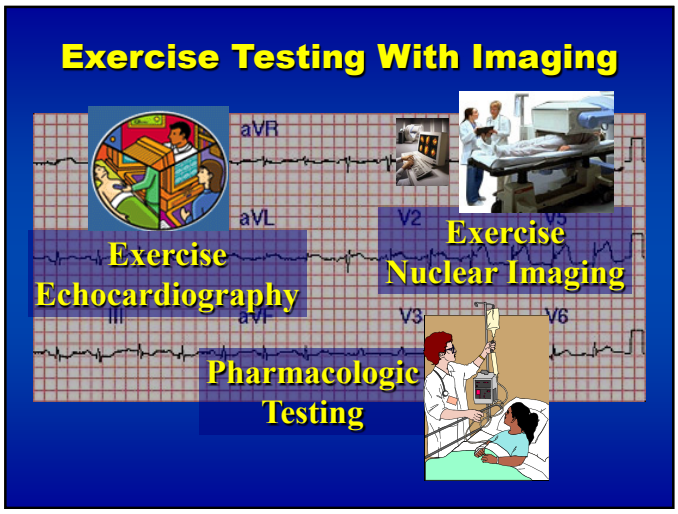

CHF Patient
Slope = 39.0
↑VCO2
• Early lactate accumulation
• Ventilation/perfusion mismatching
• Deconditioning
• Chemo/ergoreceptor hyperactivity
• Hyperventilation
Normal Subject
Slope = 25.1
VE L/min
VCO2 L/min
180
160
140
120
100
80
60
40
20
0
0
2
4
6
8


Risk Stratification Algorithm
PVO2
≤ 10 ml/kg/min
10-18 ml/kg/min
≥ 18 ml/kg/min
RER < 1.15
RER ≥ 1.15
VE/Vco2 slope ≥ 35
VE/Vco2 slope < 35
Low Risk
High Risk
Very High Risk
Mod-High Risk
Mod. Risk
Corra U et al. Chest 2004;126:942

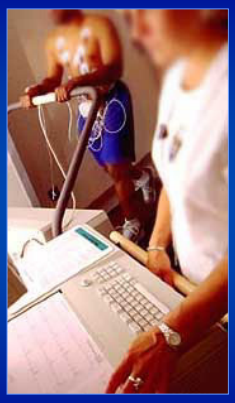

DYSPNEA AND
CARDIAC PROGNOSIS


Probability of Survival Free of Coronary Disease
1.00
0.98
0.96
0.94
0.92
0.90
0.88
0.86
0
0
400
800
1200
1600
2000
Days
No symptoms
Atypical angina
Nonanginal chest pain
Typical angina
Dyspnea
P<0.001
Abidov A et al. NEJM 2005;353:1889


Conclusion
Last 7 slides


Exercise Testing With Imaging
Exercise Echocardiography
Exercise Nuclear Imaging
Pharmacologic Testing

The limited sensitivity and specificity of standard exercise ECG testing for the detection of CAD have stimulated increased use and development of non-invasive stress imaging technologies. An alternative to the use of more expensive tests is the more efficient use of available low-cost data.



Take Home Messages

- Beyond ST-depression and MPI, non-ECG variables can provide considerable diagnostic/prognostic information
- A blunted exercise heart rate and/or systolic blood pressure response suggests a poorer prognosis
- Cardiorespiratory fitness, expressed as METs, is inversely related to all-cause and cardiovascular mortality (ie., each 1-MET increase in fitness is associated with a 15-20 percent [%] decrease in mortality)

Take Home Messages

- Resting bundle branch block (right or left), frequent exercise-induced PVCs, especially in recovery, and dyspnea are associated with a poorer prognosis
- The Duke Treadmill Score (low, moderate, or high risk) represents a major advance in exercise testing
- The value of routine exercise testing to identify occult coronary artery disease in asymptomatic persons remains controversial

SELF EVALUATION

Interpreting the Conventional Exercise Stress Test

1. According to the AHA/ACC Guidelines, protocol selection for treadmill exercise testing is critically important. If the evaluation is not terminated due to volitional fatigue, the duration of the stress test should ideally last _____ minutes.

a. 3-5
b. 5-7
c. 9-12
d. 13-15
e. None of the above

2. If you are conducting a graded exercise treadmill test, and want to start the patient at a 3-metabolic equivalent (MET) workload, what grade and/or speed would you select?

a. 1.0 mph, 0% grade
b. 2.0 mph, 0% grade
c. 2.0 mph, 3.5% grade
d. 3.0 mph, 0% grade
e. Two of the above

3. Stage 2 of the conventional Bruce treadmill protocol, that is, 2.5 mph, 12% grade, when performed for 3 minutes, approximates an energy requirement of ____ metabolic equivalents (METs).

a. 3.5
b. 5.5
c. 7.0
d. 9.5
e. 12.0

4. Which of the following would not be a reason to terminate a progressive exercise stress test?

a. ≥ 2 mm ST-segment depression
b. Exercise-induced ventricular tachycardia
c. Exertional hypotension (> 20 mmHg drop in SBP)
d. Perceived exertion (>15 – signifying 'hard work')
e. Two of the above

5. The annual rate of sudden cardiac death, per 1,000, for a patient who demonstrates a markedly blunted systolic blood pressure response (<140 mmHg) to maximal exercise testing is _____?

a. 150.0
b. 97.0
c. 25.3
d. 6.6
e. None of the above

6. An abnormal 1-minute value for the recovery heart rate from maximal exercise stress testing is defined as a reduction of _____ or less from the peak or maximal heart rate.

a. 12 beats/min
b. 15 beats/min
c. 18 beats/min
d. 21 beats/min
e. None of the above

7. T/F - Complete right or left bundle branch block as determined from the resting electrocardiogram, prior to exercise testing, are associated with a higher risk of subsequent all-cause mortality, even after adjusting for potential confounders.

Answer Key: 1. C, 2. E, 3. C, 4. D, 5. B, 6. A, 7. T

FACULTY

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Sleep Disorders and their Management

Contents

- The burden and prevalence of sleep disorders
- Recent insights on the functions of sleep
- The patient who can't fall asleep: A clinical approach for insomnia
- Snoring and sleep apnea: Finding treatments that work for patients and bedpartners
- Sleepwalking and dream enactment: Common parasomnias and what to know about them

The burden of sleep disorders

- Inadequate and poor-quality sleep is ubiquitous
  - Modern life has been structured so that sleep is dispensable
  - Exogenous light exposure is disrupting to natural circadian rhythms.
  - The most common consumed drug (caffeine) is self medication on global scale.
- Consequences
  - Sleepiness and impaired performance
  - Cardiovascular disease
  - Mental illness
  - Impaired brain development in children
  - Dementia and malignancy

(Institute of Medicine 2006, NSF 2014, Wheaton et al 2013, Wickwire et al 2016)

The prevalence and costs of sleep disorders

- Sleep deprivation
  - 50-70 million Americans
- Insomnia
  - 30% of American adults have intermittent insomnia
  - 15% have chronic insomnia
  - Direct health care costs-$3 billion
  - Indirect costs US Economy-$32 billion

(Institute of Medicine 2006, NSF 2014, Wheaton et al 2013, Wickwire et al 2016)

The prevalence and costs of sleep disorders

- Obstructive Sleep Apnea as noted by sleep study
  - 34% of adult men
  - 17% of adult women
- Obstructive Sleep Apnea Syndrome
  - 14% of adult men
  - 5% of adult women
  - Direct health care costs-$6 billion
  - Indirect costs US economy-84 billion
    - Indirect health care costs $60 billion
    - OSA related motor vehicle accidents-$14 billion
    - Absenteeism $10 billion

(McKinsey 2010, NSF 2014, ICSD 2014, Wickwire et al 2016)

The prevalence of sleep disorders

- Restless Legs Syndrome
  - 5% general population
- REM sleep Behavior Disorder-dream enactment
  - 1% General Population
  - 5% Elderly
- 1 out of every 25 drivers admit to having dozed off in the last month while driving.
- 20% of adolescent's have chronic excessive daytime sleepiness.

(ICSD 2014, Howell 2020)

Recent insights on the functions of sleep

Adaptive Inactivity

Memory Consolidation

Synaptic Homeostasis

Replenish CNS ATP

Toxic Clearance

Functions of Sleep

Adaptive Inactivity	Adaptive Inactivity
Memory Consolidation	Memory Consolidation
Synaptic Homeostasis	**Synaptic Homeostasis**
Replenish CNS ATP	Replenish CNS ATP
Toxic Clearance	Toxic Clearance

(Abel et al 2013)

Functions of Sleep

Adaptive Inactivity	Adaptive Inactivity
Memory Consolidation	Memory Consolidation
Synaptic Homeostasis	Synaptic Homeostasis
Replenish CNS ATP	Cortical Development
Toxic Clearance	**Toxic Clearance**

(Landolt 2008)

Insomnia: a common clinical presentation

- 5.5 million office visits annually
- Growth in sedative medication prescriptions
  - 1999-5.3 million
  - 2010-20.8 million
    - 55% of whom were on 2 or >
    - 25% on an opioid as well
- Daytime consequences
  - Chronic Insomnia (15% of American adults) have daytime dysfunction from insomnia.
    - Hyperarousal 24 hours a day
    - Anxiety and mood disruption
    - Poor working memory

(Roth 2007, Ford et al 2014)

Insomnia: more then a nighttime problem

- Daytime consequences
  - Chronic Insomnia (15% of American adults) have daytime dysfunction from insomnia.
    - Hyperarousal 24 hours a day
    - Anxiety and mood disruption
    - Poor working memory
    - Impaired emotional facial recognition
- Prospective studies-insomnia at baseline predicts:
  - Pediatric population
    - Anxiety mood and attention disorders
    - Oppositional defiant disorder
  - Adult population
    - Stroke-particularly stroke in the young adult
    - Cognitive decline

(Shekleton et al 2014, Kyle et al 2014, Fortier-Brochu et al 2014)

Insomnia: more then a nighttime problem

- Insomnia trap
  - Impaired mood caused by a poor night of sleep.
  - Growing anxiety over the course of a day regarding impending inability to fall asleep at night.
  - Nighttime hypervigilance makes it more difficult to fall asleep.
- Frustrated patients looking for a solution

When to prescribe a sedative?

- Insomnia is often chronic
- Benzodiazepines (BZDs) and Benzodiazepine Receptor Agonists (BRAs) have concerning adverse effects side effects.
- Sedating psychotropic medications (trazodone, quetiapine, mirtazapine) minimal safety data in a non-psychiatric population
  - Short term efficacy-modest
  - Long term efficacy-absent

(Mendelson et al 2005, Rosenberg et al 2006)

JCSM
Journal of Clinical Sleep Medicine

SPECIAL ARTICLES

Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia in Adults: An American Academy of Sleep Medicine Clinical Practice Guideline

Michael J. Sateia, MD[1]; Daniel J. Buysse, MD[2]; Andrew D. Krystal, MD, MS[3]; David N. Neubauer, MD[4]; Jonathan L. Heald, MA[5]

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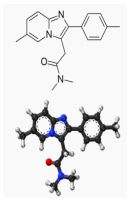
We suggest that clinicians NOT use trazadone for the treatment of sleep onset or maintenance insomnia.

(Sateia et al 2017)

Benzodiazepine receptor agonists (BRA)

- Commonly prescribed (zolpidem, eszopiclone)
- Only modest improvement on *objective* sleep efficiency
  - Primarily improve *subjective* sleep efficiency



Examples of a patient prescribed a BRA

	Pre-Treatment	Post Treatment
Subjective Sleep Efficiency	40%	
Objective Sleep Efficiency	66%	

Examples of a patient prescribed a BRA

	Pre-Treatment	Post Treatment
Subjective Sleep Efficiency	40%	95%
Objective Sleep Efficiency	66%	75%

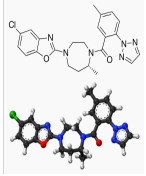
BRA adverse events

- Residual morning sedation even after 8 hours of sleep
- Falls, hip fractures
- Worsens mood and sleep apnea
- Visual hallucinations
- Sleepwalking, sleep eating
- Association with Alzheimer's, malignancy and mortality

(Kripke et al 2012, Gunia et al 2013, Lin et al 2014, Li et al 2014, Billioti de Gage et al 2014)

Orexin receptor antagonism

- Orexin is the neurotransmitter lost in narcolepsy.
  - These agents (suvorexant, lemborexant) reproduce narcolepsy somnolence.
  - Increase total sleep time approximately 30 minutes a night
- Adverse effects
  - Morning sedation
  - Middle of the night postural imbalance
- Does not suppress respiration



(Michelson et al 2014, Herring et al 2016)

Can't fall asleep: a practical clinical strategy

- Premise:

  Many if not most patients who present with "Insomnia" do not have hypervigilance but instead a distinct easily identifiable, and reversible, process leading to sleep initiation failure.

  First carefully consider:

  Circadian Rhythm Delay

  Restlessness

  Once ruled out these two conditions then consider:

  Cognitive hypervigilant insomnia.

26 y.o. male with "insomnia"

A 26-year-old male arrives in your office to discuss his troubles falling asleep before 2 AM. "My brain won't shut down", he says. In the morning he hits the snooze button 4-5 times before getting up. He sleeps in on the weekends.

Previous trial of zolpidem resulted in visual hallucinations at bedtime and he felt "hungover" in the AM.

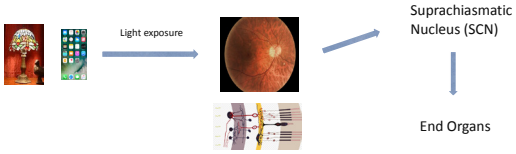
Circadian Rhythm Delay

- A problem of sleep timing
  - Natural fall asleep time and wake up time is later than desired.
  - Incredibly common
    - Especially among adolescents and young adults.
- Can present as trouble falling asleep, too sleepy in the day or both
  - Difficulty initiating sleep.
    - Often misdiagnosed as an Insomniac
    - Sedating agents can frequently lead to nighttime visual hallucinations and morning sedation because underlying circadian rhythm still promotes sleepiness until late into the AM.

(Culnan et al 2019)

Circadian Rhythm Delay

- Related to the brain's response to evening light exposure.
  - In large part a modern disorder.
    - In 1700—approx. 500 lumen hours/year
    - In 2010—approx. 500,000 lumen hours/year
    - Often minimal light exposure in the AM



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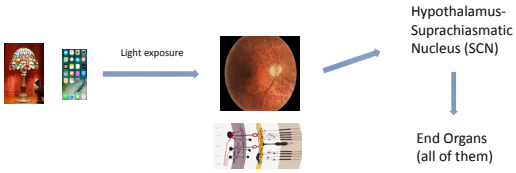


Clinical approach-Hawaii thought experiment

- Explore ad lib sleep-wake cycle
- Emphasize:

  "Don't tell me what you *want* your sleep-wake rhythm to be, tell me what *it is*"

Makena State Park, Maui

Treatment-Circadian Rhythm Delay

- Avoid sleeping pills and avoid daytime stimulants
- Morning
  - Sunlight or a 10,000-lux light box
  - Use at a consistent time (7 days a week) for 30—120 minutes
- Evening
  - Melatonin 0.5-1.0mg po 3-4 hours before bedtime.
  - Dim screens and use blue light blocking software
- Be mindful of meal timing

(Culnan et al 2019)

Clinical approach-One important question

- Distinguishing Circadian Delay from Hypervigilance

  "Tell me what happens in the morning?"
  - Circadian Rhythm Delay-tired and sleepy
  - CNS hypervigilant Insomnia-tired and not sleepy

32 y.o. female with "insomnia"

A 32-year-old female arrives in your office to discuss her troubles falling asleep before midnight. By the end of the day she is exhausted and craves sleep. She feels sleepy but she can't because of body discomfort that is "impossible to describe". She will get up and walk around which helps with the discomfort but within a couple minutes the discomfort is back, and she cannot fall asleep.

Previous trial of zolpidem resulted in sleepwalking and one morning she woke up to realize she had raided the refrigerator.

Restlessness (AKA Restless Legs Syndrome)

- Common reason for trouble falling asleep
- Often difficulty for patients to describe the discomfort and may not be located in the legs
  - Discomfort causes an urge to move
  - Movement relieves the urge (although often only momentarily)
  - Worsens at night thus interferes with sleep
- Frequently the presenting complaint is often only "I can't fall asleep"

(ICSD 2014, Avni et al 2019)

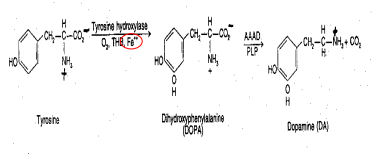
Etiology of restlessness

- CNS dopamine deficiency a primary cause of restlessness.
- Common in the setting of neuropsychiatric illness
  - Neuropathy
  - Pain syndromes
  - Spinal cord disease
  - Stroke
  - Antidopaminergic psychoactive agents

(ICSD 2014)

Iron deficiency in restlessness

- Co-factor in the tyrosine hydroxylase
  - Rate limiting step in the production of CNS dopamine
- Common in young healthy women.
  - Vegans/Vegetarians at higher risk.
  - Pregnancy exacerbates relative iron deficiency



Nap drunkenness

- Occurs when napping brain is trying to fall asleep for the "night"
- Occurs when naps are
  - Out of timing
  - Out of duration
  - Out of practice
- Untreated sleep disorder
  - Sleep deprived

Restlessness treatment-first iron replacement

- Oral iron supplementation is challenging
  - Poor intestinal absorption of elemental iron
  - GI side effects.
- Increased absorption with iron gluconate formulation.
  - Recommend 325mg
  - Absorption improved when combined with 100mg Vitamin C.
- IV Iron replacement an option
  - Ferric carboxymaltose

(Allen et al 2018, Avni et al 2019)

Restlessness treatment-second pharmacotherapies

- Alpha 2 delta ligands
  - Gabapentin, pregabalin
  - Side effects: sedation, imbalance, depression, weight gain
- Dopaminergic agonists
  - Pramipexole, ropinirole
  - Side effects: nausea, headache, impulsive behavior, augmentation
- Severe refractory cases
  - Methadone
  - Adverse effects: constipation, QT prolongation, ventilatory suppression, dependence

(Wijemanne and Ondo 2018)

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(Wijemanne and Ondo 2018)

42 y.o. female with insomnia

A 42-year old female arrives in your office to discuss her troubles falling asleep and staying asleep. By the end of the day she is exhausted and tired but not sleepy. She lays in bed and her mind won't shut down. She is frequently awakening throughout the night and often can't fall back asleep for an hour or longer. When the alarm clock goes off in the morning it is a relief. She is tired and does not feel rested but at least she can now get out of bed.

Previous trial of zolpidem resulted in a "great night of sleep".

CNS hypervigilant insomnia etiology-a conditioned response

- Trying to sleep becomes an insomnia trap
  - Despite feeling tired the act of climbing into bed is an alerting not sedating response. Psychophysiological Insomnia develops as a conditioned response.
- Feel tired and sleepy outside of the bedroom
  - Alert once an insomniac climb into bed.
  - May sleep better in hotels and out of the typical sleeping environment.

(Mitchel et al 2019)

CNS hypervigilant insomnia treatment-pharmacotherapies

- Sedating antidepressants
  - Trazodone, quetiapine, mirtazapine
  - Lack of efficacy data
- Benzodiazepines
  - Temazepam, diazepam
  - Morning sedation, balance difficulties, cognitive impairment, dependence
- Benzodiazepine receptor agonists
  - Zolpidem, eszopiclone
  - Morning sedation, balance difficulties, cognitive impairment, dependence

(Sateia et al 2017)

CNS hypervigilant insomnia treatment-pharmacotherapies

- Orexin antagonists
  - Suvorexant, lemborexant
  - Morning sedation, imbalance
  - Does not suppress respiration
- Orexin antagonists
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- Gold Standard Therapy

(Mitchel et al 2019)

CNS hypervigilant insomnia treatment-pharmacotherapies

- Orexin antagonists
  - Suvorexant, lemborexant
  - Morning sedation, imbalance
  - Does not suppress respiration
- Gold Standard Therapy
  - Cognitive Behavioral Therapy for Insomnia (CBT-I)
    - Best chance of curing insomnia
    - Administered by a licensed psychologist or online program

(Mitchel et al 2019)

First step in CBT-I treatment:

- **Primum non nocere** – First do no harm
- Stop promoting the adverse conditioned response
  - Stop lying in bed when not sleeping
  - The bedroom should be reserved for sleeping and sexual activity.
- Often requires difficult behavioral change
  - Patient often see recommendations as paradoxical

(Mitchel et al 2019)

CBT-I

- Cognitive Behavioral Therapy for Insomnia
  - Using Stimulus control, bedroom restriction and mindfulness you gradually decrease the adverse (wakeful) conditioning and promote positive (soporific) conditioning to the bedroom environment.
- The two essential rules:
  - Get out of bed if you are not sleeping
  - Don't fall asleep outside of the bedroom.

(Mitchel et al 2019)

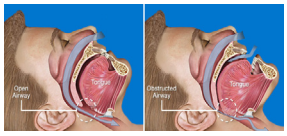
Snoring and obstructive sleep apnea (OSA)

- Collapse of the upper airway
  - Snoring-vibration of tissue
  - Hypopneas-partial restriction of airflow
  - Apneas-complete restriction of airflow
- OSA is a common condition
  - Relatively to pliable upper airway evolved for vocalization
  - Higher risk: men, weight gain, family history, increased neck circumference.

(ICSD 2014)

OSA-spectrum of disease

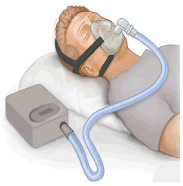
- Apnea-Hypopnea Index (AHI): number of times an individual stops breathing or nearly stops breathing per hour.
- Polysomnogram (sleep study) thresholds for diagnosis and severity in adults (consensus based)
  - Ideal for adults: AHI < 5/hr.
  - Mild: AHI 5-15/hr.
  - Moderate: AHI 15-30/hr.
  - Severe: AHI > 30/hr.



(ICSD 2014)

OSA-mechanical problem in need of a mechanical solution

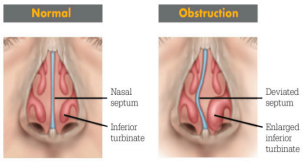
- Positive Airway Pressure (PAP) Therapy
  - Seals over the nose or mouth/nose.
  - Acts as a pneumatic splint to the upper airv
- Adherence challenges
  - Works very well about 50% of the time it is
  - Numerous reasons for poor adherence
    - Mask discomfort
    - Claustrophobia
    - Untreated co-morbid sleep problems
    - Nasal obstruction



(ICSD 2014)

OSA-what to do when PAP is not working

- Evaluate for possible nasal obstruction
  - Nasal endoscopy
- Relieve nasal obstruction-three benefits
  - Directly decreases AHI
  - Improve PAP and other OSA treatment adherence
  - Improved nasal breathing during the day



(ICSD 2014)

OSA-what to do when PAP is not working

- Consider oral appliance
  - Stabilize the mandible and prevent collapse
  - Similar to athletic mouthguards
  - See a AADSM Mastery certified dentist
- Consider upper airway stimulation
  - Stimulation of the hypoglossal nerve (CN XII).
  - Pacemaker for the tongue

(ICSD 2014)

OSA-what to do when PAP is not working

- Consider that OSA is not the etiology to the patient's symptoms
  - Mild OSA is frequently found on a PSG.
    - Sleep Heart Health Study data average AHI in US population older than 40 is 8.5 (mild OSA).
    - High likelihood that a patient with other underlying sleep or circadian rhythm problems will be given a diagnosis of OSA.
  - Medication effects
  - Suboptimal duration and/or circadian timing of sleep

(ICSD 2014)

Parasomnias-abnormal nocturnal behaviors

- Sleepwalking and dream enactment are underreported
  - Embarrassment
  - No bedpartner to witness behaviors
  - Mild behaviors-especially in childhood
  - Misattribution to mental illness
  - Cultural taboos regarding disclosure of bedroom activities
  - Assign supernatural or religious explanation to these behaviors

Fuseli—Sleepwalking Lady Macbeth)

(ICSD 2014, Howell 2020)

Sleepwalking

- Disorder of arousal emanating from deep NREM sleep
  - Minimal to no dream enactment
  - Difficult to awaken, often amnestic for behaviors
  - Occur in the first half of the night
- Nearly universal to some degree in childhood.
  - Can occasionally result in significant injury.
- Etiology-Failure to transition from sleep to wakefulness
  - Predisposed by underlying sleep disorders such as restless legs syndrome
  - Primed by processes that increase sleep drive: sleep deprivation, sedating medications
  - Precipitated by sleep fragmenting conditions such as OSA or noise

(ICSD 2014, Howell 2012)

Sleepwalking treatment

- Address underlying sleep conditions nearly universally takes care of sleepwalking.
  - Optimize the duration and timing of sleep.
    - Address sleep deprivation
    - Align circadian rhythm
  - Treat sleep disorders such as restless legs syndrome and OSA
  - Minimize sedating medications.

(ICSD 2014, Howell 2012)

Parasomnias-dream enactment

- Dream enactment-dream enactment occurring during REM sleep
- REM sleep Behavior Disorder (RBD)
  - Results in dream enactment, often vigorous, violent and potentially injurious to patients and bed partners.
    - 1% of the general population
    - 5% of elderly
  - Easy to awaken, clearly recall dream and behaviors
  - Occurs in the second half of the night
- Etiology-loss of normal REM motor paralysis

(ICSD 2014, Howell 2020)

REM sleep Behavior Disorder-treatment

- Bedroom safety
  - Discuss sleeping separately from bed partners
- Melatonin in high doses 6-18mg at bedtime
- Clonazepam in low doses 0.25-1.0mg at bedtime
  - Morning sedation, balance difficulties, depression

(ICSD 2014, Howell 2020)

RBD-prodromal syndrome

- RBD is a prodromal syndrome for Parkinson's disease (PD) and related neurodegenerative disorders.
  - Dementia with Lewy Bodies
  - Multiple System Atrophy
- Etiology-progressive alpha synuclein pathology.
  - 75% of surviving RBD patients convert to PD in 12 years.

(Charcot 1879)

(ICSD 2014, Howell 2020)

RBD and Parkinson's disease-quest for a cure

- Important to have often extended conversation to help understand their risks.
  - Loss of smell and constipation places an individual at higher risk for conversion within 5 years.
- RBD provides a unique opportunity for the development of disease modifying therapies-neuroprotection
- NAPS (North American Prodromal Synucleinopathy) Consortium
  - NIH funded study of 10 sites in the United States and Canada.
  - https://www.naps-rbd.org/

(ICSD 2014, Howell 2020)

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SELF EVALUATION

Sleep Disorders and their Management

1. Compared to placebo, benzodiazepine receptor agonists such as zolpidem…
   a. Improve subjective sleep efficiency
   b. Increase deep NREM sleep (N3)
   c. Increase REM sleep
   d. Decrease objective sleep efficiency

2. Which of the following is NOT a function of sleep?
   a. Adaptive Inactivity
   b. Memory Consolidation
   c. Increase in synaptic density
   d. Replenish CNS ATP
   e. Toxic Clearance

3. In regards to commonly employed sleeping pills which of the following have been demonstrated to have long-term efficacy?
   a. Trazadone
   b. Mirtazapine
   c. Quetiapine
   d. All of the above
   e. Non-of the Above

4. A 17-year old male presents with his parents who indicate that he sleeps all day long. He tells you that his mind won't shut down when he goes to bed. What is his condition?
   a. Hypervigilant Insomnia
   b. Circadian Rhythm Delay
   c. Restless Legs Syndrome
   d. Narcolepsy
   e. Non-of the above

5. Insomnia leads to…
   a. Anxiety and depression
   b. Poor working memory
   c. Impaired emotional intelligence.
   d. Fatigue
   e. All of the above

6. A 34-year old female has trouble falling asleep. She states that she goes to bed and can't get comfortable. She will then get up to pace the floor. After taking zolpidem once she sleepwalked and ate a large meal in the middle of the night. What is her most likely condition?
   a. Restlessness
   b. Circadian rhythm delay
   c. Hypervigilant Insomnia
   d. Sleepwalking Disorder
   e. Non-of the above

7. Which of the following RLS medication(s) have a high risk of augmentation (tolerance)?
   a. Gabapentin
   b. Pregabalin
   c. Pramipexole
   d. Ropinirole
   e. C and D

8. Which of the following is NOT a side effect of benzodiazepine receptor agonists?
   a. Falls
   b. Depression
   c. Visual hallucinations
   d. Cataplexy
   e. sleepwalking

9. Which of the following strategies may help an OSA patient who is unable to tolerate positive airway pressure (PAP) therapy.
   a. Evaluation by ENT for nasal obstruction
   b. Evaluation by ENT for possible hypoglossal nerve stimulator
   c. Reconsider whether OSA is the etiology of the patients presenting symptoms
   d. Evaluation by an AADSM Mastery Certified sleep dentist for possible oral appliance.
   e. All of the above

Answer Key: 1. A, 2. C, 3. E, 4. B, 5. E, 6. A, 7. E, 8. D, 9. E

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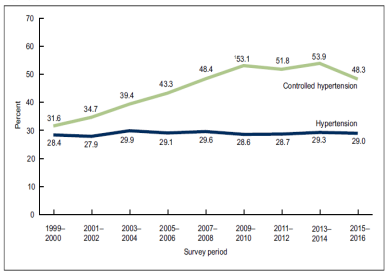
Strategies for Managing Hypertensive Patients to Goal

Hypertension a "Neglected Disease"

- **Hypertension is a "neglected disease," according to a report released 2/22/2010 by the Institute of Medicine. Despite high blood pressure being the cause of death in 1 of 6 US adults, and the greatest single risk factor for deaths from cardiovascular disease,** millions of Americans are developing, living with, and dying from hypertension. The decade **from 1995 to 2005 saw a 25% increase in the death rate from high blood pressure.**
  - The full text of the report is available at http://www.nap.edu.

Hypertension Prevalence and Control Among Adults: United States, 2015–2016

Figure 5. Age-adjusted trends in hypertension and controlled hypertension among adults aged 18 and over: United States, 1999–2016



[1]Significant increasing trend for 1999–2010, $p < 0.001$.
NOTES: Hypertension estimates are age adjusted by the direct method to the 2000 U.S. Census population using age groups 18–39, 40–59, and 60 and over. Estimates of controlled hypertension are age adjusted by the direct method using computed weights based on the subpopulation of persons with hypertension in the 2007–2008 National Health and Nutrition Examination Survey, using age groups 18–39, 40–59, and 60 and over. Access data table for Figure 5 at: https://www.cdc.gov/nchs/data/databriefs/db289_table.pdf#5.
SOURCE: NCHS, National Health and Nutrition Examination Survey, 1999–2016.

Lifestyle Modification

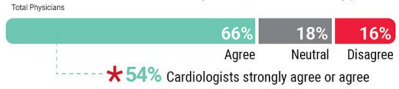
Modification	Approximate SBP reduction (range)
Weight reduction	5–20 mmHg/10 kg weight loss
Adopt DASH eating plan	8–14 mmHg
Dietary sodium reduction	2–8 mmHg
Physical activity	4–9 mmHg
Moderation of alcohol consumption	2–4 mmHg

Addressing CV Risk (Medscape/ACC Survey) February 25, 2019

Importance of Diet and Lifestyle

Diet and lifestyle modification is the most important treatment for CV risk reduction.

I have the tools I need to make lifestyle recommendations to my patients.



*54% Cardiologists strongly agree or agree

Source: Medscape/ACC Survey of 471 physicians; June 21, 2018 to October 8, 2018.

Medscape

2017 Hypertension Clinical Practice Guidelines

Blood Pressure Categories

American Heart Association | American Stroke Association

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

With the new target, the overall prevalence of hypertension among U.S. adults will jump to 45.6% compared with 31.9% based on the JNC7's 140/90 mm Hg threshold. That represents an additional 31.1 million people -- based on National Health and Nutrition Examination Survey data through 2014 -- for a total prevalence of 103.3 million,

Key Steps for Proper BP Measurements

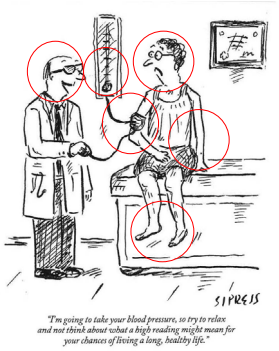
- Step 1: Properly prepare the patient
  - **1. Have the patient relax, sitting in a chair (feet on floor, back supported) for >5 min.**
  - **2. The patient should avoid caffeine, exercise, and smoking for at least 30 min before measurement.**
  - **3. Ensure patient has emptied his/her bladder.**
  - **4. Neither the patient nor the observer should talk during the rest period or during the measurement.**
  - **5. Remove all clothing covering the location of cuff placement.**
  - **6. Measurements made while the patient is sitting or lying on an examining table do not fulfill these criteria.**
- Step 2: Use proper technique for BP measurements
  - 1. Use a BP measurement device that has been validated, and ensure that the device is calibrated periodically.*
  - **2. Support the patient's arm (e.g., resting on a desk).**
  - 3. Position the middle of the cuff on the patient's upper arm at the level of the right atrium (the midpoint of the sternum).
  - 4. Use the correct cuff size, such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used (Table 9).
  - 5. Either the stethoscope diaphragm or bell may be used for auscultatory readings (5, 6).

Hypertension. 2017;71:e13–e115

Key Steps for Proper BP Measurements

- Step 3: Take the proper measurements needed for diagnosis and treatment of elevated BP/hypertension
  - **1. At the first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings.**
  - **2. Separate repeated measurements by 1–2 min.**
  - 3. For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20–30 mm Hg above this level for an auscultatory determination of the BP level.
  - 4. For auscultatory readings, deflate the cuff pressure 2 mm Hg per second, and listen for Korotkoff sounds.
- Step 4: Properly document accurate BP readings
  - 1. Record SBP and DBP. If using the auscultatory technique, record SBP and DBP as onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number.
  - **2. Note the time of most recent BP medication taken before measurements.**
- **Step 5: Average the readings Use an average of ≥2 readings obtained on ≥2 occasions to estimate the individual's level of BP.**
- Step 6: Provide BP readings to patient Provide patients the SBP/DBP readings both verbally and in writing.
  - Hypertension. 2017;71:e13–e115

What's wrong with this picture?



From Jan Basile, MD
Seinsheimer Cardiovascular Health Program
Professor of Medicine
Medical University of South Carolina

Automated Office Blood Pressure (AOBP) Readings

- Data were compiled from 31 articles comprising 9279 participants (4736 men and 4543 women). In samples with systolic AOBP of 130 mm Hg or more, **routine office and research systolic BP readings were substantially higher than AOBP readings, with a pooled mean difference of 14.5 mm Hg** (95% CI, 11.8-17.2 mm Hg; P < .001) **for routine office systolic BP readings and 7.0 mm Hg** (95% CI, 4.9-9.1 mm Hg; P < .001) **for research systolic BP readings**. Systolic awake ambulatory BP and AOBP readings were similar, with a pooled mean difference of 0.3 mm Hg (95% CI, −1.1 to 1.7 mm Hg; P < .001).
- **Based on the evidence, AOBP should now be the preferred method for recording BP in routine clinical practice.**
  - JAMA Intern Med. Published online February 4, 2019. doi:10.1001/jamainternmed.2018.6551

USPSTF Recommendation for Ambulatory BP Monitoring

- **The USPSTF found that elevated 24-hour ambulatory systolic blood pressure was consistently and significantly associated with stroke and other cardiovascular outcomes, independent of office blood pressure and with greater predictive value. Because of its large evidence base, ABPM is considered the best confirmatory test for hypertension.**
- Home blood pressure monitoring may also be a reasonable confirmatory method but has less evidence to support its use.
  - Ann Intern Med. 2015; 162(3):192-204

2017 Hypertension Clinical Practice Guidelines

Table 23. BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

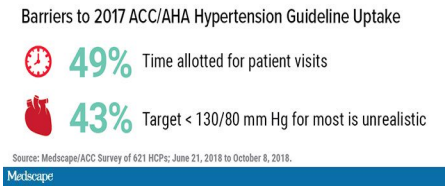
Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk ≥10%	≥130/80	<130/80
No clinical CVD and 10-year ASCVD risk <10%	≥140/90	<130/80
Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥130 (SBP)	<130 (SBP)
Specific comorbidities		
Diabetes mellitus	≥130/80	<130/80
Chronic kidney disease	≥130/80	<130/80
Chronic kidney disease after renal transplantation	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Secondary stroke prevention (lacunar)	≥130/80	<130/80
Peripheral arterial disease	≥130/80	<130/80

ASCVD indicates atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; and SBP, systolic blood pressure.

American Heart

Addressing CV Risk (Medscape/ACC Survey)

February 25, 2019

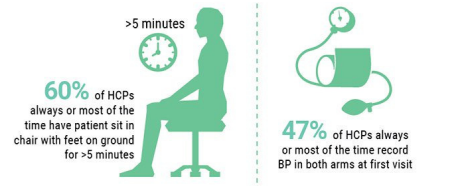


Medscape and ACC asked 621 full-time practicing clinicians involved in the diagnosis and/or treatment of patients with or at risk for cardiovascular disease (CVD) for their views on diet/lifestyle, hypertension, and type 2 diabetes. Responses came from 204 cardiologists; 101 endocrinologists; 166 primary care physicians (PCPs); and 150 allied healthcare professionals comprising nurse practitioners (NPs), physician assistants (PAs), and registered nurses (RNs).

Addressing CV Risk (Medscape/ACC Survey)

February 25, 2019

Following 2017 ACC/AHA BP Guidelines



Source: Medscape/ACC Survey of 621 HCPs; June 21, 2018 to October 8, 2018.

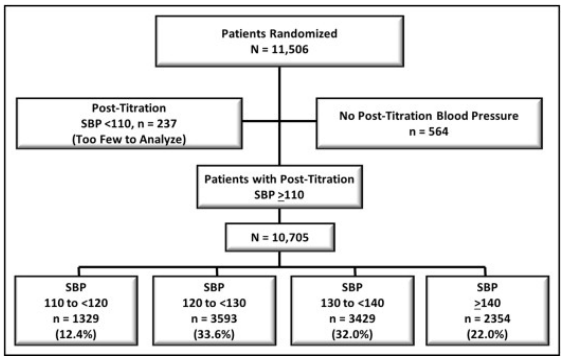
Medscape

ACCOMPLISH Trial NEJM 2008;359:2417-28

- ACCOMPLISH was a randomized**, multinational double-blind trial (n=11,506).** The aim was to determine the most effective therapeutic pharmacotherapy for controlling systolic hypertension and preventing CVD events in high risk patients. Participants were included if they were ≥ 60 Years with 1 risk factor and ≥ 55 years with 2 risk factors. One group received a **single pill combination fixed dose of an ACE inhibitor (benazepril) and a calcium channel blocker (CCB). The other group received a single pill fixed dose combination of an ACE inhibitor and a diuretic (HCTZ).** The primary endpoint was CV morbidity and mortality (mean duration 36 mo).
  - **66% >/=65 yrs of age, 40% >/= 70 yrs of age**;
  - 60% male and 84% white, 12% black;
  - **69% hx of diabetes, 23% post MI, 13% hx CVA, eGFR <60 18**

Systolic Blood Pressure and Cardiovascular Outcomes During Treatment of Hypertension

American Journal of Medicine 2013 (June) 126: 501-508



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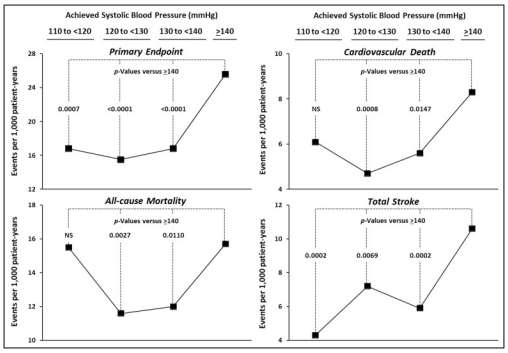

Systolic Blood Pressure and Cardiovascular Outcomes During Treatment of Hypertension

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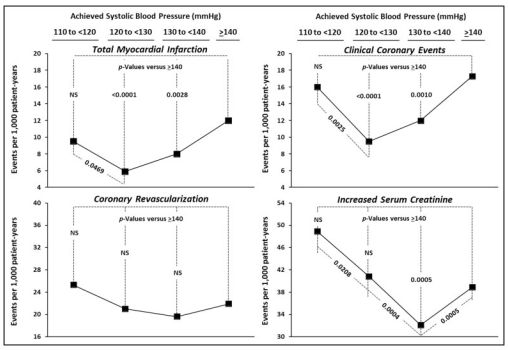


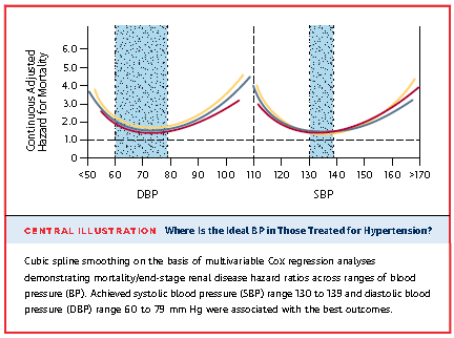
Systolic Blood Pressure and Cardiovascular Outcomes During Treatment of Hypertension

American Journal of Medicine 2013 (June) 126: 501-508

Conclusions:

- "In high-risk hypertensive patients, major **cardiovascular events are significantly lower in those with systolic blood pressures < 140 mm Hg and < 130 mm Hg than in those with levels > 140 mm Hg. There are stroke benefits at levels < 120 mm Hg, but they are offset by increased coronary events. Renal function is best protected in the 130 to 139 mm Hg range."**

398,419 Treated Hypertensive from Kaiser Southern California (JACC 2014;64:588-97)



CENTRAL ILLUSTRATION Where Is the Ideal BP in Those Treated for Hypertension?

Cubic spline smoothing on the basis of multivariable Cox regression analyses demonstrating mortality/end-stage renal disease hazard ratios across ranges of blood pressure (BP). Achieved systolic blood pressure (SBP) range 130 to 139 and diastolic blood pressure (DBP) range 60 to 79 mm Hg were associated with the best outcomes.

SPRINT Trial

- **9361 patients with systolic BP >/=130 mm Hg and at least one risk factor were randomized in a 1:1 fashion to either intensive SBP lowering (target <120 mm Hg) or routine SBP management (target <140 mm Hg).**
- The **primary composite outcome was myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes**. Renal outcomes also assessed.
- Patients were to be followed for 5 years but the **trial was stopped early (median 3.26 years) owing to a significantly lower rate of the primary composite outcome** in the intensive-treatment group than in the standard-treatment group.
  - N Engl J Med 2015; 373:2103-2116

BP Measurement in SPRINT (Automated)

- Visit BP was the average of 3 seated office BP measurements obtained using an automated measurement device: Omron 907XL.
- Appropriate cuff size was determined by arm circumference.
- Participant was seated with back supported and arm bared and supported at heart level.
- Device was set to delay 5 minutes and then take/average 3 BP measurements, during which time participant refrained from talking.

Cushman, et al. Hypertension. 2016;67:263-5

Omron Hem 907XL IntelliSense Professional Digital Blood Pressure Monitor

- Automatic cuff inflation and deflation eliminates the need to predetermine inflation level setting
- Average mode measures up to three readings and averages the total, for a more accurate measurement
- Greater choice of arm cuff circumferences with four cuff sizes included -- small, medium, large and extra-large
- Reliable power supply through included AC adapter or rechargeable battery pack
- Cost ~$650.00

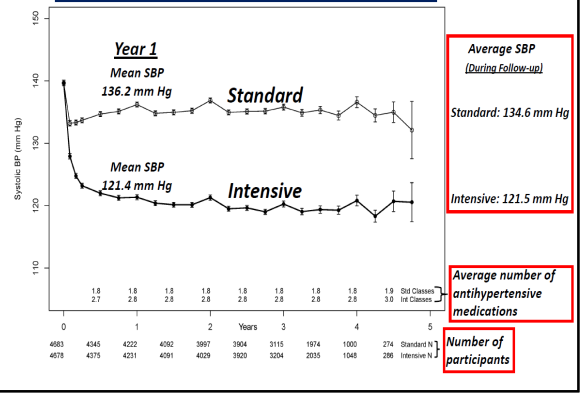
Routine Office BP versus Automated Office BP

Study	N	Routine Office BP	Automated Office BP
Graves	104	152/84	136/79
Beckett	481	151/83	140/80
Myers-16	309	153/87	132/75
Myers-18	254	150/89	133/80
Myers-19	303	150/81	133/74
Mean		**151/85**	**135/78**
		Δ = 16/7 mmHg	

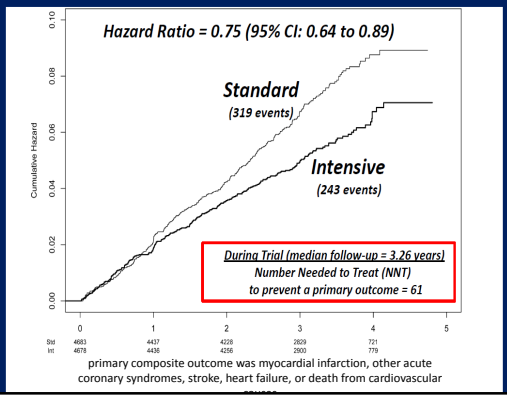
SPRINT Demographic and Baseline Characteristics

	Total N=9361	Intensive N=4678	Standard N=4683
Mean (SD) age, years	67.9 (9.4)	67.9 (9.4)	67.9 (9.5)
% ≥75 years	28.2%	28.2%	28.2%
Female, %	35.6%	36.0%	35.2%
White, %	57.7%	57.7%	57.7%
African-American, %	29.9%	29.5%	30.4%
Hispanic, %	10.5%	10.8%	10.3%
Prior CVD, %	20.1%	20.1%	20.0%
Mean 10-year Framingham CVD risk, %	20.1%	20.1%	20.1%
Taking antihypertensive meds, %	90.6%	90.8%	90.4%
Mean (SD) number of antihypertensive meds	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)
Mean (SD) Baseline BP, mm Hg			
Systolic	139.7 (15.6)	139.7 (15.8)	139.7 (15.4)
Diastolic	78.1 (11.9)	78.2 (11.9)	78.0 (12.0)

Systolic BP During Follow-up



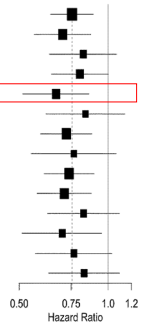
SPRINT Primary Outcome
Cumulative Hazard



primary composite outcome was myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular

Primary Outcome Experience in the Six Pre-specified Subgroups of Interest

Subgroup	HR	P*
Overall	0.75 (0.64,0.89)	
No Prior CKD	0.70 (0.56,0.87)	0.36
Prior CKD	0.82 (0.63,1.07)	
Age < 75	0.80 (0.64,1.00)	0.32
Age ≥ 75	0.67 (0.51,0.86)	
Female	0.84 (0.62,1.14)	0.45
Male	0.72 (0.59,0.88)	
African−American	0.77 (0.55,1.06)	0.83
Non African−American	0.74 (0.61,0.90)	
No Prior CVD	0.71 (0.57,0.88)	0.39
Prior CVD	0.83 (0.62,1.09)	
SBP ≤ 132	0.70 (0.51,0.95)	0.77
132 < SBP < 145	0.77 (0.57,1.03)	
SBP ≥ 145	0.83 (0.63,1.09)	

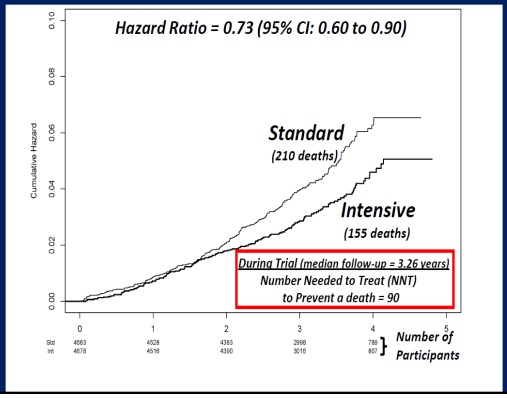


*Unadjusted for multiplicity
*Treatment by subgroup interaction

SPRINT Senior Cohort

- **The SPRINT-Senior cohort is representative of community dwelling older adults 75 and older**
- Rates of hypotension, syncope, electrolyte abnormalities, kidney injury were higher in the intensive arm, but not rates of injurious falls or orthostatic hypotension
- **Overall, benefits of more intensive BP lowering 33% reduction in primary CV outcome and 32% reduction in total mortality – exceeded the potential for harm, even among the most frail older patients**
  - JAMA. Published online May 19, 2016. doi:10.1001/jama.2016.7050

All-cause Mortality
Cumulative Hazard



SPRINT Primary Outcome and its Components
Event Rates and Hazard Ratios

		Intensive		Standard			
		No. of Events	Rate, %/year	No. of Events	Rate, %/year	HR (95% CI)	P value
Primary Outcome	NNT 61	243	1.65	319	2.19	0.75 (0.64, 0.89)	<0.001
All MI		97	0.65	116	0.78	0.83 (0.64, 1.09)	0.19
Non-MI ACS		40	0.27	40	0.27	1.00 (0.64, 1.55)	0.99
All Stroke		62	0.41	70	0.47	0.89 (0.63, 1.25)	0.50
All HF	NNT 125	62	0.41	100	0.67	0.62 (0.45, 0.84)	0.002
CVD Death	NNT 172	37	0.25	65	0.43	0.57 (0.38, 0.85)	0.005

Renal Disease Outcomes

		Intensive		Standard			
		Events	%/yr	Events	%/yr	HR (95% CI)	P
Participants with CKD at Baseline							
	Primary CKD outcome	**14**	**0.33**	**15**	**0.36**	**0.89 (0.42, 1.87)**	**0.76**
	≥50% reduction in eGFR*	10	0.23	11	0.26	0.87 (0.36, 2.07)	0.75
	Dialysis	6	0.14	10	0.24	0.57 (0.19, 1.54)	0.27
	Kidney transplant	0	-	0	-	-	.
	Secondary CKD Outcome						
	Incident albuminuria**	49	3.02	59	3.90	0.72 (0.48, 1.07)	0.11
Participants without CKD at Baseline							
	Secondary CKD outcomes						
	≥30% reduction in eGFR*	127	1.21	37	0.35	3.48 (2.44, 5.10)	<.0001
	Incident albuminuria**	110	2.00	135	2.41	0.81 (0.63, 1.04)	0.10

*Confirmed on a second occasion ≥90 days apart **Doubling of urinary albumin/creatinine ratio from <10 to >10 mg/g

Serious Adverse Events* (SAE) During Follow-up

	Number (%) of Participants		
	Intensive	Standard	HR (P Value)
All SAE reports	1793 (38.3)	1736 (37.1)	1.04 (0.25)
SAEs associated with Specific Conditions of Interest			
Hypotension	110 (2.4)	66 (1.4)	1.67 (0.001)
Syncope	107 (2.3)	80 (1.7)	1.33 (0.05)
Injurious fall	105 (2.2)	110 (2.3)	0.95 (0.71)
Bradycardia	87 (1.9)	73 (1.6)	1.19 (0.28)
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35 (0.020)
Acute kidney injury or acute renal failure	193 (4.1)	117 (2.5)	1.66 (<0.001)

*Fatal or life threatening event, resulting in significant or persistent disability, requiring or prolonging hospitalization, or judged important medical event.

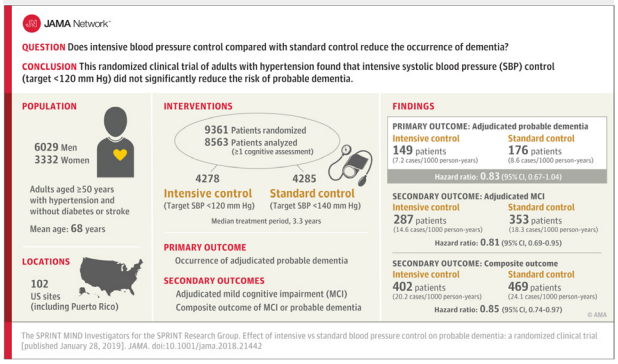
BP Measurement?

- Remember BPs were taken with no observer in the room, readings taken with a fully automatic device. Therefore, **the achieved BP of 120 mm Hg in SPRINT translates into a BP of 136 mm Hg in all prior trials, related to the "white-coat" effect.**
- One **cannot just subtract X mmHg from a poorly done office BP to approximate SPRINT BP since the variation is large and unpredictable in an individual patient.**

JAMA Network

From: **Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia: A Randomized Clinical Trial**

JAMA. Published online January 28, 2019. doi:10.1001/jama.2018.21442

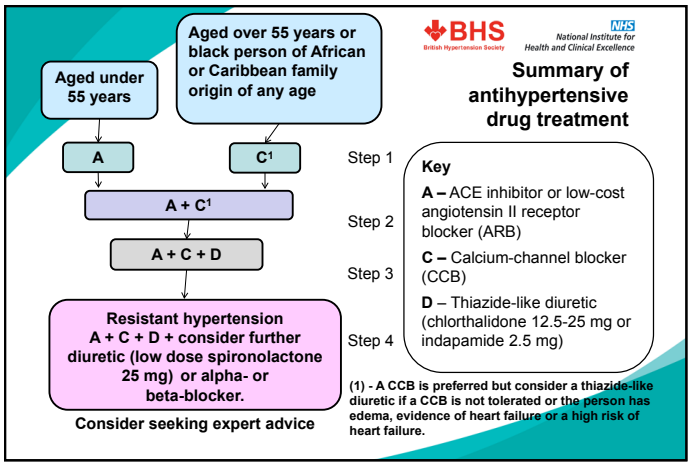


SPRINT MIND Trial

- The SPRINT MIND Research Group, including corresponding author Jeff D. Williamson, M.D., M.H.S., from Wake Forest School of Medicine, Winston-Salem, North Carolina, noted that **the primary results of this analysis found no statistically significant difference between standard and intensive treatment in the proportion of participants that were diagnosed with dementia.** The **study, however, had fewer cases of dementia than expected. Nevertheless, the secondary results suggested that the intensive treatment reduced the risk of MCI and the combined risk of MCI and dementia.** Due to the success of the SPRINT trial on the cardiovascular outcomes, the study intervention was stopped early; as a result, participants were treated for a shorter period than originally planned. The **authors concluded that the shorter time and the unexpected fewer cases of dementia may have made it difficult to determine the role of intensive blood pressure control on dementia.**
  - https://www.nih.gov/news-events/news-releases/does-intensive-blood-pressure-control-reduce-dementia

SPRINT MIND Trial 2.0

- **To further the investigation, the Alzheimer's Association has awarded more than $800,000 to fund a 2-year extension of the trial**, named SPRINT MIND 2.0, to help clarify the impact of aggressive BP treatment on reducing the risk of dementia.
- **Overall, the SPRINT MIND results are "compelling and offer real hope." Maria C. Carrillo, PhD. chief science officer for the Alzheimer's Association.**



Compelling Indications for Individual Drug Classes

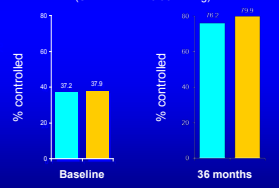
Compelling Indication	Initial Therapy Options	Clinical Trial Basis
Heart failure	THIAZ, **BB, ACEI**, ARB, **ALDO ANT** **2017 also an ARNI instead of an ACEI or ARB**	ACC/AHA Heart Failure Guideline, MERIT-HF, COPERNICUS, CIBIS, SOLVD, AIRE, TRACE, ValHEFT, RALES
Postmyocardial infarction	**BB, ACEI, ALDO ANT** **2017 could also use an ARB**	ACC/AHA Post-MI Guideline, BHAT, SAVE, Capricorn, EPHESUS
High CAD risk	THIAZ, ACE, ARB, CCB	ALLHAT, HOPE, ANBP2, LIFE, CONVINCE, ACCOMPLISH

ACCOMPLISH

American Heart Association
Learn and Live

Trial Design: ACCOMPLISH was a randomized, multinational double-blind trial (n=11,508). The aim was to determine the most effective therapeutic pharmacotherapy for controlling systolic hypertension and preventing CVD events in high risk patients. Participants were included if they were ≥ 60 Years with 1 risk factor and ≥ 55 years with 2 risk factors. One group received a single pill combination fixed dose of an ACE inhibitor (benazepril) and a calcium channel blocker (CCB). The other group received a single pill fixed dose combination of an ACE inhibitor and a diuretic (HCTZ). The primary endpoint was CV morbidity and mortality (mean duration 36 mo).

Blood Pressure % control Rates (SBP/DBP < 140/90 mmHg)



Jamerson et al., Presented at ACC, 2008.

Results

- **Primary endpoints of composite CV morbidity and mortality were significantly reduced by 21% in the CCB/ACEI group RR=1.21[CI 95%, (1.06-1.37)]**
- **ARR 2.2% NNT = 46**
  - **Men NNT = 40; Women NNT = 63**
  - **Diabetes NNT = 46; No Diabetes NNT = 48**
  - **Age 70 or > NNT = 36**
- Secondary endpoint of Systolic blood pressure was reduced significantly over time (42 months) with both treatments.

Conclusions

- The study demonstrated the effectiveness of a single pill fixed dose combination therapy of amlodipine/benazepril compared to HCTZ/benazepril on CV morbidity and mortality.
- Future initial hypertension pharmacotherapy could be impacted by these findings.

ACCOMPLISH Results: ACEI/CCB vs. ACEI/Diuretic

CV Morbidity and Mortality (Primary Endpoint)

- **Men** RRR 20% ARR 2.5% NNT 40
- **Women** RRR 17% ARR 1.6% NNT 63
- **>/= 65y/o** RRR 19% ARR 2.3% NNT 44
- **>/= 70y/o** RRR 21% ARR 2.8% NNT 36
- **Diabetes** RRR 21% ARR 2.2% NNT 46
- **No Diabetes** RRR 18% ARR 2.1% NNT 48

(66% >/=65 yrs of age, 40% >/= 70 yrs of age; 60% male and 84% white, 12% black; 69% hx of diabetes, 23% post MI, 13% hx CVA, eGFR <60 18%)

– **NEJM 2008;359:2417-28**

ACCOMPLISH: Outcomes in the intention-to-treat population

End point	Benazepril plus amlodipine (n=5744), %	Benazepril plus hydrochlorothiazide (n=5762), %	Hazard ratio (95% CI)/NNT
Progression to CKD (primary end point)	1.97	3.73	0.52/57 (0.41–0.65)
Doubling of serum creatinine	1.83	3.61	0.51/57 (0.39–0.63)
Dialysis	0.12	0.23	0.53 (0.21–1.35)
eGFR <15 mL/min/1.73 m²	0.31	0.30	1.06 (0.54–2.05)
Progression to CKD and cardiovascular death	3.83	5.99	0.63/47 (0.53–0.74)
Progression to CKD and all-cause mortality	6.02	8.07	0.73/50 (0.64–0.84)

Bakris GL et al. *Lancet* 2010; available at: http://www.thelancet.com.

Influence of Circadian Time of Hypertension Treatment on CV Risk: The MAPEC Trial

- **2156 hypertensive subjects**, 1044 men/1112 women, 55.6 ± 13.6 (mean ± SD) yrs of age, were randomized to ingest all their prescribed hypertension medications upon awakening or ≥1 of them at bedtime.
- At baseline, **BP was measured at 20-min intervals from 07:00 to 23:00 h and at 30-min intervals at night for 48 hours**.
  – **Chronobiology International 2010; 27(8): 1629–1651**

MAPEC Trial Results

- The median time to follow up was 5.6 yrs.
  - 187 events were seen in the a.m. arm versus 68 in the bedtime arm, p <0.001
  - 28 total deaths in the a.m. arm versus 12 in the bedtime arm, p <0.008

Endpoints	Control (n=1084)	Treatment (n=1072)	RR p-value	RRR	ARR	NNT
Death	28 (2.6%)	12 (1.1%)	0.42 (0.008)	57.7%	1.5%	67
CV Events	187 (17.3%)	68 (6.3%)	0.36 (<0.001)	63.6%	11%	9

  - CV events include–death, MI, stroke, heart failure, etc.
    - Chronobiology International 2010; 27(8): 1629–1651

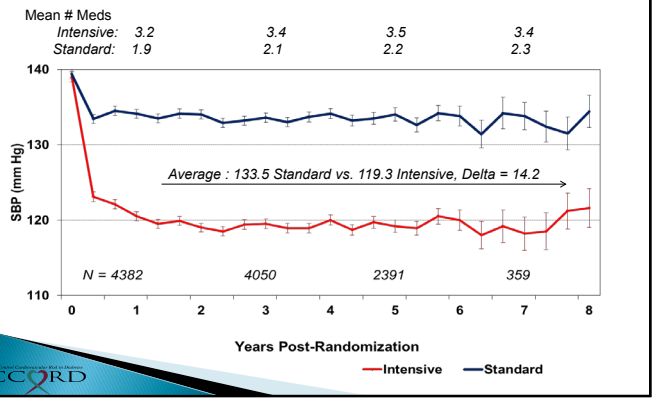
Effects of Intensive Blood Pressure Control on Cardiovascular Events in Type 2 Diabetes Mellitus: The Action to Control Cardiovascular Risk in Diabetes (ACCORD) Blood Pressure Trial

William C. Cushman, MD, FACP, FAHA
Veterans Affairs Medical Center, Memphis, TN

For The ACCORD Study Group

Action to Control Cardiovascular Risk in Diabetes
ACCORD

Systolic Pressures (mean ± 95% CI)



ACCORD

Primary & Secondary Outcomes

	Intensive Events (%/yr)	Standard Events (%/yr)	HR (95% CI)	P
Primary	208 (1.87)	237 (2.09)	0.89 (0.73-1.07)	0.20
Total Mortality	150 (1.28)	144 (1.19)	1.07 (0.85-1.35)	0.55
Cardiovascular Deaths	60 (0.52)	58 (0.49)	1.06 (0.74-1.52)	0.74
Nonfatal MI	126 (1.13)	146 (1.28)	0.87 (0.68-1.10)	0.25
Nonfatal Stroke	34 (0.30)	55 (0.47)	**0.63 (0.41-0.97)**	**0.03**
Total Stroke	36 (0.32)	62 (0.53)	**0.59 (0.39-0.89)**	**0.01**

Also examined Fatal/Nonfatal HF (HR=0.94, p=0.67), a composite of fatal coronary events, nonfatal MI and unstable angina (HR=0.94, p=0.50) and a composite of the primary outcome, revascularization and unstable angina (HR=0.95, p=0.40)

ACCORD

ADA and ACE/AACE 2019 Blood Pressure Goals

- **For individuals with diabetes and hypertension at lower risk for cardiovascular disease (10-year atherosclerotic cardiovascular disease risk, 15%), treat to a blood pressure target of <140/90 mmHg. A**
- **For individuals with diabetes and hypertension at higher cardiovascular risk (existing atherosclerotic cardiovascular disease or 10-year atherosclerotic cardiovascular disease risk >15%), a blood pressure target of <130/80mm Hg maybe appropriate, if it can be safely attained. C**
- **ACE/AACE a target BP of <130/80 mm Hg is appropriate for most patients.**
  - Diabetes Care Volume 42, Supplement 1, January 2019 S104
  - Endocrine Practice 2019; 25:73-74

ADA 2019 Treatment of Blood Pressure

- **Treatment for hypertension should include drug classes demonstrated to reduce cardiovascular events in patients with diabetes (ACE inhibitors, angiotensin receptor blockers, thiazide-like diuretics, or dihydropyridine calcium channel blockers).**
  - Multiple drug therapy is generally required to achieve blood pressure targets (but not a combination of ACE inhibitors ARBs). (A)
- **An ACE inhibitor or ARB, at the maximum tolerated dose indicated for blood pressure treatment, is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin – to – creatinine ratio >/= 300 mg/g creatinine (A)or 30 - 299 mg/g creatinine (B).**
  - If one class is not tolerated, the other should be substituted. (B)
    - Diabetes Care Volume 42, Supplement 1, January 2019 S107

AHA Scientific Statement

Principles of ACE Inhibitor Therapy: Renal Considerations

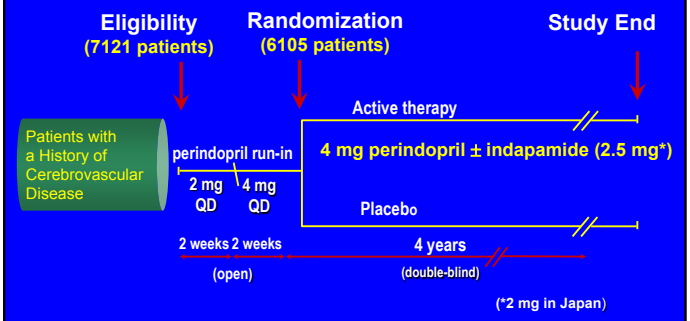
1. **ACE inhibitors improve RBF and stabilize GFR in most patients with CHF.**
2. ACE inhibitor therapy is indicated in patients with diabetic nephropathy and in patients with nondiabetic nephropathies when protein excretion exceeds 1 g/d.
3. **A rise in serum creatinine may occur after initiation of therapy in patients with CHF. This rise usually occurs promptly, is less than 10% to 20%, is not progressive, and is a consequence of the renal hemodynamic changes brought about by ACE inhibitor therapy. Serum creatinine often stabilizes and may decline thereafter.**
4. **Although there is no serum creatinine level per se that contraindicates ACE inhibitor therapy, greater increases in serum creatinine occur more frequently when ACE inhibitors are used in patients with underlying chronic renal insufficiency.**

Circulation. 2001;104:1985–1991

ACEI and Elevated Serum Creatinine

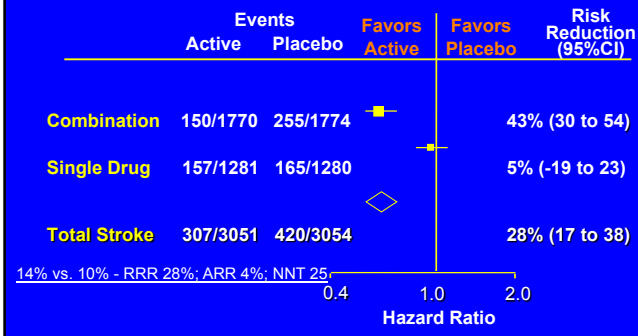
- **A recommendation from Drs Bakris and Weir Arch Intern Med 2000;160:685-93**
  - **A strong association exists between acute increases in serum creatinine of up to 30% that stabilize within the first 2 months of ACEI therapy and long-term preservation of renal function**
  - **Withdrawal of an ACEI should only occur when the rise in serum creatinine exceeds 30% above baseline within the first 2 months of ACEI therapy, or hyperkalemia (5.6mEq/L or greater) develops**

PROGRESS: Study Design



Neal B, et al. *J Hypertens.* 1995;13:1869-73.

Stroke: Combination versus Monotherapy



PROGRESS Group. *Lancet* 2001; 358: 1033-41.

PRoFESS® Trial: Study Design

20,332 patients ≥ 50 years with at least ischemic stroke* (see inclusion criteria)
Double-blind. Placebo-controlled. Simultaneous randomization.
Doses: (200 mg ER-DP + 25 mg Aspirin) 2x/day, 80 mg Telmisartan, 75 mg Clopidogrel 1x/day

R

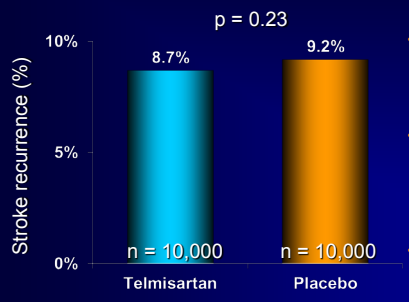
ER-DP + Aspirin + Telmisartan	Clopidogrel + Telmisartan	ER-DP + Aspirin + Placebo	Clopidogrel + Placebo
n= 5,000	n= 5,000	n=5,000	n=5,000

2.5 yrs. mean follow-up

- Primary Endpoint: rate of first recurrent stroke
- Secondary Endpoints: stroke, MI, vascular death, rate of new diabetes mellitus
- Tertiary Endpoints: major hemorrhagic event, all deaths, new or worsening congestive heart failure

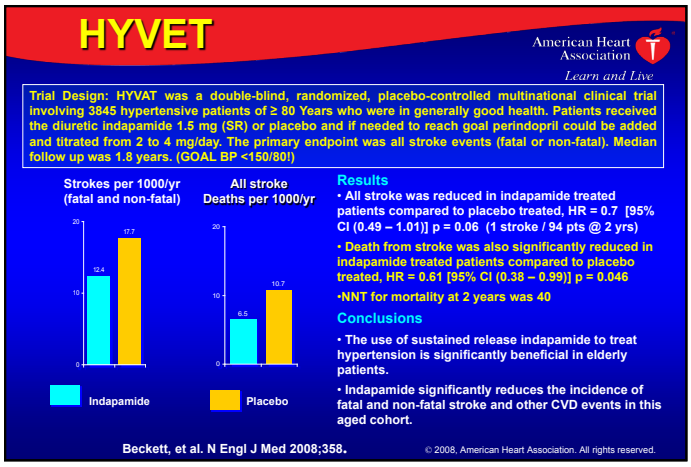
Cerebrovascular Dis. 2007; 23/ESC 2008

PRoFESS® Trial: Primary Endpoint



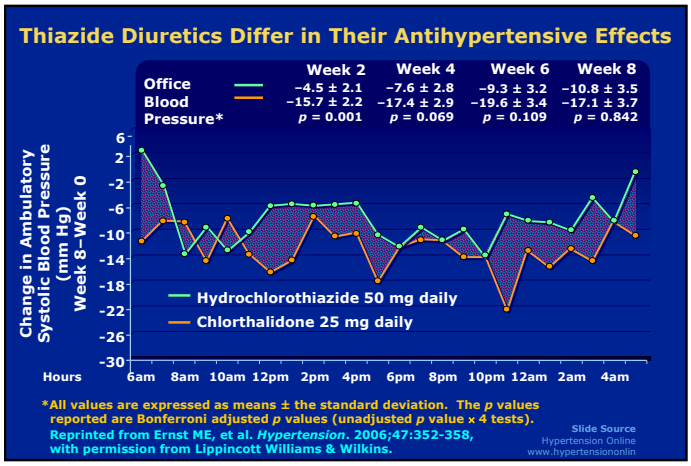
- Telmisartan demonstrated no significant benefit over placebo in the rate of recurrent stroke.
- Lowering blood pressure with Telmisartan for 2.5 years after a stroke does not significantly reduce the rate of stroke.
- HR 0.9 ; 95% CI 0.86-1.04

Cerebrovascular Dis. 2007; 23/ESC 2008



Questions

- Which diuretic would you prescribe for initial treatment of hypertension?
- Would you change diuretic therapy in a patient with resistant hypertension (not controlled on a 3 drug regimen that includes hydrochlorothiazide 25-50 mg/day)?



Indapamide vs. HCTZ in Patients with Impaired Renal Function and Hypertension

- **28 patients with impaired renal function and moderate hypertension**. The patients had elevated blood pressure for 2-27 years and impaired renal function for 1-15 years before entering the study. Their ages ranged between ,32-70 years and their **initial creatinine clearance was between 32 and 80 ml/min/1.73 m2 body surface area.** There were 16 female and 12 male patients. They were **randomly assigned for treatment with 2.5 mg of indapamide/day (14 patients) or with 50 mg of hydrochlorothiazide/day (14 patients) all patients were seen every 3 months and followed for 24 months.**
- **BP reductions were similar and maintained for the 24 months of follow-up**
  - (Am J Cardiol l996;77:23B-25B)

Indapamide vs. HCTZ in Patients with Impaired Renal Function and Hypertension

- **Creatinine clearance increased progressively in 13 of the 14 patients treated with indapamide; it rose from 58 +/- 4.4 to 72 +/- 4.4 ml/min/1.73 m2 body- surface area (p < 0.01)** by the end of the treatment. In contrast, **creatinine clearance fell progressively in 13 of the 14 patients who were managed with hydrochlorothiazide; it fell from 65 +/- 3.0 to 53 +/- 3.0 ml/min/1.73 m2 body surface area (p < 0.01)** by the end of the study.
- Creatinine clearance increased by 28.5 +/- 4.4% with indapamide treatment and decreased by 17.4 +/- 3.0% with thiazide therapy, a statistically significant difference (p < 0.01).
  - (Am J Cardiol l996;77:23B-25B)

Aldosterone Antagonists

- **Adding aldosterone antagonists (IE spironolactone) to the therapeutic regimen of patients with resistant hypertension can reduce or normalize elevated blood pressure in as many as 30% of these patients.**
  - **Avoid when potassium is >/=5.0 mEq/L**
  - **Avoid with elevated serum creatinine >/= 2-2.5 mg/dl**
  - **Ask about salt substitutes**

Spironolactone for Hypertension. *Cochrane Database of Systematic Reviews* 2010

- **Meta-analysis of the 5 cross-over studies found a reduction in SBP of 20.09 mmHg (95%CI:16.58-23.06,p<0.00001) and a 6.75 mmHg (95%CI:4.8-8.69,p<0.00001) reduction in DBP.** These results were statistically significant and there was no evidence of heterogeneity between the studies. There may be a dose response effect with spironolactone up to 50 mg/day, but the confidence intervals around the mean end-of-study blood pressure for doses ranging 25-500 mg/day all overlapped.
- **In other words, it appears that doses >50mg/day do not produce further reductions in either SBP or DBP.**
- One cross-over study found that spironolactone 25 mg/day did not statistically significantly change SBP or DBP compared to placebo, SBP: -9.9 (95%CI:-21.15,1.35); DBP -2.34 (95%CI:-7.92,3.06).

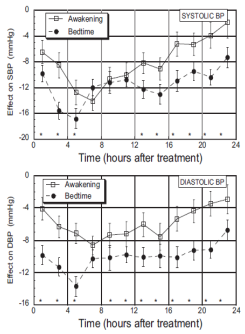
Diuretics

Cost and T1/2:

- **Chlorthalidone 25 and 50 mg tabs generic $17-38.00/30 tabs**
  - **T1/2: 40-60 hrs**
- **Indapamide 1.25 and 2.5 mg tabs generic $4-20.00/30 tabs**
  - **T1/2: 14-26 hrs**
- Hydrochlorothiazide 12.5, 25 and 50 mg tabs generic $4-11.00/30 tabs
  - T1/2: 6-15 hrs
- **Spironolactone 25 and 50 mg tabs generic $4-15.00/30 tabs**
  - **T1/2: 1.4 – 16.5 hrs active metabolite**
- Eplerenone 25 and 50 mg tabs generic $38-150.00/30 tabs
  - T1/2: 3-6 hrs

Morning vs. Bedtime Dosing of Ramipril?

115 untreated hypertensive patients, 46.7 +\- 11.2 years of age, **randomly assigned to receive ramipril (5 mg/d) as a monotherapy either on awakening or at bedtime. Blood pressure was measured for 48 hours before and after 6 weeks of treatment.**
The proportion of patients with **controlled ambulatory blood pressure increased from 43% to 65% (P< 0.019) with bedtime treatment.** Nocturnal blood pressure regulation is significantly better achieved at bedtime as compared with morning administration of ramipril, without any loss in efficacy during diurnal active hours. This might be clinically important, because **nighttime blood pressure has been shown to be a more relevant marker of cardiovascular risk**. (Hypertension 2009;54:40-46)



Efficacy and safety of once vs. twice daily dosing of lisinopril for hypertension

- Patients previously receiving lisinopril 20 mg were placed into the once- daily cohort if changed to **40 mg once daily or into the twice- daily cohort if changed to 20 mg twice daily.** Efficacy outcome measures were change in systolic blood pressure and diastolic blood pressure and achievement of blood pressure control (<140/90 mm Hg). **(Lisinopril the second most prescribed antihypertensive has a T1/2 of 12 hours)**
- Of 90 patients included (45 per cohort), the mean age was 61.8 years and 17.8% were black. **Once- and twice- daily administrations were associated with blood pressure reductions of 6.2/1.5 mm Hg and 16.5/5.9 mm Hg, with a 10.2/4.3 mm Hg greater reduction with twice- daily administration** (systolic blood pressure, P=.016; diastolic blood pressure, P=.068).
- **Twice- daily lisinopril dosing was associated with greater systolic blood pressure reductions compared with the same total daily dose administered once daily.**
  - J Clin Hypertens. 2017;19:868–873 (Univ of Colorado and Univ Florida)

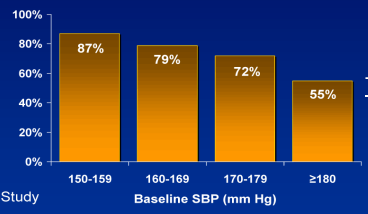
AHA Scientific Statement: Resistant Hypertension

- **Resistant hypertension (RH) is defined as above-goal elevated blood pressure (BP) in a patient despite the concurrent use of 3 antihypertensive drug classes, commonly including a long-acting calcium channel blocker, a blocker of the renin-angiotensin system (angiotensin-converting enzyme inhibitor or angiotensin receptor blocker), and a diuretic.**
- **Management of RH includes** maximization of lifestyle interventions, **use of or substitution of long-acting thiazide-like diuretics (chlorthalidone or indapamide), addition of a mineralocorticoid receptor antagonist (spironolactone or eplerenone),** and, if BP remains elevated, stepwise addition of antihypertensive drugs with complementary mechanisms of action to lower BP. If BP remains uncontrolled, referral to a hypertension specialist is advised.
  - (Hypertension. 2018;72:e53-e90).

Many Providers Not Motivated to Initiate or Change Treatment

Retrospective Analysis

Percentage of Visits *Without* Medication Intensification[1]



Therapeutic Inertia

Retrospective Study

Failure to titrate or combine medications and to reinforce lifestyle modifications despite knowing that the patient is not at goal BP represents clinical inertia that must be overcome.- *JNC 7*[2]

1. Adapted from Andrade et al. *Am J Manag Care.* 2004;10:481-486.
2. Chobanian AV et al. *Hypertension* 2003;42;1206-1252.

Issues Dealing with Adherence to Regimens

- Hypertension is typically asymptomatic for the first 20–25 years (The "Silent Killer")
- Involve the patient in his or her own care and therapy (The patient is the most important member of the team!)
- Patients must be motivated and assume responsibility for their blood pressure and health-promoting lifestyle
- Consider cost, potential adverse effects of medications and potential drug interactions (NSAIDs, SNRIs, triptans, etc.)
- Simplify the regimen as much as possible
  - Consider once a day medications and combination products if appropriate

What do the Numbers Suggest?

According to the National Heart, Lung, and Blood Institute (NHLBI):

- Up to 50% of patients who begin antihypertensive therapy drop out of care within one year
- 50% of those who remain in treatment take less than 80% of their medication
- Who knows or should know this better than anyone except the patient? Ask the pharmacist

Conclusion

- Why do we treat? To reduce events!
- Hypertension is called the "Silent Killer"
- Patients need to know their numbers
- Hypertension effects over 65 million adults in the US and it is a leading cause of cardiovascular disease
- Most important – Control the BP!
- Hypertension is readily treated with a combination of evidence based life style changes and pharmacotherapy resulting in significant reductions in morbidity and mortality
- Even after 30 years of JNC 1-7 we are still a long way from where we need to be but we can help make a difference!
- Use evidence-based and affordable therapy!

SELF EVALUATION

Strategies for Managing Hypertensive Patients to Goal

1. The 2017 American Heart Association/American College of Cardiology Hypertension Guidelines have redefined Stage 2 Hypertension as?

a. BP >130/80 mm Hg
b. BP > 140/90 mm Hg
c. BP > 150/90 mm Hg
d. BP > 160/100 mm Hg
e. None of the above

2. Which of the following patient groups does not have a goal BP of <130/80 mm Hg?

a. Diabetes mellitus
b. Chronic kidney disease
c. Heart failure
d. Secondary stroke prevention
e. None of the above all have a goal < 130/80 mm Hg

3. Which statement about an ACE inhibitor is **not correct**?

a. An ACE inhibitor or an ARB are preferred in patients with chronic kidney disease
b. An ACE inhibitor or ARB, at the maximum tolerated dose indicated for blood pressure treatment, is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin – to – creatinine ratio >/= 30 mg/g creatinine
c. There is no serum creatinine level per se that contraindicates ACE inhibitor therapy
d. Withdrawal of an ACEI should only occur when the rise in serum creatinine exceeds 30% above baseline within the first 2 months of ACEI therapy, or hyperkalemia (5.6mEq/L or greater) develops.
e. None of the above, all are correct.

4. Which diuretic is not recommended in both the UK NICE BP Guidelines and the new American Heart Association Scientific Statement on Resistant Hypertension?

a. Hydrochlorothiazide
b. Chlorthalidone
c. Indapamide
d. Spironolactone

5. T/F - According to the National Heart, Lung, and Blood Institute (NHLBI): Up to 50% of patients who begin antihypertensive therapy drop out of care within one year and 50% of those who remain in treatment take less than 80% of their medication.

Answer Key: 1. B, 2. E, 3. E, 4. A, 5. T