50th Annual Primary Care Review

Monday

OHSU

Challenges in Management of the Older Patient with CKD

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Oregon Health & Science University
VA Portland Health Care System
February 2019

DISCLOSURES

Nothing to Disclose

CKD is Common in the U.S.

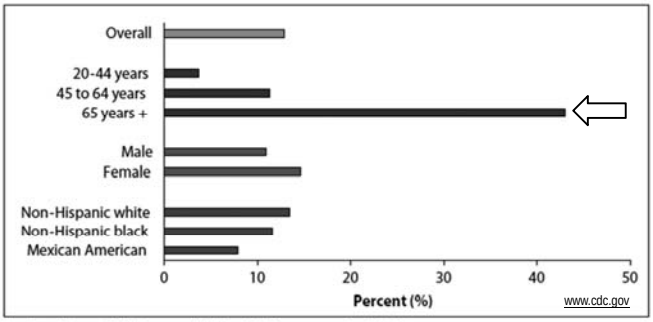


Figure legend: Percent with CKD among adult U.S. population by age, sex, and race/ethnicity.

Incorporating Lag Time to Benefit into Prevention Decisions for Older Adults

- The question "when will it help?" is just as important as "how much will it help?"
- If a person's life expectancy is substantially shorter than the lag time to benefit, then administering the intervention poses immediate risks, with little likelihood of surviving long enough to benefit

Lee SJ, JAMA 310: 2609–2610, 2013

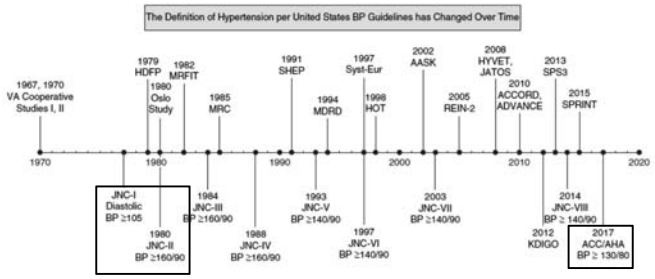
An Older Woman with CKD

- 84 year old Caucasian female with hypertension, Type 2 diabetes, GERD, atrial fib
- Meds: Lisinopril; metoprolol; glipizide; warfarin; atorvastatin; omeprazole
- BP = 146/62 mmHg
- Cr = 1.2 mg/dl; eGFR = 45 ml/min/1.73m^2, stable x 4 years; nonproteinuric

Management Questions

- Hypertension target and therapy
- Diabetes target and therapy
- GERD therapy
- Anticoagulation
- Hyperlipidemia
- Renal prognosis/risk of ESRD

The Changing Definition of HTN over Time



Alex R. Chang et al. CJASN doi:10.2215/CJN.07440618

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

AMERICAN COLLEGE of CARDIOLOGY

Whelton PK, JACC 2017

American Heart Association. life is why

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.

Age-Related Issues

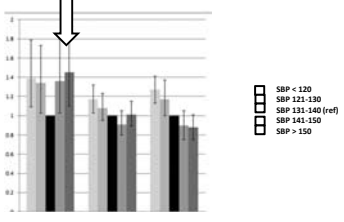
COR	LOE	Recommendations for Treatment of Hypertension in Older Persons
I	A	Treatment of hypertension with a SBP treatment goal of less than 130 mm Hg is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age) with an average SBP of 130 mm Hg or higher.
IIa	C-EO	For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit is reasonable for decisions regarding intensity of BP lowering and choice of antihypertensive drugs.

SBP and Mortality in Older CKD Patients

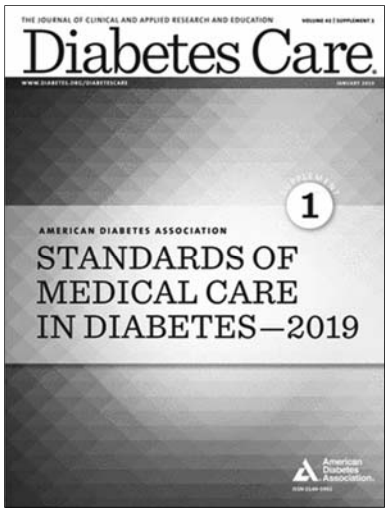
Weiss JW, et al. CJASN 10:1553, 2015

- Retrospective cohort study of 21,015 patients aged ≥ 65 years with eGFR < 60; 11 year follow-up

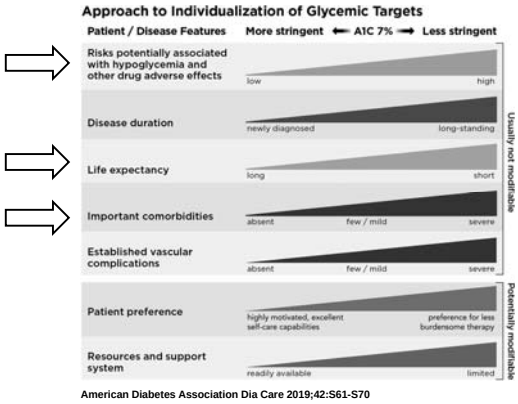
Hazard Ratio for Mortality



- Risk of death was highest for patients with lowest SBP in all age groups
- Only in those aged 65-70 was SBP > 140 mmHg associated with higher risk of death



Patient and Disease Factors used to Determine Optimal A1C Targets



American Diabetes Association Dia Care 2019;42:S61-S70

American Diabetes Association.

Management of Diabetic CKD

- Glycemic control
  - Metformin: ↑ risk of lactic acidosis
    - Contraindicated if eGFR < 30
    - If eGFR falls below 45 in patient already on metformin, OK to continue if stable, but d/c when eGFR < 30
  - Avoid glyburide
    - ↑ half-life, prolonged hypoglycemia
  - Glipizide preferred; glimepiride OK (low dose)
  - DPP4 inhibitors may be OK; avoid SGLT2 inhibitors
  - In CKD: always advise patients about risk of hypoglycemia, need to ↓ hypoglycemic meds

PPIs and Risk of CKD

- Increasing evidence has linked PPIs with risk of CKD, becoming apparent after 3 months of use
- PPI use is associated with a 20-50% ↑ risk of incident CKD
- Risk is seen in all demographic groups
- Twice daily dosing carries higher risk than once daily

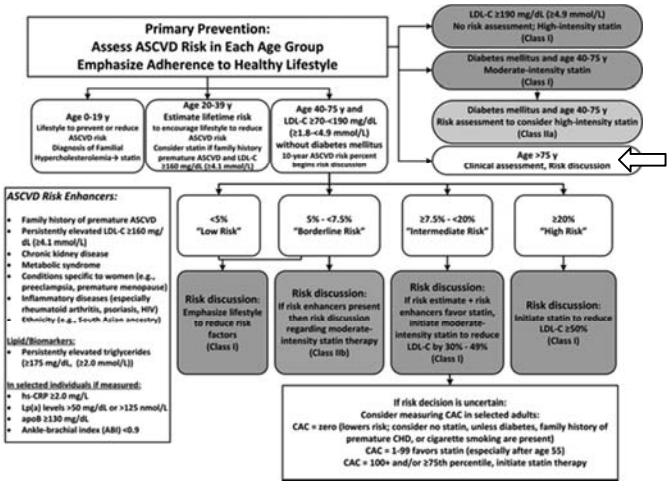
Lazarus B, JAMA IM 176:238, 2016

Grundy SM, et al.
2018 Cholesterol Clinical Practice Guidelines

2018
AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA
Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Grundy SM. Circulation 2018, Nov. 10



Anticoagulation in CKD Patients

Eur J Haematol. 2018 Dec 28. doi: 10.1111/ejh.13206. [Epub ahead of print]

The Efficacy and Safety of Direct Oral Anticoagulants in Patients with Chronic Renal Insufficiency: A Review of the Literature.

Weber J[1], Olyaei A[2,3], Shatzel J[1].

- Warfarin: decades of experience
- Newer anticoagulants:
  - Possible ↑ risk of bleeding (compared with warfarin) in advanced CKD
  - Similar benefit in stroke prevention
  - Apixaban (low dose) appears to be the safest option

Nephropharmacology for the Clinician

Medication Safety Principles and Practice in CKD

Chanel F. Whittaker,[1] Margaret A. Miklich,[2] Roshni S. Patel,[3] and Jeffrey C. Fink[4]

Abstract

Ensuring patient safety is a priority of medical care because iatrogenic injury has been a primary concern. Medications are an important source of medical errors, and kidney disease is a thoroughfare of factors threatening safe administration of medicines. Principal among these is reduced kidney function because almost half of all medications used are eliminated *via* the kidney. Additionally, kidney patients often suffer from multimorbidity, including diabetes, hypertension, and heart failure, with a range of prescribers who often do not coordinate treatments. Patients with kidney disease are also susceptible to further kidney injury and metabolic derangements from medications, which can worsen the disease. In this review, we will present the key issues and threats to safe medication use in kidney disease, with a focus on predialysis CKD, as the scope of medication safety in ESKD and transplantation are unique and deserve their own consideration. We discuss drugs that need to be avoided or dose modified, and review the complications of a range of medications routinely administered in CKD, as these also call for cautious use.

Clin J Am Soc Nephrol 13: 1738–1746, 2018. doi: https://doi.org/10.2215/CJN.00580118

Whittaker CF, CJASN 13:1738, 2018

An Older Woman with CKD

- 84 year old Caucasian female with hypertension, Type 2 diabetes, GERD, atrial fib
- Meds: Lisinopril; metoprolol; glipizide; warfarin; atorvastatin; omeprazole
- BP = 146/62 mmHg
- Cr = 1.2 mg/dl; eGFR = 45 ml/min/1.73m^2, stable x 4 years; nonproteinuric

Prognosis?

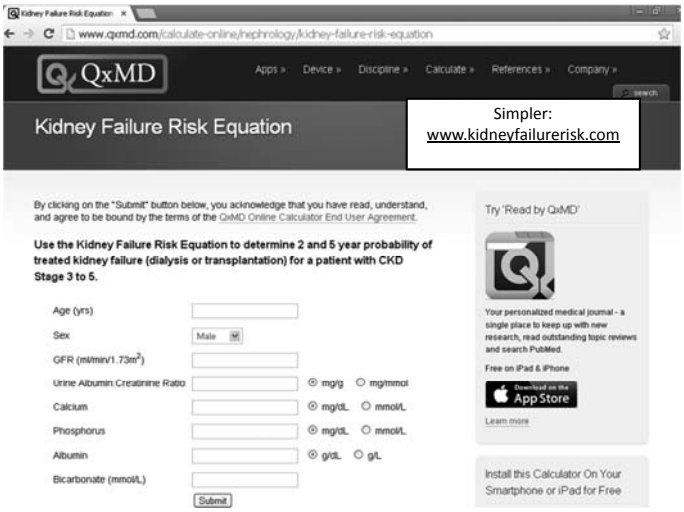
Stage 3 CKD in the Era of Precision Medicine

- 84-year old Caucasian female

eGFR 45 ml/min/1.73m^2

- 35-year old African-American male

eGFR 45 ml/min/1.73m^2



Progression Risk Calculator

Tangri N, et al. JAMA 305:1553, 2011

- 84 year old female with eGFR 45, nonproteinuric
- Risk of progression to ESRD:
  - Over 2 years: 0.4%
  - Over 5 years: 1.4%

IF NOTHING ELSE HAPPENS

www.qxmd.com

Questions

- Will diagnosis and treatment of early CKD in older persons confer **benefit** (survival, CVD, CKD)?
- Do the benefits > the **harms** of diagnosis and treatment?

OPEN ACCESS Freely available online PLOS | MEDICINE

Essay

Using Evidence to Combat Overdiagnosis and Overtreatment: Evaluating Treatments, Tests, and Disease Definitions in the Time of Too Much

Ray Moynihan[1]*, David Henry[2,3], Karel G. M. Moons[4]

- Over-diagnosis and related overtreatment are major problems
- "Positive" average results from treatment trials can mask situations where patients at low risk may receive no benefit

Most older patients with CKD do NOT need ACEI/ARBs

PLOS Medicine 11(7):e1001655, 2014
JAMA Intern Med. 2014 Mar;174(3):391-7

OPEN ACCESS Freely available online PLOS | MEDICINE

Essay

Using Evidence to Combat Overdiagnosis and Overtreatment: Evaluating Treatments, Tests, and Disease Definitions in the Time of Too Much

Ray Moynihan[1]*, David Henry[2,3], Karel G. M. Moons[4]

- Over-diagnosis and related overtreatment are major problems
- "Positive" average results from treatment trials can mask situations where patients at low risk may receive no benefit
- Evaluation of diagnostic tests usually looks at how well they detect presence or absence of disease, but not how well they detect clinically meaningful stages of disease
- Changes to disease definitions often do not involve evaluation of potential harms of over-diagnosis – and are often conducted by heavily conflicted panels

PLOS Medicine 11(7):e1001655, 2014

What About Number Needed to Harm?

Zermansky A. BMJ 317:1014, 1998

- A possible solution is to separate adverse effects into several grades:
  - Number needed to kill
  - Number needed to disable
  - Number needed to make you ill
  - Number needed to annoy
- The concept of attaching a price list to the therapeutic agent should not stop at the cost of the pills

Concerns re CKD G3A

Moynihan R, et al. BMJ 347:f4298, 2013

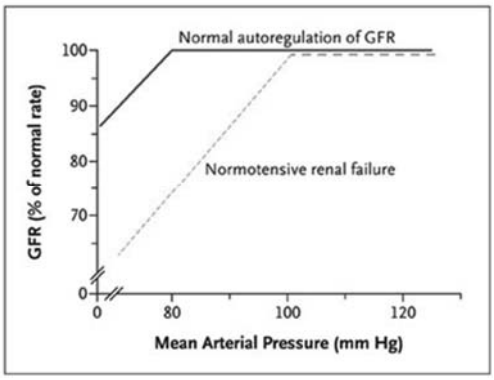
- Why is eGFR < 60 considered abnormal at all ages?
  - This may be 50% of "normal" GFR for young adults, but not older adults
- ¾ of CKD3A patients have no albuminuria
- In older patients, is this really a *disease*, or medicalization of the normal aging process?

An Older Woman with CKD

- 84 year old Caucasian female with hypert
  Type 2 diabetes, atrial fib
- Meds: Lisinopril; metoprolol; glipizide; warfarin
- BP = 146/62 mmHg
- Cr = 1.2 mg/dl; eGFR = 45 ml/min/1.73m^2, stable x 4 years; nonproteinuric
- She develops hip pain, for which she takes naproxen. When seen by her PCP, Cr = 2.2 mg/dl

Normotensive Ischemic AKI

Abuelo JG. NEJM 357:797-805, 2007



What is her prognosis?

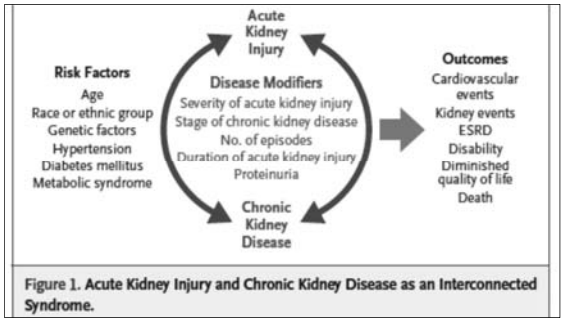


Figure 1. **Acute Kidney Injury and Chronic Kidney Disease as an Interconnected Syndrome.**

Chawla LS, et al. Nat Rev Neph 2017 Apr;13(4):241-257

An Older Woman with CKD

- 84 year old Caucasian female with hypertension, Type 2 diabetes, atrial fib
- Cr = 1.2 mg/dl; eGFR = 45 ml/min/1.73m^2, stable x 4 years; nonproteinuric
- She develops hip pain, for which she takes naproxen. When seen by her PCP, Cr = 2.2 mg/dl
- ACEI and NSAIDs are stopped. Her serum Cr settles at 1.8 mg/dl [eGFR 22 ml/min/1.73m^2]

An Older Woman with CKD

- She is referred to a nephrologist
- A brief discussion introduces the topic of dialysis, with plan to further explore goals of care in subsequent visits

Choosing Wisely
An initiative of the ABIM Foundation

American Society of Nephrology
ASN

Five Things Physicians and Patients Should Question

5 **Don't initiate chronic dialysis without ensuring a shared decision-making process between patients, their families, and their physicians.**

The decision to initiate chronic dialysis should be part of an individualized, shared decision-making process between patients, their families, and their physicians. This process includes eliciting individual patient goals and preferences and providing information on prognosis and expected benefits and harms of dialysis within the context of these goals and preferences. Limited observational data suggest that survival may not differ substantially for older adults with a high burden of comorbidity who initiate chronic dialysis versus those managed conservatively.

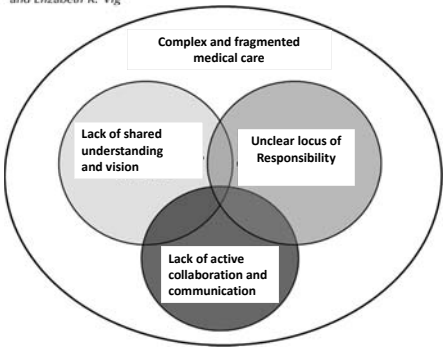
www.choosingwisely.org
Williams AW, CJASN 7:1664, 2012

Talking about Dialysis is like Talking about Cancer

- Patients and families would rather not think about it and wish it would go away
- Providers would prefer not to talk about it
- Discussions are difficult
- But – patients want the information; they expect their providers to initiate the conversation; and they want to know all their options

Provider Perspectives on Advance Care Planning for Patients with Kidney Disease: Whose Job Is It Anyway?

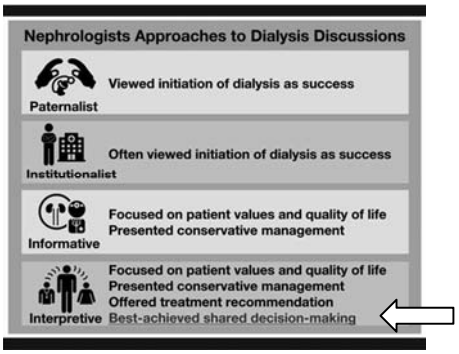
Ann M. O'Hare,†‡ Jackie Szarka,* Lynne V. McFarland,* Janelle S. Taylor,§ Rebecca L. Sudore,‖¶ Ranak Trivedi,**†† Lynn F. Reinke,*† and Elizabeth K. Vig‡‡*



CJASN 11:855, 2016

How do nephrologists' approaches influence variation in dialysis decision-making among older patients?

CJASN



Keren Ladin et al. CJASN 2018;13:1188-1196

An Older Woman with CKD

- She is referred to a nephrologist
- A brief discussion introduces the topic of dialysis, with plan to further explore goals of care in subsequent visits
- Subsequent discussions are inconclusive
- Over the next year, her renal function declines to Stage 5; it's time to make a decision

Should we dialyze grandma?

HEALTH POLICY

Dialysis in the Frail Elderly — A Current Ethical Problem, an Impending Ethical Crisis

Bjorg Thorsteinsdottir, MD[1], Keith M. Swetz, MD, MA[2,3], and Jon C. Tilburt, MD, MPH[2,3,4,5]

The Ethics of Chronic Dialysis for the Older Patient: Time to Reevaluate the Norms

Bjorg Thorsteinsdottir,*† Keith M. Swetz,‡†§ and Robert C. Albright‖

Practice Change Is Needed for Dialysis Decision Making with Older Adults with Advanced Kidney Disease

Jennifer S. Scherer*† and Alvin H. Moss*§

Clin J Am Soc Nephrol 11: 1732–1734, 2016. doi: 10.2215/CJN.08770816

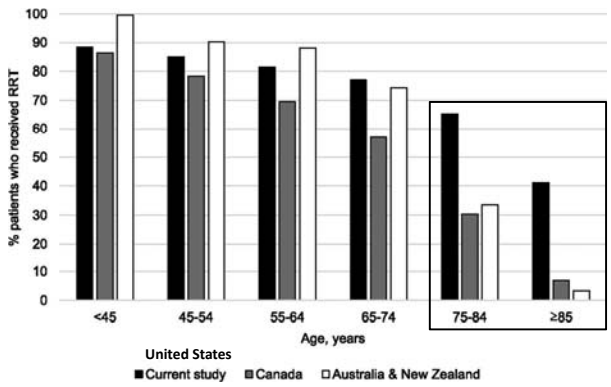
Ethics of Chronic HD in the Elderly

- Overall benefit is modest at best for frail elderly patients with multimorbidity

Table 1. Six commonly articulated goals of care
1. Be cured 2. Live longer 3. Improve or maintain function/quality of life/ independence 4. Be comfortable 5. Achieve life goals 6. Provide support for family/caregiver
Adapted from reference 8, with permission.*

*Kaldjian LC, et al Am J Hosp Pall Care 25:501, 2008

International Differences in Use of RRT in Advanced CKD



Susan P.Y. Wong et al. CJASN 2016;11:1825-1833

CJASN

Prognosis: Elderly Patients on Hemodialysis

Kurella Tamura M, et al. NEJM 361:1539, 2009

- Used registry to examine all 3702 U.S. nursing home residents starting HD 1998-2000

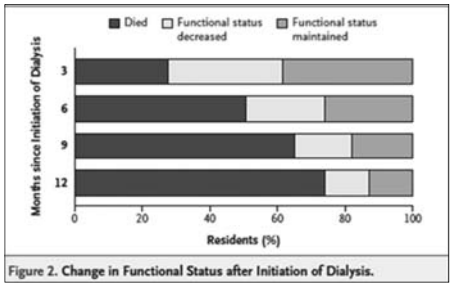


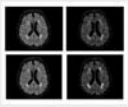
Figure 2. Change in Functional Status after Initiation of Dialysis.

Investigating the relationship between cerebral blood flow and cognitive function in hemodialysis patients

METHODS

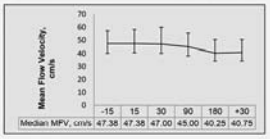
97 Hemodialysis patients

Prospective cohort study with 12 month follow-up Correlating transcranial Doppler mean flow velocity (MFV), cognitive function during & out-with hemodialysis (HD) and cerebral MRI in 40 participants.



RESULTS

HD induces a transient decline in cerebral blood flow, correlating with intradialytic & longer-term cognitive dysfunction & associates with progressive cerebral white matter hyper-intensities.



CONCLUSION Hemodialysis is capable of inducing transient cerebral stunning, offering one mechanism of cerebral injury in ESRD

doi: 10.1681/ASN.2018050462

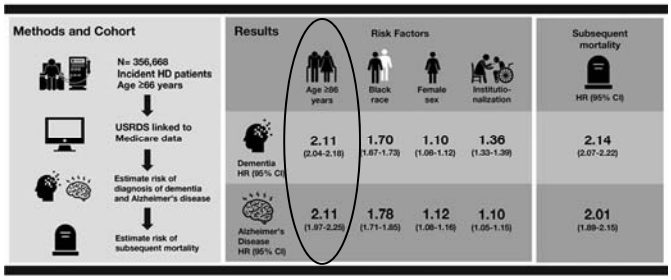
Mark Duncan Findlay et al. JASN
doi:10.1681/ASN.2018050462

JASN

JASN

Dementia, Alzheimer's Disease, and Mortality after Hemodialysis Initiation

Mara A. McAdams-DeMarco[1,2] Matthew Daubresse,[2] Sunjae Bae[1] Alden L. Gross,[2,3] Michelle C. Carlson,[3,4] and Dorry L. Segev[1,2]



McAdams MA, CJASN 13:1339, 2018

Intensity of Care During the Final Month of Life

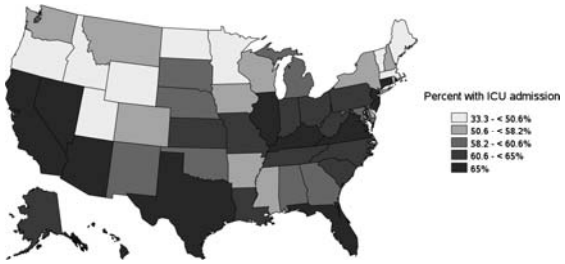
Wong SPY, et al. Arch Intern Med 172:661, 2012

Table. Intensity of Care During the Final Month of Life

	Medicare Beneficiaries		
Intensity of Care	Dialysis (Present Study)	Cancer[7]	Heart Failure[8,9]
Hospitalization, %	76.0	61.3	64.2
Days hospitalized, mean	9.8	5.1	NA
Intensive care unit admission, %	48.9	24.0	19.0
Days in an intensive care unit, mean	3.5	1.3	NA
Any intensive procedure, %	29.0	9.0	NA
Hospice use, %	20.0	55.0	39.1
Death in a hospital, %	44.8	29.0	35.2

vol 2 Figure 12.3 ICU admission during the last 90 days of life among Medicare beneficiaries with ESRD overall, and by age, race, ethnicity, sex, and modality, 2000-2014

(g) ICU admission by state



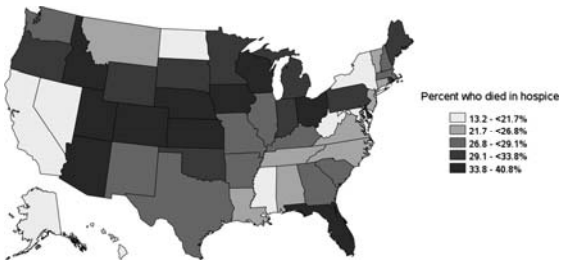
Data Source: Special Analyses, USRDS ESRD Database. Denominator is all decedents with Medicare Parts A and B throughout the last 90 days of life. ICU admission was identified using ICU revenue center codes in Medicare Institutional claims. Abbreviations: ESRD, end-stage renal disease; ICU, Intensive care unit.

2017 Annual Data Report
Volume 2, Chapter 12

www.usrds.org

vol 2 Figure 12.9 Hospice utilization at the time of death among Medicare beneficiaries with ESRD overall, and by age, race, ethnicity, sex, modality, and whether dialysis was discontinued, 2000-2014

(h) Hospice utilization by state



Data Source: Special Analyses, USRDS ESRD Database. Denominator population is all decedents with Medicare Parts A and B throughout the last 90 days of life. Receipt of hospice care at the time of death was defined as having a claim in the Hospice SAF on or after the date of death or Discharge Status from hospice=40, 41, or 42. Abbreviation: ESRD, end-stage renal disease.

2017 Annual Data Report
Volume 2, Chapter 12

www.usrds.org

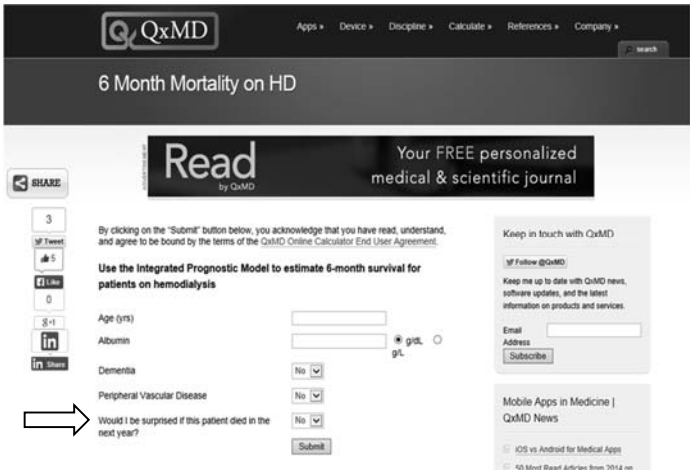
clinical investigation www.kidney-international.org

Survival among older adults with kidney failure is better in the first three years with chronic dialysis treatment than not

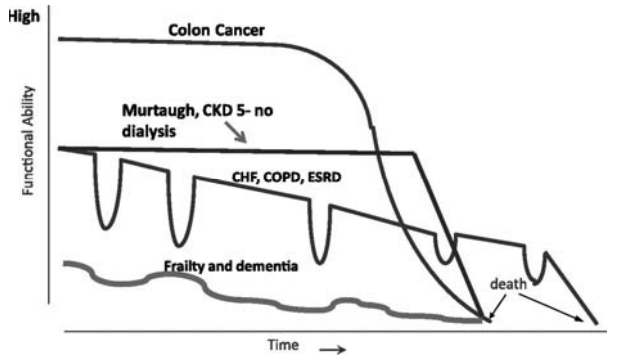
Helen Tam-Tham[1], Robert R. Quinn[1,2], Robert G. Weaver[1], Jianguo Zhang[1], Pietro Ravani[1,2], Ping Liu[1], Chandra Thomas[1], Kathryn King-Shier[2,3], Karen Fruetel[1], Matt T. James[1,2], Braden J. Manns[1,2], Marcello Tonelli[1,2], Fliss E.M. Murtagh[4] and Brenda R. Hemmelgarn[1,2]

Important Caveats:
- Functional status often declines after starting dialysis
- Up to 75% of any time gained is likely to be "medical contact time" (time in dialysis unit, in hospital, or appts addressing care related to dialysis)

Kidney International (2018) **94,** 582–588



Illness Trajectories



Holley J L CJASN 2012;7:1033-1038

CJASN

More Challenges

Zijin C, Hsu C. JAMA IM 178:664, 2018

- While a deliberate process of shared decision-making is the goal, more than half of incident ESRD patients start dialysis during a hospitalization
- Patients may be acutely ill, vulnerable, and cognitively impaired
- Momentum and pressure build from various sources, including other specialties, to "do something"
- So shared decision-making is hard to achieve

An Older Woman with CKD

- She is then admitted to the MICU with pneumonia, sepsis, and oligo-anuric AKI
- The MICU team tells the patient and family that "she needs dialysis; we'll call nephrology"
- What will be the outcome if we dialyze her?

Original Investigation

Functional Trajectories Among Older Persons Before and After Critical Illness

Lauren E. Ferrante, MD; Margaret A. Pisani, MD, MPH; Terrence E. Murphy, PhD; Evelyne A. Gahbauer, MD, MPH; Linda S. Leo-Summers, MPH; Thomas M. Gill, MD

CONCLUSIONS AND RELEVANCE Among older persons with critical illness, more than half died within 1 month or experienced significant functional decline over the following year, with particularly poor outcomes in those who had high levels of premorbid disability. These results may help to inform discussions about prognosis and goals of care before and during critical illness.

JAMA Intern Med. 2015;175(4):523-529
Published online February 9, 2015.

The Ethics of Offering Dialysis for AKI to the Older Patient: Time to Re-Evaluate?

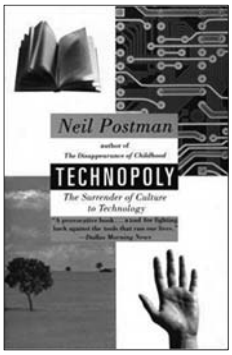
Sana Akbar and Alvin H. Moss*†*

- A major consequence of the biomedicalization of aging is . . . the relatively unquestioned provision of dialysis for AKI to older patients
- Nephrologists should not automatically recommend dialysis for older patients
- In those who can be predicted to do poorly, recommending against dialysis upholds the Hippocratic maxim to be of benefit and do no harm
- [We] challenge the automatic transformation of the technological imperative into the moral imperative for such patients

CJASN 9:1652, 2014

An Older Woman with CKD

- She is then admitted to the MICU with pneumonia, sepsis, and oligo-anuric AKI
- The MICU team tells the patient and family that “she needs dialysis; we’ll call nephrology”
- What will be the outcome if we dialyze her?
- After discussions among the patient, her family, the treatment teams, and the palliative care service, she was transitioned to comfort care, and passed away peacefully



A technopoly is founded on the belief that technique is superior to lax, ambiguous and complex human thinking and judgment

Primary Care Providers – First Line of Defense against CKD

- PCPs: significant role in early diagnosis, treatment, and patient education
- Therapeutic interventions for CKD are similar to those required for optimal cardiac care
  - Control of glucose, blood pressure, and lipids; smoking cessation, avoidance of nephrotoxins
- In goals of care discussions with older patients with advanced CKD – please talk about dialysis!

CKD is Part of Primary Care

Thank you!

A Day in the Hospital
Jose S. Perez

Non-Alcoholic Fatty Liver Disease: Where Are We and Where Are We Going

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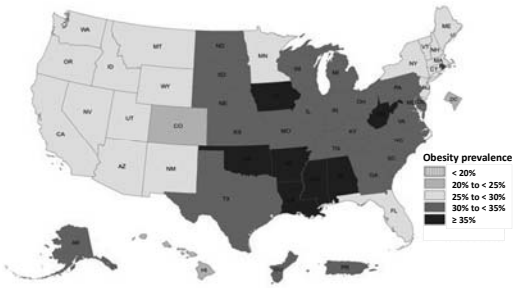
Oregon Health & Science University

Disclosures

None

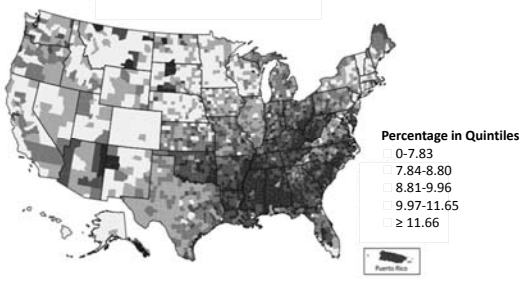
Magnitude of the Problem: Role of Obesity and T2DM

Obesity in the United States, 2017



CDC Behavioral Risk Factor Surveillance System. https://www.cdc.gov/obesity/data/prevalence-maps.html

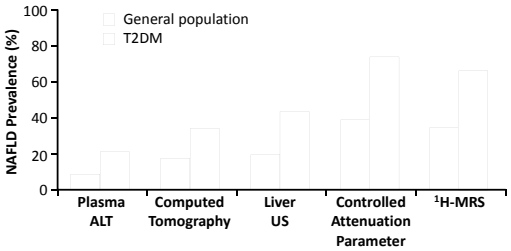
The Epidemic: 2013 Diabetes Prevalence in Adults



United States Diabetes Surveillance System. https://www.cdc.gov/diabetes/atlas/countydata/atlas.html

NAFLD in Patients With vs Without T2DM by Diagnostic Approach

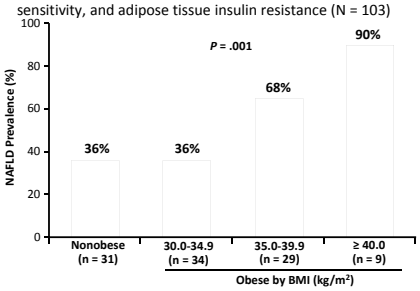
- Pooled results of patients with and without T2DM with NAFLD diagnosed by different means



Bril. Diabetes Care. 2017;40:419.

Prevalence of NAFLD and NASH in Patients With T2DM and Normal Plasma AST or ALT

- Patients with T2DM and normal AST or ALT evaluated for liver triglyceride content by H-MRS, insulin sensitivity, and adipose tissue insulin resistance (N = 103)

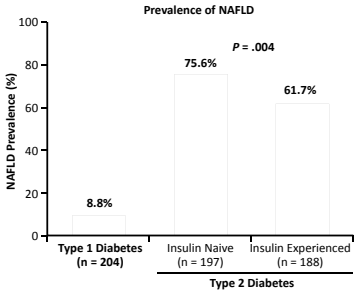


- Prevalence of NAFLD in overall cohort: 50%
  - Among these patients, prevalence of NASH: 56%

Portillo-Sanchez. J Clin Endocrinol Metab. 2015;100:2231. Stål. World J Gastroenterol. 2015;21:11077.

Prevalence of NAFLD in Patients With Type 1 and 2 Diabetes

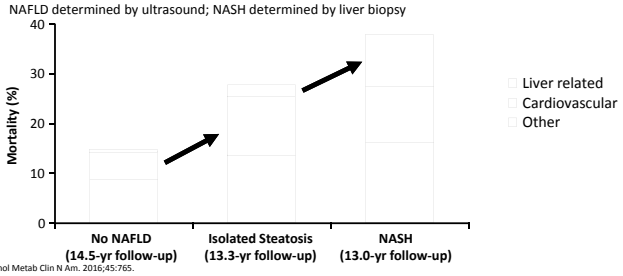
- Post hoc analysis of baseline data from 4 phase III trials (N = 589)
- Exclusion criteria: triglycerides > 400 mg/dL and ALT/AST > 2.5 x ULN



Cusi. Diabetes Obes Metab. 2017;19:1630.

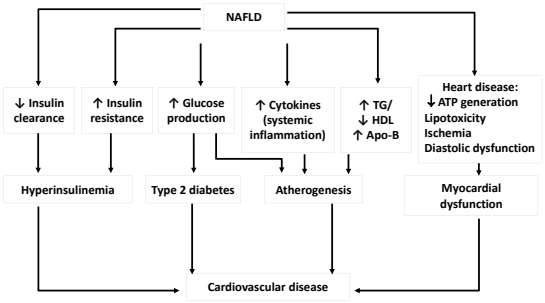
Mortality Risk Associated With Isolated Steatosis and NASH

- Analysis of all-cause mortality in 6 separate studies among patients without NAFLD vs with and without NASH
  - NAFLD determined by ultrasound; NASH determined by liver biopsy



Bril. Endocrinol Metab Clin N Am. 2016;45:765.

Metabolic Consequences of NAFLD



Cusi. Gastroenterology. 2012;142:711.

Magnitude of the Problem: Sedentary Lifestyle, Genetic Factors, Alcohol

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Sedentary Lifestyle in NAFLD

- Physical inactivity linked to
  - Increased body weight
  - Central adiposity
  - Insulin resistance
  - Increased risk of metabolic syndrome
  - NAFLD
  - Severity of NASH

Hannah. Dig Dis Sci. 2016;61:1365.

Genetic Risks for NAFLD

- Known: Patatine-like phosphatase in domain 3 (PNPLA3) polymorphism, others
- Unknown: probably many, as NAFLD, hepatic steatosis, and hepatic fibrosis are heritable traits[1]
  - Family history of diabetes, even among people without diabetes, is associated with NASH and NAFLD fibrosis[2]
  - Increased odds of advanced cirrhosis in first-degree relatives of patients with NAFLD cirrhosis[1]

1. Caussy. J Clin Invest. 2017;127:2697. 2. Loomba. Hepatology. 2012;56:943.

Moderate Alcohol Use and NASH: Inconclusive Relationship

- In separate cross-sectional or longitudinal studies of NAFLD, **no vs moderate alcohol use** associated with conflicting outcomes:
  - Key features of steatohepatitis, fibrosis[1]
  - NASH resolution (and more improvement in steatosis, ALT)[2]
- Practical recommendations
  - Conservative: occasional single drink is okay
  - Maximum: 1 drink daily for women, 2 drinks daily for men
  - Avoid binging (eg, 7 drinks on Friday, none the rest of the week)

"A strong recommendation of benefit of moderate alcohol use in NAFLD cannot be made."[3]

1. Dunn. J Hepatology. 2012;57:384. 2. Ajmera. Clin Gastroenterol Hepatology. 2018;16:1511. 3. Amjera. Hepatology. 2017;65:2090.

Considerations in Patients With Atypical NAFLD

- Be sure to fully exclude Wilson's disease (24-hr urine copper)
- Low cholesterol (eg < 100 mg/dL): check ApoB, may be hypobetalipoproteinemia
- Get a good diet history for unusual supplements
- Corroborate minimal or no alcohol (especially if AST > ALT)
- Lysosomal acid lipase deficiency?

Chalasani. Hepatology. 2018;67:328.

Diagnosis

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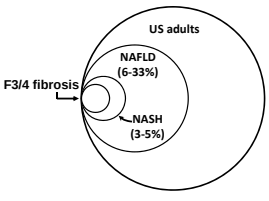
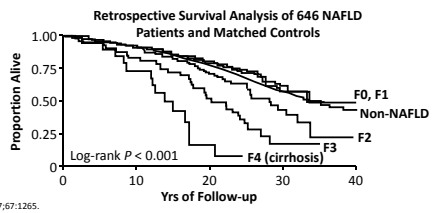
Diagnosis: Goals

- Goal 1: Identify those with NASH
  - Having NASH increases the risk of progression of fibrosis
  - Identify treatment candidates
- Goal 2: Identify those at risk for progressing to cirrhosis
  - Having advanced fibrosis is associated with increased mortality





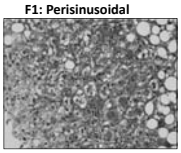
Stål . World J Gastroenterol. 2015;21:11077. Hagström. J Hepatology. 2017;67:1265.

Diagnosis: Approaches

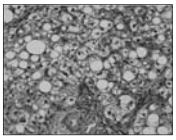
- NAFLD
  - US, CT, MRI, *FibroScan*
- NASH
  - Liver biopsy
- Advanced fibrosis
  - FIB4, APRI, proprietary panels
  - *FibroScan*/ARFI
  - MR elastography
  - Liver biopsy

Fibrosis Staging in NASH

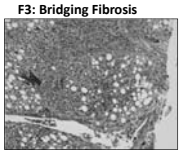
F1: Perisinusoidal



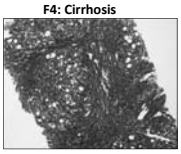
F2: Perisinusoidal + Portal



F3: Bridging Fibrosis

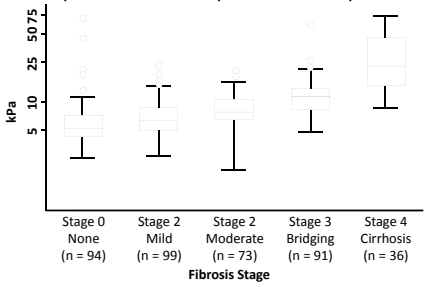


F4: Cirrhosis



Detecting Liver Fibrosis With *FibroScan*

- NASH CRN: 393 patients with biopsies within 1 yr



Trend test $P < .0001$

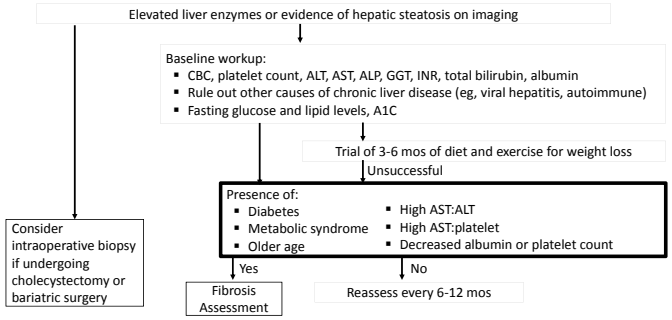
Siddiqui. Clin Gastroenterol Hepatology. 2018;18:S1542.

Detecting NASH, Fibrosis With Liver Biopsy

- **Benefits**
  - Establish diagnosis of NASH
  - Rule out other processes: alpha-1 antitrypsin, iron overload, autoimmune component
  - Assess early fibrosis
- **Limitations**
  - Risk of bleeding, pain
  - Sampling variability (especially with IR biopsies if they are small)

Rockey. Hepatology. 2009;49:1017.

Approach to Initial Assessment and Consideration for a Liver Biopsy



Noureddin. Clin Liver Dis. 2012;1:104.

Management of NAFLD/NASH

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No need to diagnose NASH

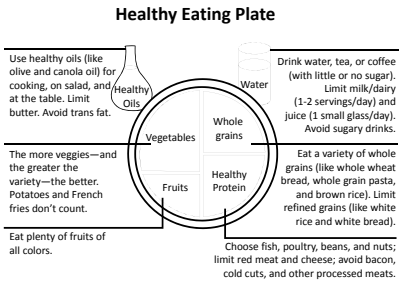
if there are no treatments . . .

Wrong!

Dietary Habits: One Approach

- "Healthy eating" (instead of "dieting")
- Mediterranean diet
- Harvard Healthy Eating Plate
- Eliminate sugar-sweetened beverages (get history from every patient—it's shocking)
- Use healthy oils (olive, canola)
- Portion control
- Minimize restaurants or split portions
- Avoid fast food
  - Calorie dense (1300 cal and more fat than a stick of butter in some commonly marketed burgers)

Harvard Healthy Eating Pyramid and Plate



https://www.hsph.harvard.edu/nutritionsource/healthy-eating-plate/

AASLD Guidance: Nonpharmacologic Approaches

- **Weight loss**
  - 3% to 5% to improve steatosis, but 7% to 10% to **improve** the majority of the histopathologic features of NASH, including **fibrosis**
- **Exercise**
  - **Exercise alone may prevent or reduce steatosis,** but its ability to improve other aspects of liver histology remains unknown
- **Bariatric surgery**
  - Can be considered in otherwise eligible obese individuals with NAFLD or NASH
  - Premature to consider bariatric surgery as an established option to treat NASH
  - The type, safety, and efficacy of bariatric surgery are not established in obese individuals with cirrhosis from NAFLD
  - In patients with compensated NASH or cryptogenic cirrhosis, bariatric surgery may be considered on a case-by-case basis by an experienced bariatric surgery program

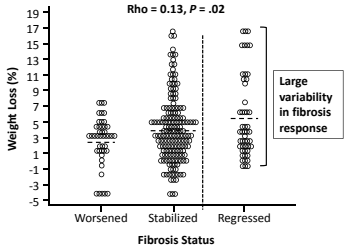
Chalasani. Hepatology. 2018;67:328.

Weight Loss Associated With NASH Improvement but Substantial Variability in Fibrosis

Probability of Improving NASH Components After 1 Yr of Lifestyle Interventions (N = 293)

	Mean Weight Loss, %			
Outcome, %	**< 5**	**5-7**	**7-10**	**> 10**
Patients achieving weight loss	70	12	9	10
Probability of improvement*				
▪ NASH resolution	10	26	64	90
▪ Fibrosis regression	45	38	50	81
▪ Steatosis improvement	35	65	76	100

*At least 1 stage.



Romero-Gomez. J Hepatology. 2017;67:829. Vilar-Gomez. Gastroenterology 2015;149:367.

Sedentary Lifestyle and Exercise in NAFLD

- Physical inactivity linked to[1]
  - Increased body weight
  - Central adiposity
  - Insulin resistance
  - Increased risk of metabolic syndrome
  - NAFLD
  - Severity of NASH
- Adults with NAFLD (N = 813)[2]
  - 54% of patients reported NO physical activity
  - Vigorous-intensity exercise (≥ 6 METs for 75 min/wk) associated with decreased odds of NASH
    - OR: 0.65 (95% CI: 0.43-0.98; *P* = .04)

1. Hannah. Dig Dis Sci. 2016;61:1365. 2. Kistler. Am J Gastroenterol. 2011;106:460.

Bariatric Surgery Improves Clinical Parameters

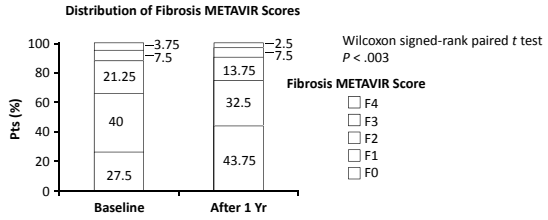
- Prospective study following bariatric surgery in pts who are severely obese with ≥ 1 comorbidity, no excessive drinking < 2 yrs, no chronic liver diseases (N = 381)
  - Liver biopsies assessed by 2 blinded reviewers for fibrosis (F0-4), NAFLD scoring to determine NASH (≥ 3, probable or definite; ≥ 5, definite)

Parameter	Before Surgery	After 5 Yrs	*P* Value
Diabetes mellitus, n (%)	94 (24.8)	24 (10.8)	.00001
Arterial hypertension, n (%)	185 (48.8)	85 (37.0)	.0005
Serum triglycerides, mean (g/L)	1.67	1.06	.00001
Fasting glucose, mean (g/L)	1.18	0.94	.00001
Insulin resistance index, mean	3.2	2.83	.00001
ALT, mean (IU/L)	30.1	22.8	.00003
GGT, mean (IU/L)	39.9	29.2	.00001

Mathurin P, et al. Gastroenterology. 2009;137:532-540.

Bariatric Surgery Improves Fibrosis in Pts With NASH

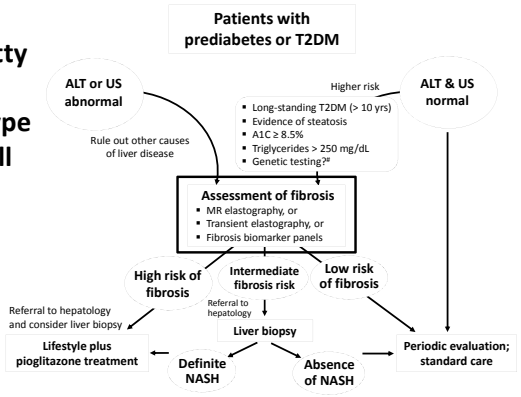
- Prospective study of bariatric surgery in pts who are morbidly obese with biopsy-validated NASH, ≥ 1 comorbidity factor for > 5 yrs, no chronic liver disease (N = 109)



Lassailly G, et al. Gastroenterology. 2015;149:379-388.

Management of Nonalcoholic Fatty Liver Disease in Patients With Type 2 Diabetes: A Call to Action

- Algorithm for endocrinologists and primary care providers



Bril. Diabetes Care. 2017;40:419.

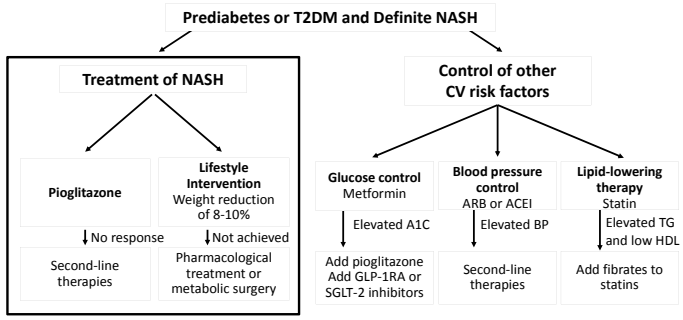
AASLD Guidance on CV Risk: Statins in Patients With NASH

- "Patients with NAFLD are at high risk for cardiovascular morbidity and mortality. Thus, **aggressive modification of CVD risk factors should be considered** in all patients with NAFLD"
- "Patients with NAFLD or NASH are not at higher risk for serious liver injury from statins. Thus, **statins can be used to treat dyslipidemia in patients with NAFLD and NASH**"

Statins recommended for reducing CV risk, not for resolving NASH
"Clinical trials of statins as treatment for NASH are limited and have shown inconsistent results"

Chalasani. Hepatology. 2018;67:328.

Treatment of NASH



Bril & Cusi, Diabetes Care 2017 40:419-430

Phase II Data on Investigational NAFLD/NASH Therapies Presented at AASLD 2018

Agent	MOA	N	Study Population
GS-9674[1]	FXR agonist	140	NASH
Obeticholic acid[2]	FXR agonist	84	NASH, fibrosis
Tropifexor[3]	FXR agonist	198	NASH
NGM282[4,5]	FGF19 analogue	38, 85	NASH
MGL-3196[6]	THR-β agonist	125	NASH, hepatic fat fraction ≥ 10%
VK2809[7]	THR-β agonist	35	NAFLD, liver fat > 8%, elevated LDL-C and TG
GS-0976[8]	ACC inhibitor	75	NASH, no cirrhosis
Aramchol[9]	SCD1 inhibitor	247	NASH, overweight or obesity, prediabetes or diabetes
Semaglutide[10]	GLP-1 receptor agonist	957	Obesity, no diabetes

1. Patel. AASLD 2018. Abstr 736. 2. Halegoua-De Marzio. AASLD 2018. Abstr 71. 3. Sanyal. AASLD 2018. Abstr LB-23. 4. Harrison. AASLD 2018. Abstr 104. 5. Paredes. AASLD 2018. Abstr LB-22. 6. Harrison. AASLD 2018. Abstr 14. 7. Loomba. AASLD 2018. Abstr LB-4. 8. Charlton. AASLD 2018. Abstr 1741. 9. Ratziu. AASLD 2018. Abstr LB-5. 10. Newsome. AASLD 2018. Abstr 105.

Summary

1. **Obesity and Diabetes are key drivers of Non-alcoholic fatty liver disease (NAFLD)**
2. **Diagnosing Non-alcoholic steatohepatitis (NASH), especially those with significant fibrosis is essential**
3. **Statins are safe in NALFD**
4. **While we wait for effective NAFLD-specific medications consider:**
   - **Diet and exercise**
   - **In diabetics consider pioglitazone**
   - **Bariatric surgeries/procedures for some**

OHSU

Anemia!

Tom DeLoughery, MD MACP FAWM
Oregon Health & Science University

GENERAL HEMATOLOGY

DISCLOSURE

Current Relevant Financial Relationship(s)

Speaker Bureau – None

Iron Deficiency

- **Common!**
- **Treatable**
- **Sign of GI pathology**

Three Types of Iron Deficiency

- **Statistical**
  - **Ferritin < 3 SD**
- **Physiological**
  - **Tissue effects beyond the blood**
- **Pharmacological**
  - **EPO**

Other Effects of Fe Deficiency

- **Iron is important in a variety of enzyme system**
- **Muscle second greatest user of iron**
- **CNS iron also important**
- **Iron deficiency important above and beyond just anemia**

Iron for Fatigue

- **DBRCT of 144 women with fatigue**
  - **Placebo**
  - **Iron: 80mg/day elemental iron**
- **Endpoints: fatigue visual analog scale**

BMJ. 2003 May 24;326(7399):1124.

Iron for Fatigue

- Mean age was 35 years
  - Inclusion 18- 55 years
- Anemia was exclusion criterion
  - 85% with ferritins < 50 ng/mL
  - 51% with ferritins < 20 ng/mL
- Good compliance with therapy

Iron for Fatigue

	N	Baseline	1 month	Decrease	p
Iron	71	6.4±1.6	4.5±1.9	1.8±1.7	P <0.01
Placebo	65	6.5±1.5	5.6±2.2	0.8±52.1	

Women with ferritin < 50 ng/mL had greatest response (3.0)

Iron for Fatigue II

- RCT = 198 women 18-53
  - Ferritin < 50 ug/l
  - Hgb > 12
- Oral iron 80mg/day
- CMAJ 184:1247-1254, 2012

Results

- Fatigue
  - Score: -12.2 vs -8.7
  - Index: -16.2 vs -11.2
  - Severity: -3.6 vs -2.7
- Ferritin up by 11.6 ug/L
- Hbg up by 0.28

Iron for Fatigue

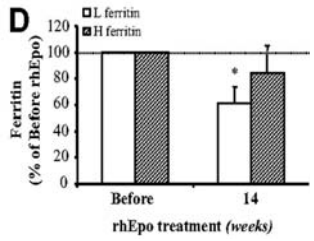
- Two RCT with oral iron show benefit with ferritin < 50
- Increasing data on symptoms with non-anemic iron deficiency
- Iron deficiency with normal blood count does lead to symptoms

Athletes: Non-Anemic Iron Deficiency

- Low iron stores inhibits performance
- Two meta-analysis shows iron repletion improves performance
- BJSM 49:1389, 2015
- J Nut 144:906, 2014

Muscle Iron

- **Ferritin 75 ng/mL → 36 ng/mL**



Blood, Vol. 113, Issue 26, 6707-6715, June 25, 2009

Iron and Athletes

- **Low iron even without anemia affects performance**
  - **Decrease muscle stores?**
- **Consider screening female athletes**
- **Check fatigued athletes**
- **RCT show improvement in performance treating non-anemic iron deficiency**

Effects of Iron Deficiency in Pregnancy

- **Increased risk of preterm birth with ferritins < 12**
  - **Decrease transfer of iron to fetus with very low ferritins**
- **Decreased birth weight**
- **Children born to iron deficient mothers more likely to be anemia at one year**

Benefits of Iron in Pregnacy

- **2015 Cochrane review**
- **70% less anemia at term**
- **20% reduction is LWB children**
- **10% reduction in preterm births**

Other Effects of Low Iron

- **Restless legs**
  - **Ferritins < 100 ng/mL**
  - **Lack of CNS Iron**
- **Alopecia**
  - **Ferritins < 100 ng/mL**
- **Pulmonary hypertension**
- **Heart failure**
  - **Improved QOL**

Iron Deficiency – alone without anemia – is detrimental

Statistical Iron Deficiency

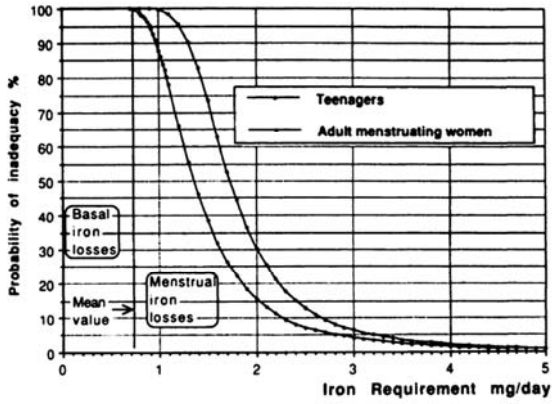
- Laboratory values for ferritin reflect arbitrary criteria and not physiology
- Ranges of "normal" unrealistic for:
  - Woman
  - Older patients

Women and Iron

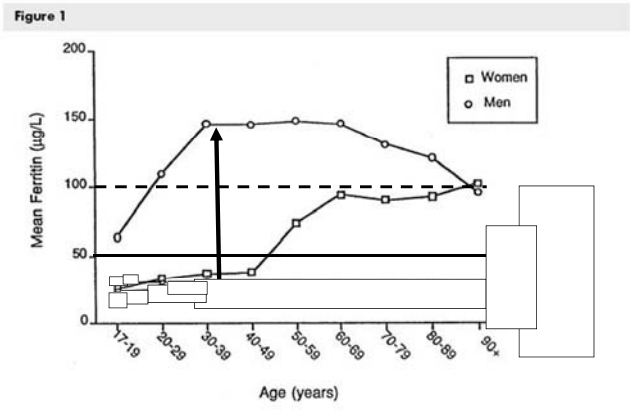
- No physiologic reason that women should have different ranges of normal for ferritin
  - 85% of 20 year old men have ferritin over 50 ng/mL
  - 25% of 20 year old women do
- Often overlooked cause of fatigue
  - Benefit of raising ferritin > 50 ng/mL

Iron Requirements

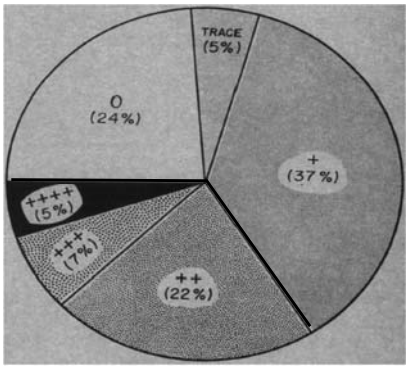
- Men: 14 ug/kg/day
  - ~ 1mg/day
- Women:
  - ~2.4-3.4 mg/day



Gender and Ferritin



Most Women have Low Iron Stores



JAMA, Mar 1967; 199: 897 - 900

Iron is Good

- Iron required by every tissue
- Laboratory ranges of "normal" do not reflect physiology

Diagnosis of Iron Deficiency Anemia

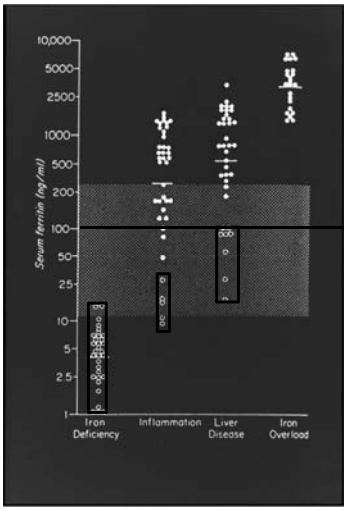
- MCV
- Serum iron
- TIBC
- Iron saturation
- Ferritin
- Bone marrow tests

Testing for Iron Deficiency

- "Classic" tests only helpful in few patients
- Tests affected by concurrent illness and age
  - Fe: VARIES WILDLY
  - MCV: lacks sensitivity and specificity
  - RDW: totally and completely worthless
  - Saturation: low in both ACD and iron deficiency

Serum Ferritin

- Serum ferritin proportional to iron stores
- Needs iron to be produced
  - Acute phase reactant only in presence of iron
- Most accurate non-invasive test of iron stores!

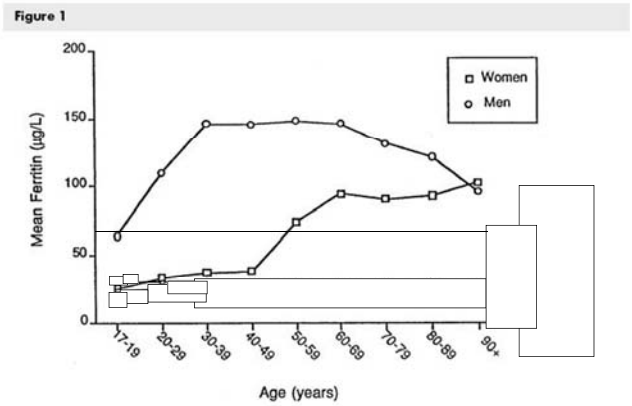


N Engl J Med. 1974 May 30;290(22):1213-6.

Iron Deficiency

- Serum ferritin is BEST non-invasive test of iron status
  - > 100 ng/mL rules out iron deficiency
  - Lower limit changes with age and condition
    - Patient over 65 with ferritin < 50 ng/mL all iron deficient

Age and Ferritin



Ferritin: Bottom Line

- Ignore lab reference ranges!
  - > 100 ng/ml rules-out
- In older patients ferritins < 100ng/ml consider GI work-up
- Remember low ferritin and:
  - Fatigue
  - Alopecia
  - Restless legs

Functional Iron Deficiency

- Good iron stores but impaired mobilization
  - ESA use
  - Heart Disease
- Good ferritins but low saturations
  - < 20-40%

Trial of Oral Iron

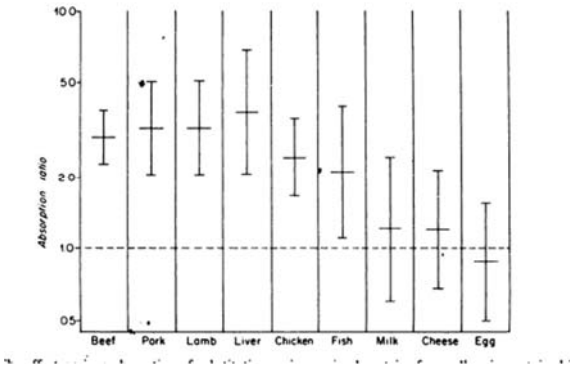
- Effected by inflammation and compliance
- Useful in young women

Summary

- RDW, serum iron, saturation: worthless
- TIBC: specific but not sensitive
- Ferritin: best non-invasive test
- Bone marrow: gold standard

Dietary Iron

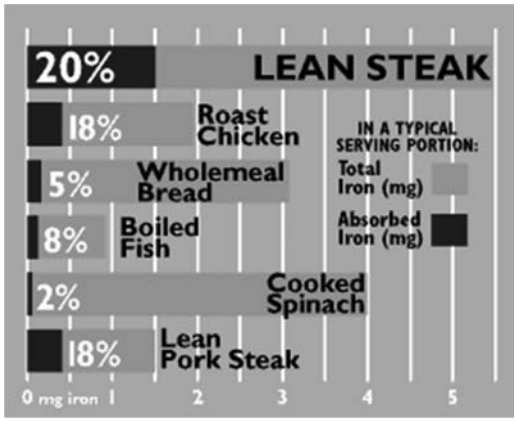
- Heme iron 10x better absorbed than non-heme iron
- Meat protein improves iron absorption



Am J Clin Nutr **August**
1976 vol. 29 no. 8
859-867

Dietary Iron

- **Calcium, fiber can block iron absorption**
  - **Overcome by vitamin C**
- **Tea decreases 75-80%**
- **Coffee decreases 60% (5 oz!)**

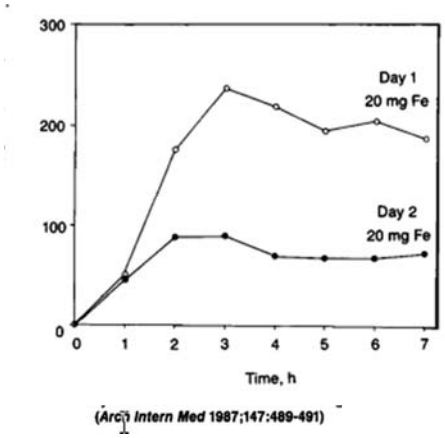


What I Tell my Patients

- **If feasible increase meat in diet**
- **Try not to drink tea or coffee with meat**
- **Vitamin C helps**
- **Maybe vitamin D?**
  - **Decreases hepcidin**

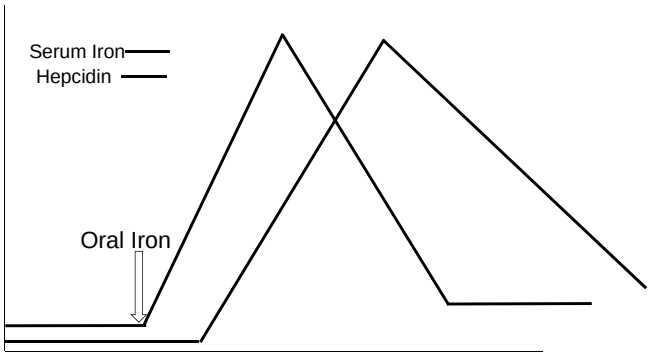
Oral Iron Pills

- **Gut can only absorb a limited amount of iron**
- **Maxed out at ~ 10mg**

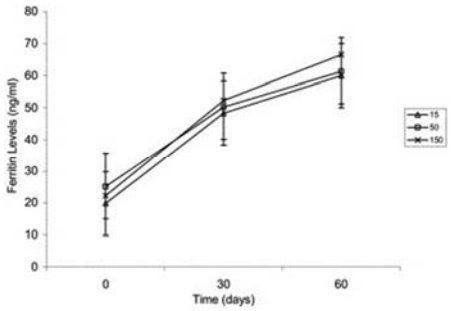


(*Arch Intern Med* 1987;147:489-491)

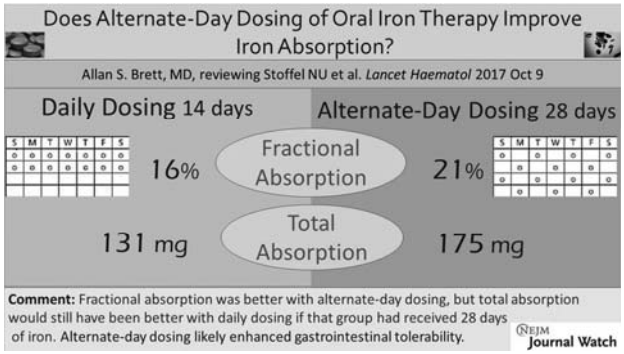
Hepcidin Response to Iron



15 vs 50 vs 150mg Oral Iron



Am J Med. 2005 Oct;118(10):1142-7.



But 28 days of daily iron = 262 mg absorbed

Oral Iron Pills

- **Years of studies have shown that the best iron preparation is….**

Oral Iron Pills

….the one that the patient can tolerate

- **No consistent difference in any brand**
- **Many patients can't tolerate any pill on an empty stomach**
  - **Ok with meals**

What I Do

- **Cheapest iron pill**
  - **Ferrous sulfate**
- **Once a day with meals**
  - **Vitamin C 500**
  - **No tea or coffee**
- **If intolerant can try lower dose**

Response to Oral Iron

- Increased retic 7-10 days
- Increased Hct 2 weeks
- Normalized 2 months

At What Ferritin are Iron Stores Replete?

- GI iron absorption goes back to backline only at ferritin of 60 ng/mL
- Falling from 70 to 35 ng/mL muscle loss iron
- Alopecia and restless legs seen at < 100 ng/mL
- Maybe 50-100 ng/mL a reasonable goal for repletion

Failure to Respond to Iron

- Blood loss
  - HHT
- Noncompliance
- Defective absorption
- Concurrent B_{12} or folate deficiency

Parental Iron Therapy

- When to use
  - Refractory to oral iron
  - Unable to take oral iron
  - Cannot keep up with blood loss
    - Bariatric surgery
    - Inflammatory bowel disease
    - Chronic GI bleeding

Safety

- Minor infusion reactions common (~1-2%) but true anaphylaxis very rare
- Death rates (per 100,000)
  - INFeD 0.8 (0-1.9)
  - Ferrlecit 6.3 (1.311.4)
  - Venofer 6.6 (3.1-9)
  - FeraHeme 3.5 (0-7.8)

Reactions

- Complement mediated pseudo-allergy
- Drug non-specific activated complement
  - Similar to rituximab etc.
- True anaphylaxis very rare
  - Negative tryptase > 200 reactions

Implication

- No value test dose
- Premedication often doesn't help
- Diphenhydramine makes things worse
- Treat as infusion reaction not allergy
- Studies show risk same with all iron preparations

Dosing IV Iron

- Replacement formulas inaccurate
- Give 1000mg
  - Recheck in 4 weeks
  - If severe anemia recheck in two weeks

IV Iron Dosing

Formulation	Recommended Dose
LMW Iron dextran	1000mg over 1 hr
Ferumoxytol	510 x 2 or 1020 over 15 min
Ferric carboxymaltose	1000mg over 15 min or 705mg x 2
Iron isomaltoside	1-2000 mg over 15 min

Refractory Iron Deficiency

- Patient is "refractory" to IV iron
- Not getting enough iron
- Frequent ferritin checks infusions
- Goal ferritin > 100

Etiology of Iron Deficiency

- All iron deficiency has a cause!
- Blood loss must always be assumed!

Contributors to Iron Deficiency

- GI
  - NSAIA 10-15%
  - Colon Ca 5-10%
  - Gastric Ca 5%
  - Ulcers 5%
  - Angiodysplasia 5%
  - Esophagitis 2-4%
  - Esophageal Ca 1-2%
- Non-GI
  - Menstruation 20-30%
  - Celiac disease 4-6%
  - Bariatric surgery 1%

Iron Deficiency: GI Evaluation

- Most patients with identifiable source of GI blood loss
- Very high number with tumors
- Most common cause of missed cancer diagnosis
- Who *not* to evaluate?

GI Work-Up

- Iron deficiency anemia
  - Men with ferritins < 100 ng/mL
  - Post-menopausal women < 50 ng/mL (?100)
  - Women > 40
- Refractory iron deficiency
- Iron deficiency and GI symptoms

Trends in Iron Deficiency

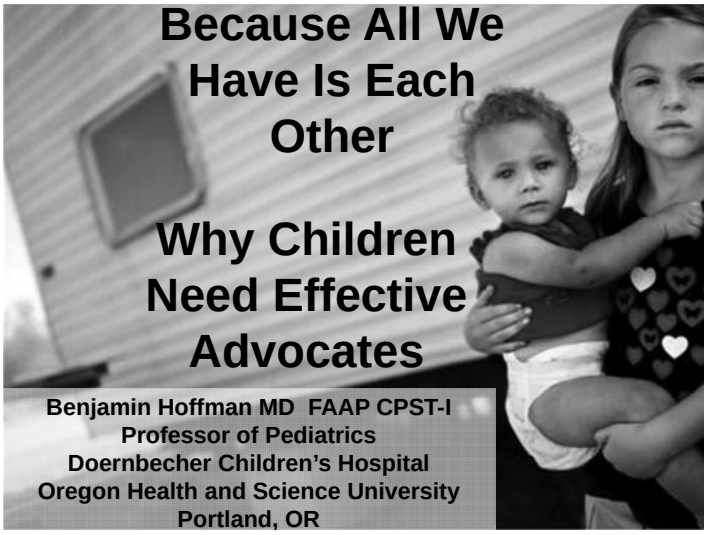
- Incidence of iron deficiency is increasing
  - Reduction in meat intake
  - Increase PPI/H2 blockers
  - Increase in bariatric procedures

Trends in Iron Deficiency

- Understanding variability in iron absorption
  - TMPRSS6
    - Key enzyme in iron metabolism
    - Multiple polymorphism in population
    - Homozygous mutations with refractory iron deficiency
    - Heterozygous with decrease absorption

Remember!

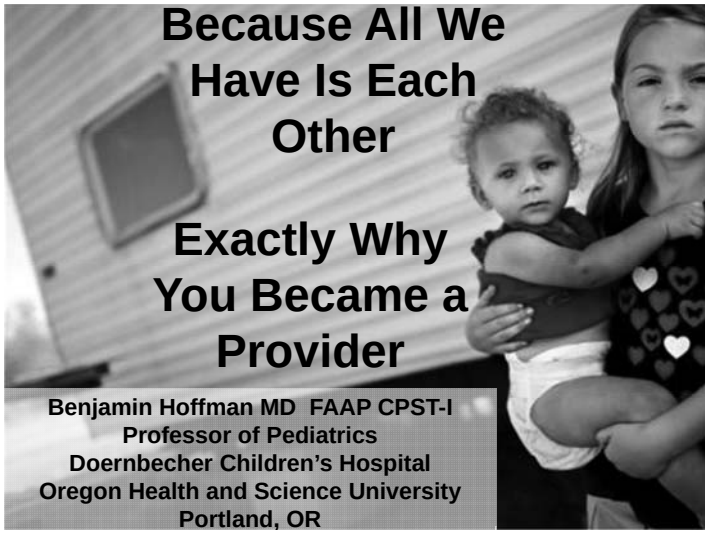
- Iron is good!
- Ferritins > 50 ng/mL are good
- Oral iron
  - One pill/day
  - With vitamin C
  - With meat if feasible



Because All We Have Is Each Other

Why Children Need Effective Advocates

Benjamin Hoffman MD FAAP CPST-I
Professor of Pediatrics
Doernbecher Children's Hospital
Oregon Health and Science University
Portland, OR



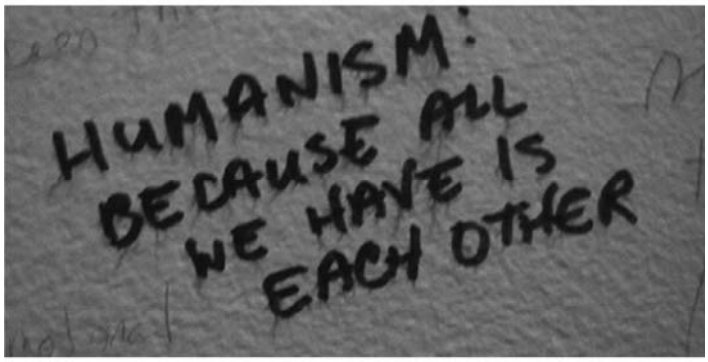
Because All We Have Is Each Other

Exactly Why You Became a Provider

Benjamin Hoffman MD FAAP CPST-I
Professor of Pediatrics
Doernbecher Children's Hospital
Oregon Health and Science University
Portland, OR

Disclosure Statement

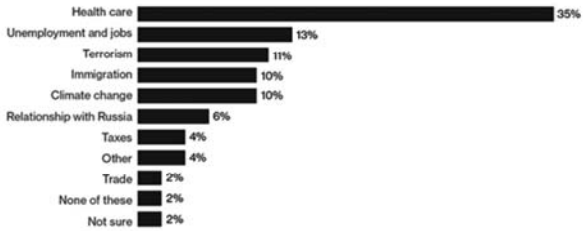
- I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this session.
- I do not intend to discuss an unapproved/investigative use of a commercial product/device in our presentation.



Why did you become a provider?

Maslow's Hierarchy of Needs

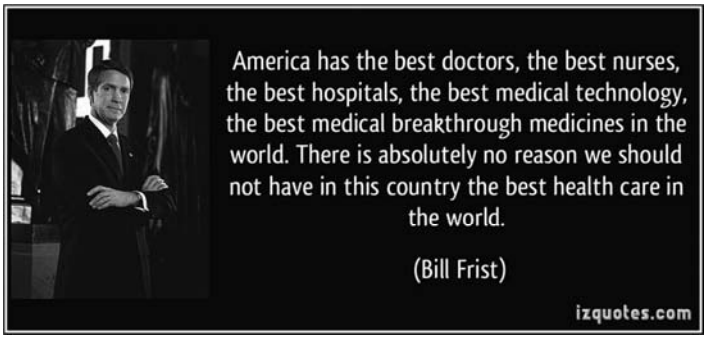
Top Issues for Americans
Which of the following do you see as the most important issue facing the country right now?



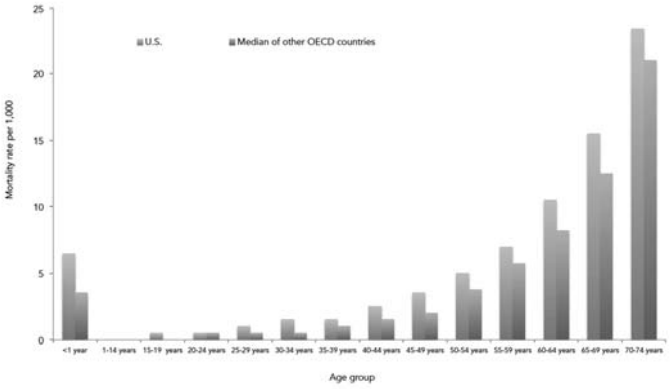
Note: Percentages may not add to 100 due to rounding.
Source: Bloomberg National Poll conducted by Selzer & Co. July 8-12, 2017, with 1,001 American adults. Margin of error +/- 3.1 percentage points.

Bloomberg

https://ricochet.com/442941/americans-care-vs-media-cares/

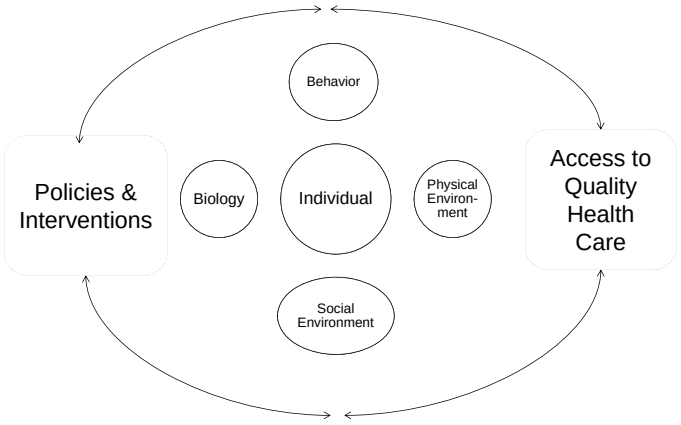


U.S. vs. median mortality rates, age 0-75



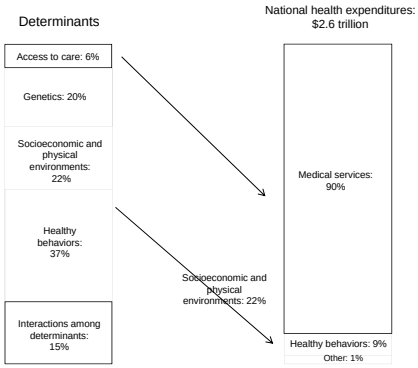
Why us?

Determinants of Health

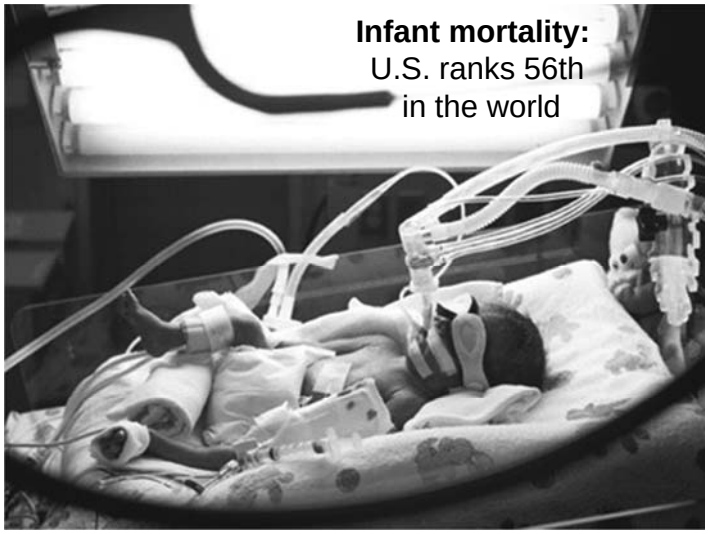


Healthy People 2010

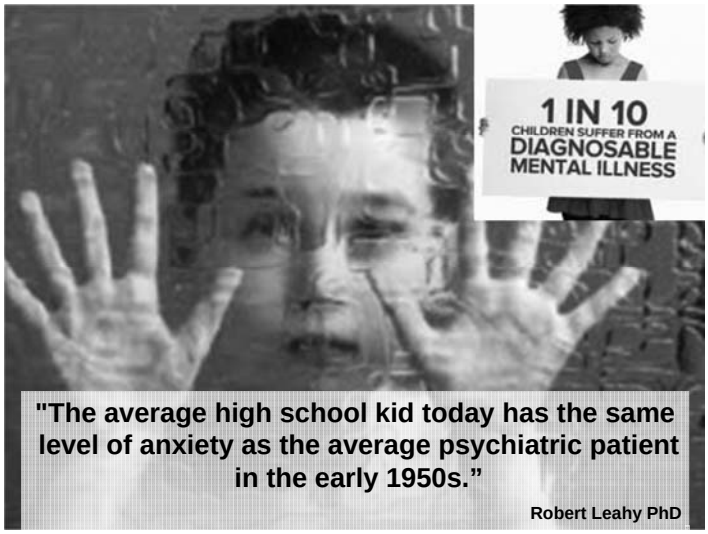
The spending mismatch: health determinants vs. health expenditures



"Healthy People/Healthy Economy: An Initiative to Make Massachusetts the National Leader in Health and Wellness." 2015. Data from NEHI 2013. <http://www.tbf.org/tbf/56/hphe/Health-Crisis>
Tarlov A. Social determinants of health: the sociobiological translation. In: Blane D, Brunner E, Wilkinson R, editors. Health and social organization: towards a health policy for the 21st century. London: Routledge; 1996 pp. 71-93.
Bostonfoundation.org



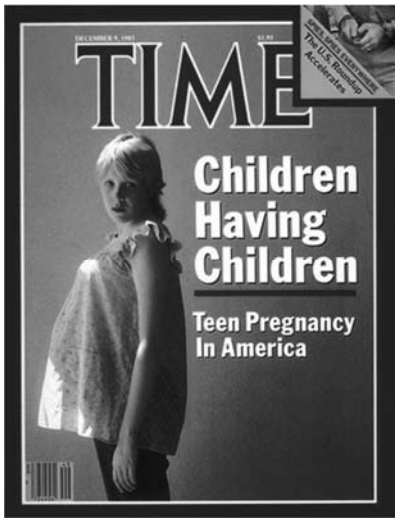
Infant mortality:
U.S. ranks 56th
in the world



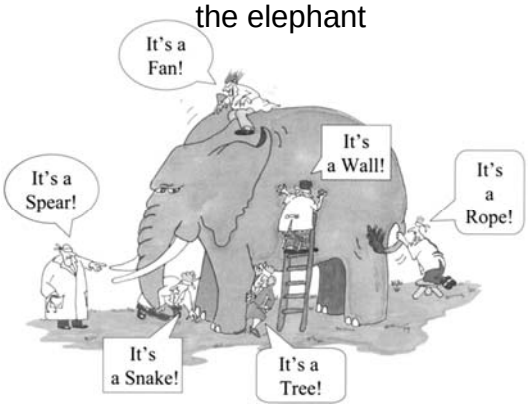
"The average high school kid today has the same level of anxiety as the average psychiatric patient in the early 1950s."

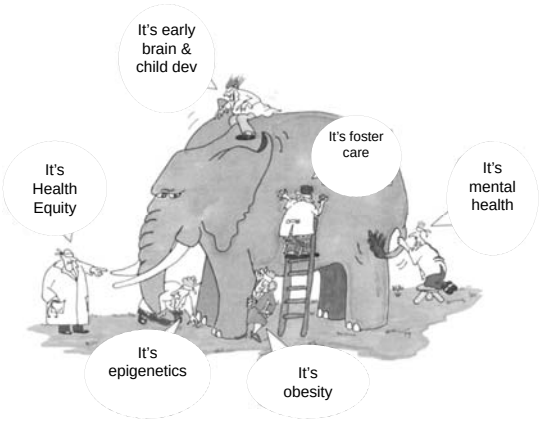
Robert Leahy PhD

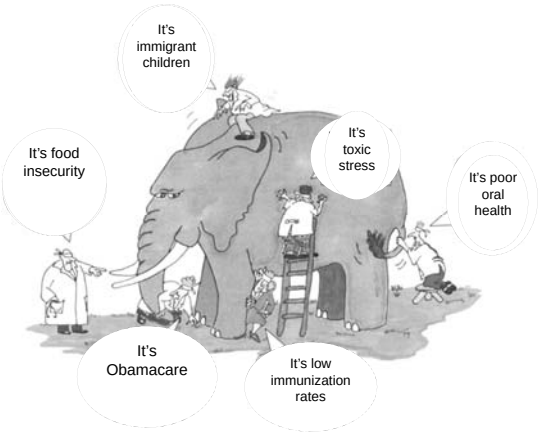
1 in 3 Children is Overweight or Obese



…it's a little like the blindfolded man feeling the elephant

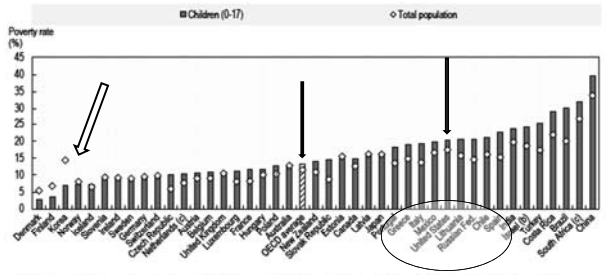






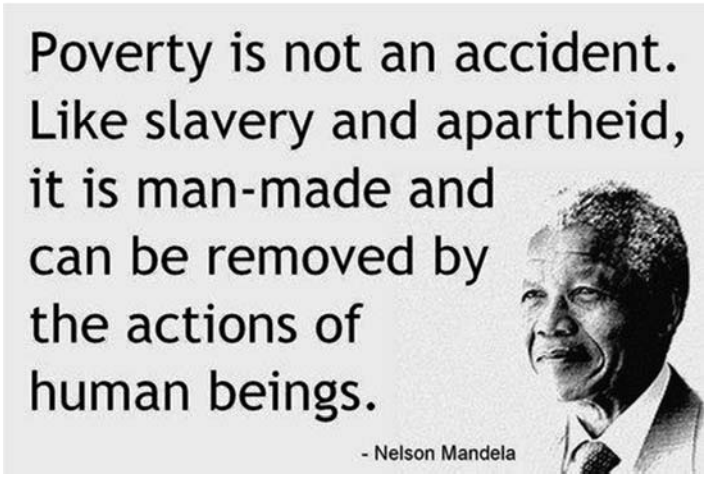
Comparison of US to Other OECD Countries

Organisation for Economic Co-operation and Development



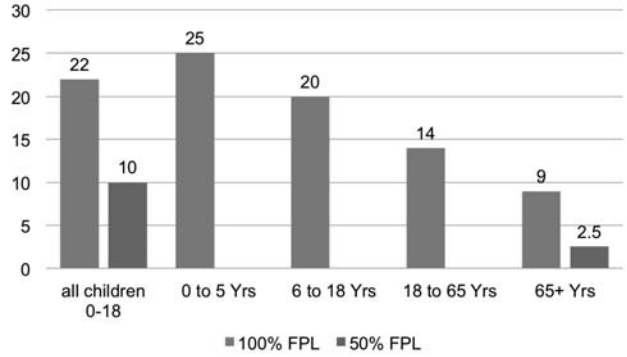
a) Data for India and the Russian Federation refer to 2011, for Japan to 2012, for Brazil and China to 2013, and for Chile and South Africa to 2015.
b) The statistical data for Israel are supplied by and under the responsibility of the relevant Israeli authorities. The use of such data by the OECD is without prejudice to the status of the Golan Heights, East Jerusalem and Israeli settlements in the West Bank under the terms of international law
c) Data for the Netherlands refer only to the European territory.
Sources: OECD Income Distribution Database

CO2.2: Child Poverty. www.oecd.org/social/family/database/



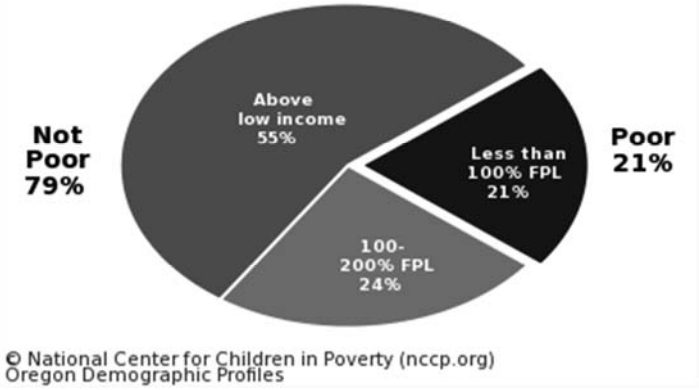
% Poverty by Age

Poverty vs. "Deep" Poverty



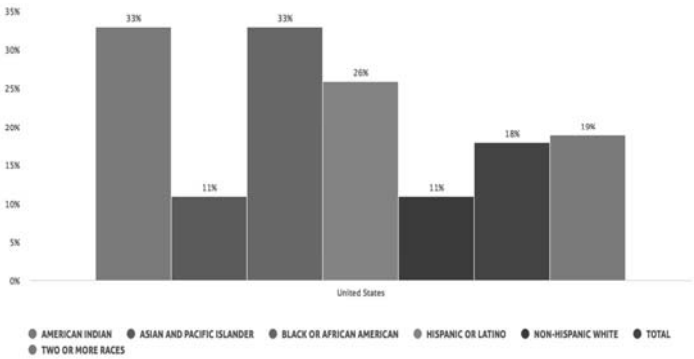
US Census Bureau: Income, Poverty, and Health Insurance Coverage in the US: 2010

Children in Oregon, by Income Level, 2015



© National Center for Children in Poverty (nccp.org)
Oregon Demographic Profiles

2019 POVERTY GUIDELINES FOR THE 48 CONTIGUOUS STATES AND THE DISTRICT OF COLUMBIA	
PERSONS IN FAMILY/HOUSEHOLD	POVERTY GUIDELINE
For families/households with more than 8 persons, add $4,420 for each additional person.	
1	$12,490
2	$16,910
3	$21,330
4	$25,750
5	$30,170
6	$34,590
7	$39,010
8	$43,430



Children In Poverty By Race And Ethnicity (Percent) - 2017

National KIDS COUNT
KIDS COUNT Data Center, datacenter.kidscount.org
A project of the Annie E. Casey Foundation

MONTHLY COSTS

2 adults *and* 2 children
Portland/Vancouver/Hillsboro metro area

HOUSING	$1,330
FOOD	$791
CHILD CARE	$1,653
TRANSPORTATION	$1,170
HEALTH CARE	$906
OTHER NECESSITIES	$856
TAXES	$1,298
Monthly Total	**$8,004**
Annual Total	**$96,047**

FPL= $2145.83

27% of monthly expenses!

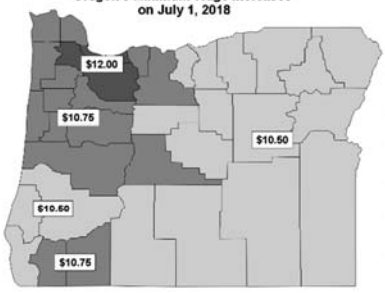
OR
Minimum Wage?

http://www.epi.org/resources/budget/

MONTHLY COSTS

2 adults *and* 2 children
Portland/Vancouver/Hillsboro metro area

Oregon's Minimum Wage Increases on July 1, 2018



Annual Total **$96,047**

FPL= $2145.83

27% of monthly expenses!

OR
Minimum Wage?

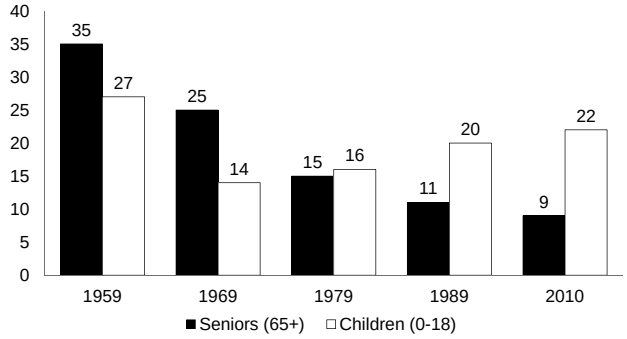
$12/hr

Full Time= $2080
22% of monthly expenses!

http://www.epi.org/resources/budget/

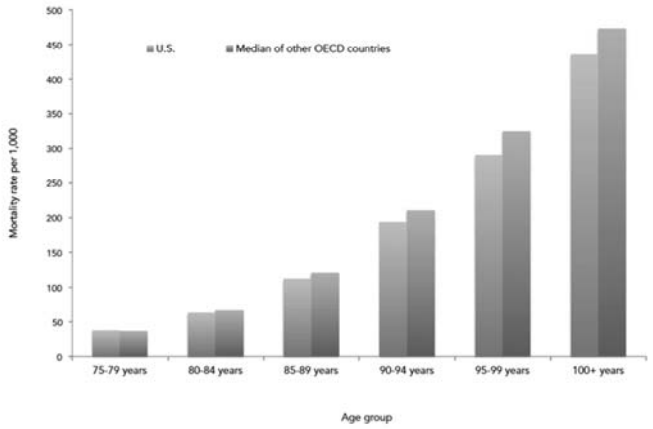
% Poverty Over Time: 1959-2010

Children and Seniors



Sachs JD. The Price of Civilization. 2011, Random House, NY. Chapter 10, pp. 185-208

U.S. vs. median mortality rates, age 75+



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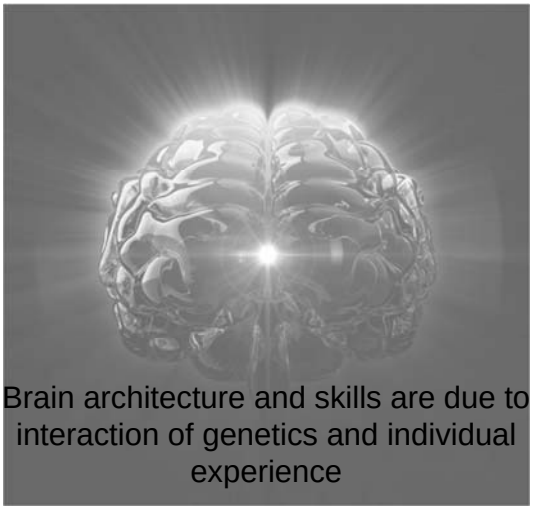
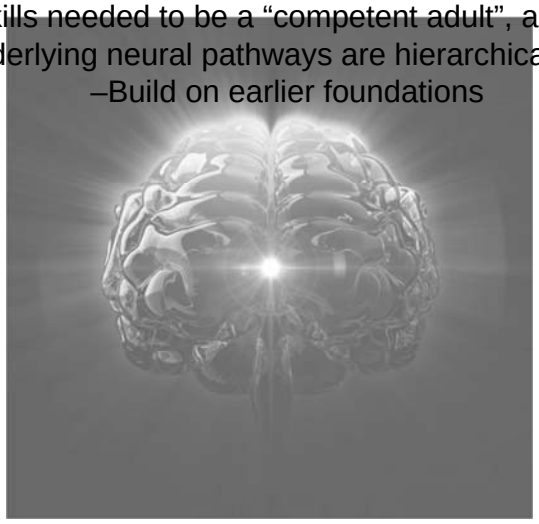
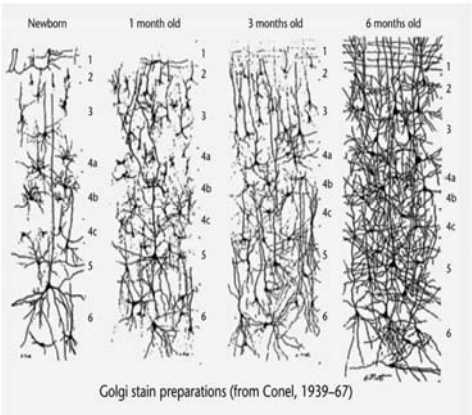


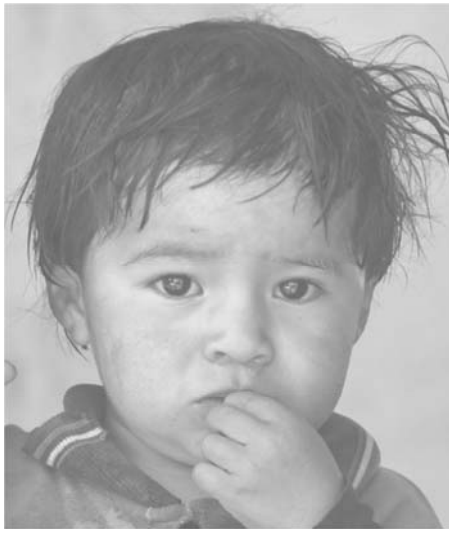
Brain architecture and skills are due to interaction of genetics and individual experience

Skills needed to be a “competent adult”, and underlying neural pathways are hierarchical…
–Build on earlier foundations



1 Million new neural connections per second!





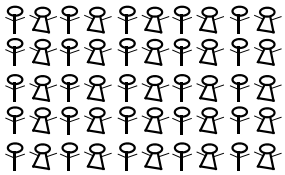
Cognitive, language, social and emotional skills are interdependent

Early childhood is the most plastic and receptive time to environmental influences

What happens in the 1st thousand days is more important than school

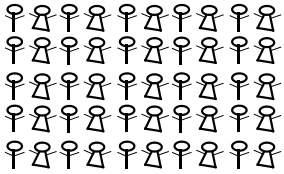
In early childhood, there is no difference between health and learning

50 first graders with reading problems

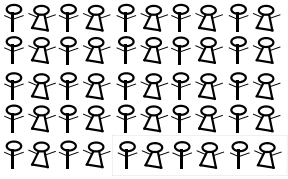


First Graders

50 first graders with reading problems



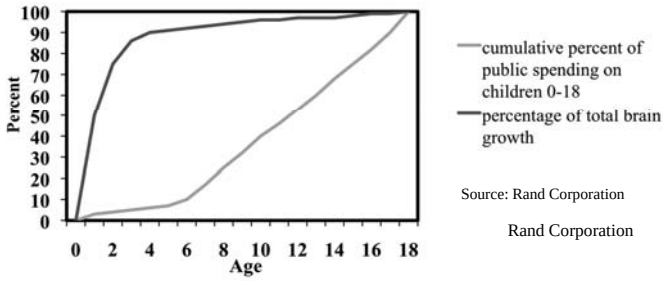
First Graders



Fourth Graders

POLICY IS LAGGING BEHIND RESEARCH

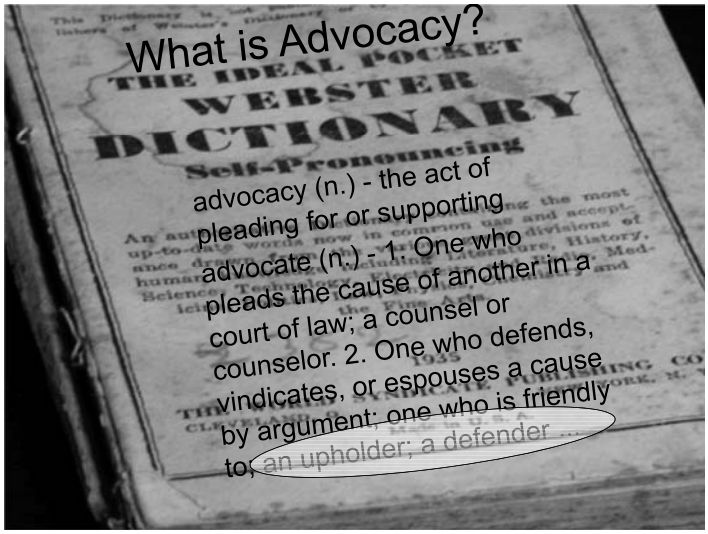
Brain growth versus public expenditures on children ages 0-18



Source: Rand Corporation

Rand Corporation

90% of public expenditures occur after age five, after up to 90% of brain development has occurred.

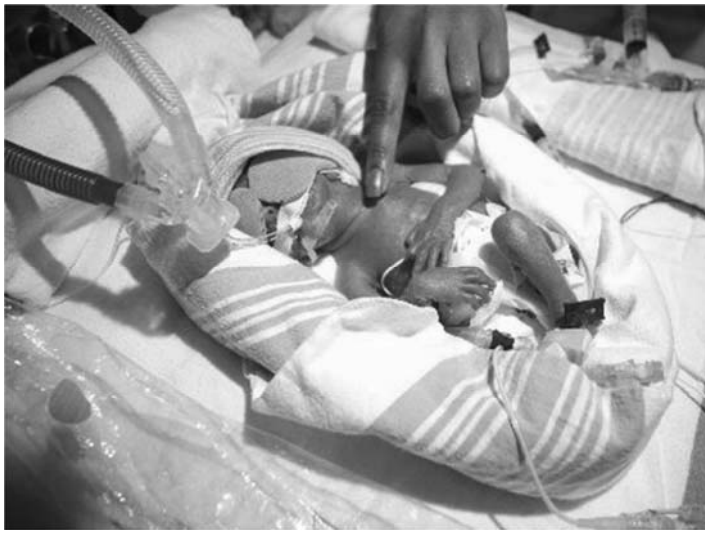


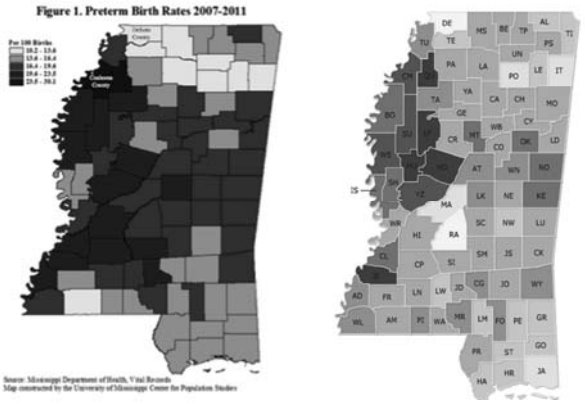
"Action by a physician to promote those social, economic, educational, and political changes that ameliorate the suffering and threats to human health and well-being that he or she identifies through his or her professional work and expertise."

Earnest et al. Acad Med 2010

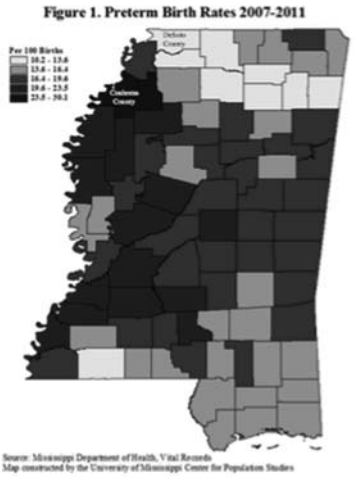
In the long run, **child health** is about **advocacy**…

Health Affairs, 2004



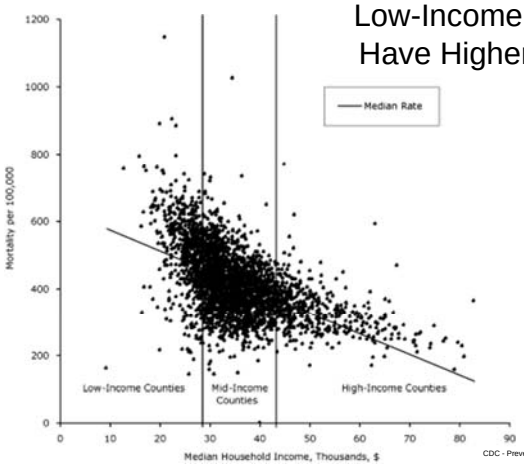


University of Mississippi Center for Population Studies, 2013



University of Mississippi Center for Population Studies, 2013

Premature Infants Born in Low-Income Counties Have Higher Mortality

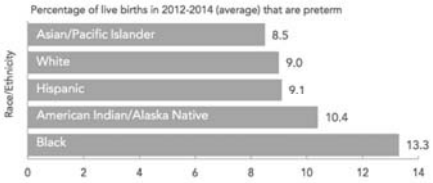


CDC - Preventing Chronic Disease: Volume 9, 2012: 11_0120

2016 PREMATURE BIRTH REPORT CARD

RACE & ETHNICITY IN THE UNITED STATES

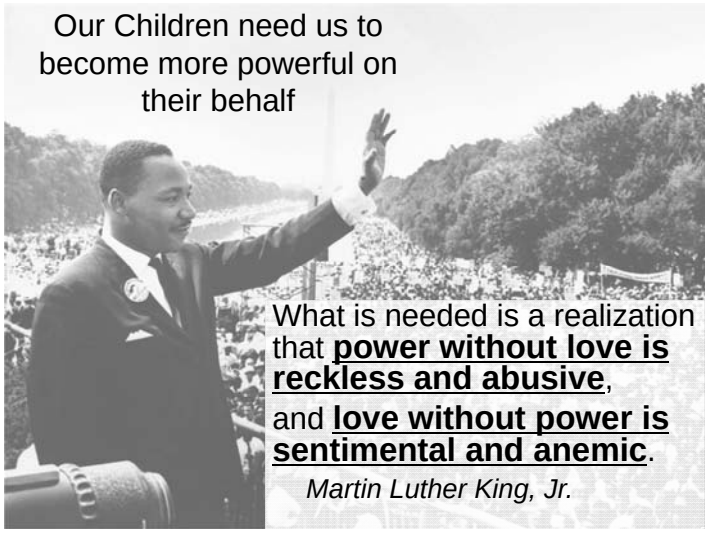
The March of Dimes uses a Disparity Index score to measure and track progress towards the elimination of racial/ethnic disparities in preterm birth. The score represents the average percent difference in the preterm birth rate across all groups compared to the group with the lowest rate in the state. Index scores range from 0 (achievement of equity) to 44 (highest score in 2016).



Disparity index
23

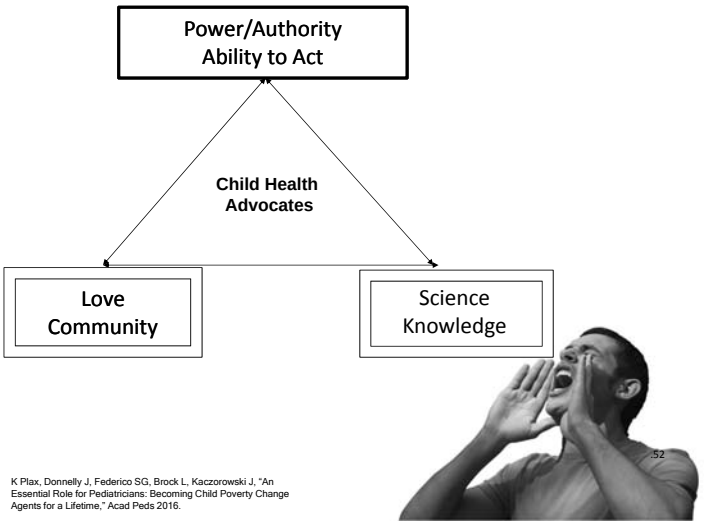
In the United States, the preterm birth rate among **black women is 48%** higher than the rate among all other women.

Our Children need us to become more powerful on their behalf



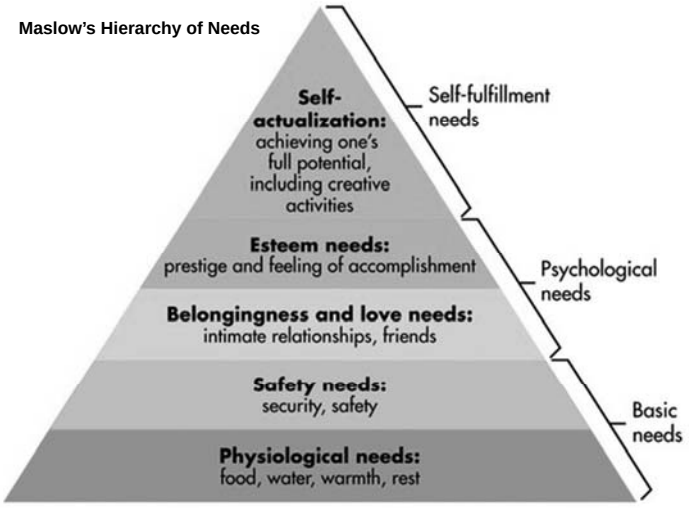
What is needed is a realization that **power without love is reckless and abusive**, and **love without power is sentimental and anemic**.

Martin Luther King, Jr.



K Plax, Donnelly J, Federico SG, Brock L, Kaczorowski J, "An Essential Role for Pediatricians: Becoming Child Poverty Change Agents for a Lifetime," Acad Peds 2016.

Maslow's Hierarchy of Needs



Take Home

- **Children need advocates by nature and necessity**
- **We must transform our system to address HEALTH**
- **It's about disparities and equity**
- **We need to harness the power of our voices to help ensure kids are heard**

What is the national membership of the AARP?

35 Million

How many of them vote?

35 Million

How many children under the age of 18 are there in the US?

72 Million

How many of them vote?

Caring for the Cancer Patient: The Central Role of the Primary Care Provider

Kevin G. Billingsley MD
Chief, Division of Surgical Oncology
Medical Director, OHSU Knight Cancer Institute

1) Diagnosis and Initial Management
    a. Taming the anxiety
    b. Building a Plan
    c. Building a Team
    d. Local versus Travel for Care

2) Preparing for Treatment
    a. Medical Preparation
    b. Prehabilitation
        i. Exercise
        ii. Diet
    c. Psychosocial Support

3) Primary Role - Integrator
    a. Oncology care is fragmented
    Surgeons, medical oncologists, radiation oncologists
    b. Have they recovered from surgery?
    c. Was care discussed in a multidisciplinary tumor board?
    d. Translate these findings?
    e. Manage medical issues during treatment
    f. Integrative medicine and complementary medicine
        i. Integrative Medicine to cope with the physical, emotional, spiritual effects of cancer and relief of symtpoms that conventional therapy does not address.
        ii. Advocate
        iii. Complementary Medicine
            1. Acupuncture
            2. Massage
            3. Meditation
            4. Yoga
            5. Nutritional Therapies
            6. Herbal Medicine
        iv. Cannabis
        v. Alternative Medicine – Education and Counseling

4) Survivorship
    a. Ask What is your survivorship plan?
    b. Opportunity to work with oncologist/ surgeon
    c. Much followup can and should be done locally
    d. Survivorship not so happy
        i. Trauma
        ii. Disruption of life an family structure
        iii. Counseling

5) Palliation/ End of Life Care
    a. Decision to no longer pursue cancer treatment
    b. When clinically meaningful benefit is unlikely and toxicity outweighs the benefits.
    c. Shifting the focus of care to comfort and support
    d. Pain and symptom management
    e. Hospice

2018
AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA

Guideline on the Management of Blood Cholesterol: Executive Summary

Cezary Wójcik MD, PhD, DSc, FNLA
Department of Family Medicine, OHSU
Diplomate, American Board of Clinical Lipidology

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Table 1. Applying Class of Recommendation and evel of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care*
(Updated August 2015)

2018 Cholesterol Guideline

High Blood Cholesterol and ASCVD

Measurements of LDL-C and Non-HDL-C

Recommendations for Measurements of LDL-C and Non-HDL-C		
COR	**LOE**	**Recommendations**
I	**B-NR**	**In adults who are 20 years of age or older and not on lipid-lowering therapy, measurement of either a fasting or a nonfasting plasma lipid profile is effective in estimating ASCVD risk and documenting baseline LDL-C.**
I	**B-NR**	**In adults who are 20 years of age or older and in whom an initial nonfasting lipid profile reveals a triglycerides level of 400 mg/dL (≥4.5 mmol/L) or higher, a repeat lipid profile in the fasting state should be performed for assessment of fasting triglyceride levels and baseline LDL-C.**

Measurements of LDL-C and Non-HDL-C

Recommendations for Measurements of LDL-C and Non-HDL-C		
COR	**LOE**	**Recommendations**
IIa	**C-LD**	**For patients with an LDL-C level less than 70 mg/dL (<1.8 mmol/L), measurement of direct LDL-C or modified LDL-C estimate is reasonable to improve accuracy over the Friedewald formula.**
IIa	**C-LD**	**In adults who are 20 years of age or older and without a personal history of ASCVD but with a family history of premature ASCVD or genetic hyperlipidemia, measurement of a fasting plasma lipid profile is reasonable as part of an initial evaluation to aid in the understanding and identification of familial lipid disorders.**

2018 Cholesterol Guideline

Patient Management Groups

Secondary Prevention

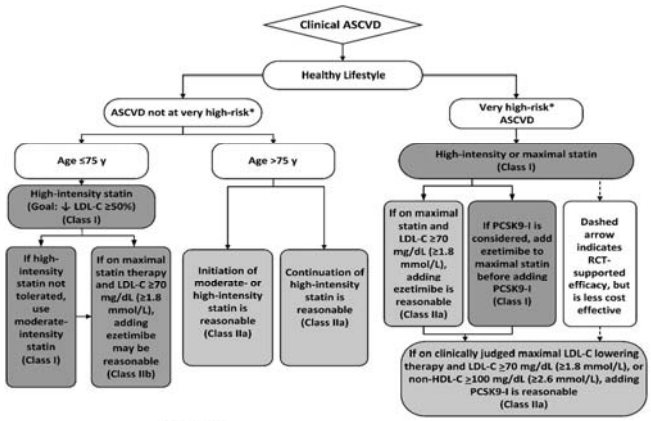


Table 4. Very High-Risk* of Future ASCVD Events

Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation)

Table 4 continued

High-Risk Conditions
Age ≥65 y
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes mellitus
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m^2)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	**LOE**	**Recommendations**
I	**A**	**In patients who are 75 years of age or younger with clinical ASCVD,* high-intensity statin therapy should be initiated or continued with the aim of achieving a 50% or greater reduction in LDL-C levels.**
I	**A**	**In patients with clinical ASCVD in whom high-intensity statin therapy is contraindicated or who experience statin-associated side effects, moderate-intensity statin therapy should be initiated or continued with the aim of achieving a 30% to 49% reduction in LDL-C levels.**

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	**LOE**	**Recommendations**
I	**B-NR**	**In patients with clinical ASCVD who are judged to be very high risk and *considered for PCSK9 inhibitor therapy,* maximally tolerated LDL-C lowering therapy should include maximally tolerated statin therapy and ezetimibe.**
IIa	**A^{SR}**	**In patients with clinical ASCVD who are judged to be very high risk and who are on maximally tolerated LDL-C lowering therapy with LDL-C 70 mg/dL (≥1.8 mmol/L) or higher or a non-HDL-C level of 100 mg/dL (≥2.6 mmol/L) or higher, it is reasonable to add a PCSK9 inhibitor following a clinician–patient discussion about the net benefit, safety, and cost.**

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	**LOE**	**Recommendations**
IIa	**B-R**	**In patients with clinical ASCVD who are on maximally tolerated statin therapy and are judged to be at very high risk and have an LDL-C level of 70 mg/dL (≥1.8 mmol/L) or higher, it is reasonable to add ezetimibe therapy.**
Value Statement: Low Value (LOE: B-NR)		**At mid-2018 list prices, PCSK9 inhibitors have a low cost value (>$150,000 per QALY) compared to good cost value (<$50,000 per QALY) (Section 7 provides a full discussion of the dynamic interaction of different prices and clinical benefit).**

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	**LOE**	**Recommendations**
IIa	**B-R**	**In patients older than 75 years of age with clinical ASCVD, it is reasonable to initiate moderate- or high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug–drug interactions, as well as patient frailty and patient preferences.**
IIa	**C-LD**	**In patients older than 75 years of age who are tolerating high-intensity statin therapy, it is reasonable to continue high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug-drug interactions, as well as patient frailty and patient preferences.**

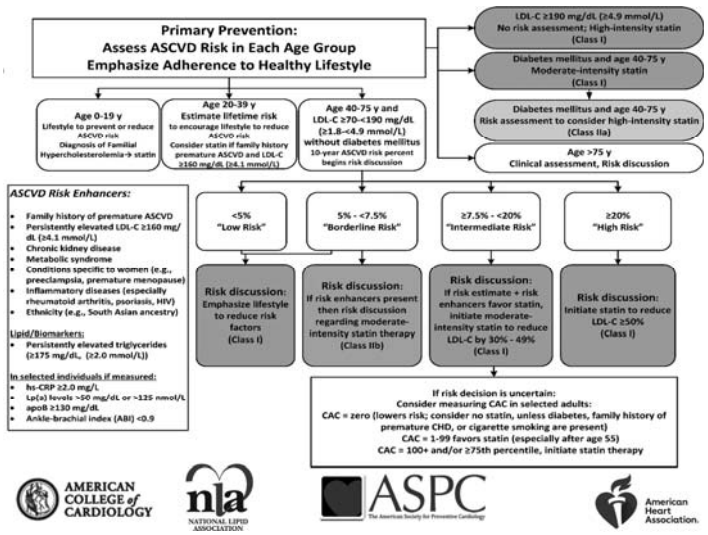
Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	**LOE**	**Recommendations**
IIb	**B-R**	**In patients with clinical ASCVD who are receiving maximally tolerated statin therapy and whose LDL-C level remains 70 mg/dL (≥1.8 mmol/L) or higher, it may be reasonable to add ezetimibe.**
IIb	**B-R**	**In patients with heart failure (HF) with reduced ejection fraction attributable to ischemic heart disease who have a reasonable life expectancy (3 to 5 years) and are not already on a statin because of ASCVD, clinicians may consider initiation of moderate-intensity statin therapy to reduce the occurrence of ASCVD events.**

Severe Hypercholesterolemia (LDL-C ≥190 mg/dL [≥4.9 mmol/L])

Recommendations for Primary Severe Hypercholesterolemia (LDL-C ≥190 mg/dL [≥4.9 mmol/L])		
COR	**LOE**	**Recommendations**
I	**B-R**	**In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL (≥4.9 mmol/L) or higher, maximally tolerated statin therapy is recommended.**
IIa	**B-R**	**In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL (≥4.9 mmol/L) or higher who achieve less than a 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of 100 mg/dL (≥2.6 mmol/L) or higher, ezetimibe therapy is reasonable.**

Primary Prevention in All Age Groups



Severe Hypercholesterolemia (LDL-C ≥190 mg/dL [≥4.9 mmol/L])

Recommendations for Primary Severe Hypercholesterolemia (LDL-C ≥190 mg/dL [≥4.9 mmol/L])		
COR	**LOE**	**Recommendations**
IIb	**B-R**	**In patients 20 to 75 years of age with a baseline LDL-C level ≥190 mg/dL (≥4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides ≤300 mg/dL (≤3.4 mmol/L). while taking maximally tolerated statin and ezetimibe therapy, the addition of a bile acid sequestrant may be considered.**
IIb	**B-R**	**In patients 30 to 75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL (≥2.6 mmol/L) or higher while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered.**

Severe Hypercholesterolemia (LDL-C ≥190 mg/dL [≥4.9 mmol/L])

Recommendations for Primary Severe Hypercholesterolemia (LDL-C ≥190 mg/dL [≥4.9 mmol/L])		
COR	**LOE**	**Recommendations**
IIb	**C-LD**	**In patients 40 to 75 years of age with a baseline LDL-C level of 220 mg/dL (≥5.7 mmol/L) or higher and who achieve an on-treatment LDL-C level of 130 mg/dL (≥3.4 mmol/L) or higher while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered.**
Value Statement: Uncertain Value (B-NR)		**Among patients with FH without evidence of clinical ASCVD taking maximally tolerated statin and ezetimibe therapy, PCSK9 inhibitors provide uncertain value at 2018 U.S. list prices.**

Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	**LOE**	**Recommendations**
I	**A**	**In adults 40 to 75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated.**
IIa	**B-NR**	**In adults 40 to 75 years of age with diabetes mellitus and an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it is reasonable to assess the 10-year risk of a first ASCVD event by using the race and sex-specific PCE to help stratify ASCVD risk.**

Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	**LOE**	**Recommendations**
IIa	**B-R**	**In adults with diabetes mellitus who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more.**
IIa	**B-NR**	**In adults older than 75 years of age with diabetes mellitus and who are already on statin therapy, it is reasonable to continue statin therapy.**
IIb	**C-LD**	**In adults with diabetes mellitus and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL-C levels by 50% or more.**

Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	**LOE**	**Recommendations**
IIb	**C-LD**	**In adults older than 75 years with diabetes mellitus, it may be reasonable to initiate statin therapy after a clinician–patient discussion of potential benefits and risks.**
IIb	**C-LD**	**In adults 20 to 39 years of age with diabetes mellitus that is either of long duration (≥10 years of type 2 diabetes mellitus, ≥20 years of type 1 diabetes mellitus), albuminuria (≥30 mcg of albumin/mg creatinine), estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2, retinopathy, neuropathy, or ankle-brachial index (ABI; <0.9), it may be reasonable to initiate statin therapy.**

Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

Risk Enhancers
• Long duration (≥10 years for type 2 diabetes mellitus (S.4.3-20) or ≥20 years for type 1 diabetes mellitus)
• Albuminuria ≥30 mcg of albumin/mg creatinine
• eGFR <60 mL/min/1.73 m^2
• Retinopathy
• Neuropathy
• ABI <0.9

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	**LOE**	**Recommendations**
I	A	In adults at intermediate-risk, statin therapy reduces risk of ASCVD, and in the context of a risk discussion, if a decision is made for statin therapy, a moderate-intensity statin should be recommended.
I	A	In intermediate-risk patients, LDL-C levels should be reduced by 30% or more, and for optimal ASCVD risk reduction, especially in high-risk patients, levels should be reduced by 50% or more.

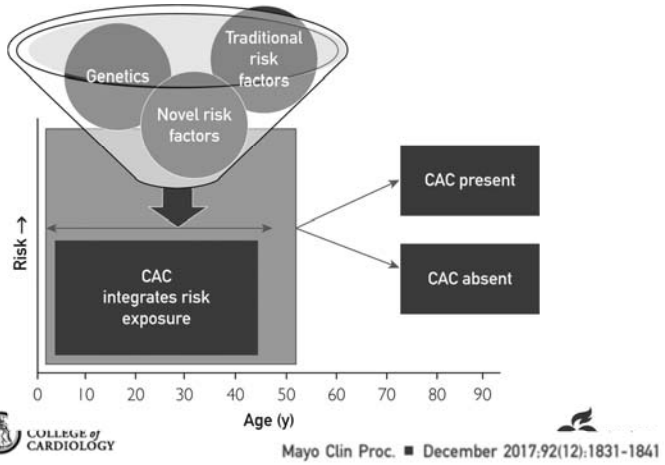
Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	**LOE**	**Recommendations**
I	B-NR	For the primary prevention of clinical ASCVD* in adults 40 to 75 years of age without diabetes mellitus and with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), the 10-year ASCVD risk of a first "hard" ASCVD event (fatal and nonfatal MI or stroke) should be estimated by using the race- and sex-specific PCE, and adults should be categorized as being at low risk (<5%), borderline risk (5% to <7.5%), intermediate-risk (≥7.5% to <20%), and high-risk (≥20%).
I	B-NR	Clinicians and patients should engage in a risk discussion that considers risk factors, adherence to healthy lifestyle, the potential for ASCVD risk-reduction benefits, and the potential for adverse effects and drug–drug interactions, as well as patient preferences, for an individualized treatment decision.

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	**LOE**	**Recommendations**
IIa	B-R	In intermediate-risk adults, risk-enhancing factors favor initiation or intensification of statin therapy.
IIa	B-NR	In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone or initiate statin therapy.

CORONARY CALCIUM SCORING



Mayo Clin Proc. ■ December 2017;92(12):1831-1841

CORONARY CALCIUM SCORING

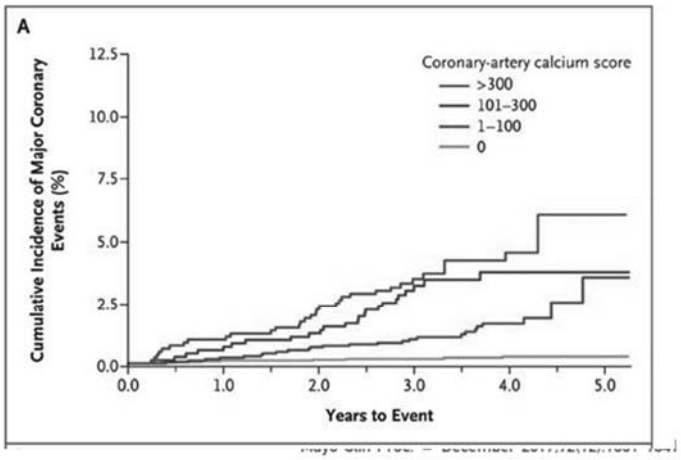


Table 6. Risk-Enhancing Factors for Clinician–Patient Risk Discussion

Risk-Enhancing Factors
• **Family history of premature ASCVD** (males, age <55 y; females, age <65 y) • **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L); non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])* • **Metabolic syndrome** (increased waist circumference, elevated triglycerides [>175 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis) • **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation) • **Chronic inflammatory conditions** such as psoriasis, RA, or HIV/AIDS • **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia** • **High-risk race/ethnicities** (e.g., South Asian ancestry)

Table 6 continued

Risk-Enhancing Factors
• **Lipid/biomarkers**: Associated with increased ASCVD risk o Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dL); o If measured: ▪ **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L) ▪ **Elevated Lp(a):** A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor especially at higher levels of Lp(a). ▪ **Elevated apoB** ≥130 mg/dL: A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor ▪ **ABI** <0.9

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	**LOE**	**Recommendations**
IIa	B-NR	In intermediate-risk adults or selected borderline-risk adults in whom a CAC score is measured for the purpose of making a treatment decision, AND •If the coronary calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher risk conditions are absent (diabetes mellitus, family history of premature CHD, cigarette smoking); •If CAC score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥55 years of age; •If CAC score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy.

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	**LOE**	**Recommendations**
IIb	B-R	In intermediate-risk adults who would benefit from more aggressive LDL-C lowering and in whom high-intensity statins are advisable but not acceptable or tolerated, it may be reasonable to add a nonstatin drug (ezetimibe or bile acid sequestrant) to a moderate-intensity statin.
IIb	B-R	In patients at borderline risk, in risk discussion, the presence of risk-enhancing factors may justify initiation of moderate-intensity statin therapy.

Monitoring in Response to LDL-C–Lowering Therapy

Recommendation for Monitoring		
COR	**LOE**	**Recommendation**
I	A	Adherence to changes in lifestyle and effects of LDL-C–lowering medication should be assessed by measurement of fasting lipids and appropriate safety indicators 4 to 12 weeks after statin initiation or dose adjustment and every 3 to 12 months thereafter based on need to assess adherence or safety.

Primary Prevention in Other Age Groups (Older Adults)

Recommendations for Older Adults		
COR	**LOE**	**Recommendations**
IIb	B-R	In adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable.
IIb	B-R	In adults 75 years of age or older, it may be reasonable to stop statin therapy when functional decline (physical or cognitive), multimorbidity, frailty, or reduced life-expectancy limits the potential benefits of statin therapy.
IIb	B-R	In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it may be reasonable to measure CAC to reclassify those with a CAC score of zero to avoid statin therapy.

Primary Prevention in Other Age Groups (Children and Adolescents)

Recommendations for Children and Adolescents		
COR	**LOE**	**Recommendations**
I	A	In children and adolescents with lipid disorders related to obesity, it is recommended to intensify lifestyle therapy, including moderate caloric restriction and regular aerobic physical activity.
I	B-NR	In children and adolescents with lipid abnormalities, lifestyle counseling is beneficial for lowering LDL-C.

Primary Prevention in Other Age Groups (Children and Adolescents)

Recommendations for Children and Adolescents		
COR	**LOE**	**Recommendations**
IIa	B-R	In children and adolescents 10 years of age or older with an LDL-C level persistently 190 mg/dL (≥4.9 mmol/L) or higher or 160 mg/dL (4.1 mmol/L) or higher with a clinical presentation consistent with FH (see Section 4.2.) and who do not respond adequately with 3 to 6 months of lifestyle therapy, it is reasonable to initiate statin therapy.
IIa	B-NR	In children and adolescents with a family history of either early CVD* or significant hypercholesterolemia,† it is reasonable to measure a fasting or nonfasting lipoprotein profile as early as age 2 years to detect FH or rare forms of hypercholesterolemia.

Primary Prevention in Other Age Groups (Children and Adolescents)

Recommendations for Children and Adolescents		
COR	**LOE**	**Recommendations**
IIa	B-NR	In children and adolescents found to have moderate or severe hypercholesterolemia, it is reasonable to carry out reverse-cascade screening of family members, which includes cholesterol testing for first-, second-, and when possible, third-degree biological relatives, for detection of familial forms of hypercholesterolemia.
IIa	C-LD	In children and adolescents with obesity or other metabolic risk factors, it is reasonable to measure a fasting lipid profile to detect lipid disorders as components of the metabolic syndrome.

Primary Prevention in Other Age Groups (Children and Adolescents)

Recommendations for Children and Adolescents		
COR	**LOE**	**Recommendations**
IIb	B-NR	In children and adolescents without cardiovascular risk factors or family history of early CVD, it may be reasonable to measure a fasting lipid profile or nonfasting non HDL-C once between the ages of 9 and 11 years, and again between the ages of 17 and 21 years, to detect moderate to severe lipid abnormalities.

Other Populations at Risk (Ethnicity)

Recommendation for Other Populations at Risk		
COR	**LOE**	**Recommendation**
IIa	B-NR	For clinical decision-making in adults of different race/ethnicities, it is reasonable for clinicians to review race/ethnic features that can influence ASCVD risk so as to adjust choice of statin or intensity of treatment.

Hypertriglyceridemia

Recommendations for Hypertriglyceridemia		
COR	**LOE**	**Recommendations**
I	B-NR	In adults 20 years of age or older with moderate hypertriglyceridemia (fasting or nonfasting triglycerides 175 to 499 mg/dL [1.9 to 5.6 mmol/L]), clinicians should address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes mellitus, chronic liver or kidney disease and/or nephrotic syndrome, hypothyroidism), and medications that increase triglycerides.
IIa	B-R	In adults 40 to 75 years of age with moderate or severe hypertriglyceridemia and ASCVD risk of 7.5% or higher, it is reasonable to reevaluate ASCVD risk after lifestyle and secondary factors are addressed and to consider a persistently elevated triglyceride level as a factor favoring initiation or intensification of statin therapy (see Section 4.4.2.).

Hypertriglyceridemia

Recommendations for Hypertriglyceridemia		
COR	**LOE**	**Recommendations**
IIa	B-R	In adults 40 to 75 years of age with severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL [≥5.6 mmol/L]) and ASCVD risk of 7.5% or higher, it is reasonable to address reversible causes of high triglyceride and to initiate statin therapy.
IIa	B-NR	In adults with severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL [≥5.7 mmol/L]), and especially fasting triglycerides ≥1000 mg/dL (11.3 mmol/L)), it is reasonable to identify and address other causes of hypertriglyceridemia), and if triglycerides are persistently elevated or increasing, to further reduce triglycerides by implementation of a very low-fat diet, avoidance of refined carbohydrates and alcohol, consumption of omega-3 fatty acids, and, if necessary to prevent acute pancreatitis, fibrate therapy.

Issues Specific to Women

Recommendations for Issues Specific to Women		
COR	**LOE**	**Recommendations**
I	B-NR	Clinicians should consider conditions specific to women, such as premature menopause (age <40 years) and history of pregnancy-associated disorders (hypertension, preeclampsia, gestational diabetes mellitus, small-for-gestational-age infants, preterm deliveries), when discussing lifestyle intervention and the potential for benefit of statin therapy.
I	C-LD	Women of childbearing age who are treated with statin therapy and are sexually active should be counseled to use a reliable form of contraception.
I	C-LD	Women of childbearing age with hypercholesterolemia who plan to become pregnant should stop the statin 1 to 2 months before pregnancy is attempted, or if they become pregnant while on a statin, should have the statin stopped as soon as the pregnancy is discovered.

Adults With Chronic Kidney Disease

Recommendations for Adults With CKD		
COR	**LOE**	**Recommendations**
IIa	B-R	In adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL (1.7 to 4.8 mmol/L) who are at 10-year ASCVD risk of 7.5% or higher, CKD not treated with dialysis or kidney transplantation is a risk-enhancing factor and initiation of a moderate-intensity statin or moderate-intensity statins combined with ezetimibe can be useful.
IIb	C-LD	In adults with advanced kidney disease that requires dialysis treatment who are currently on LDL-lowering therapy with a statin, it may be reasonable to continue the statin.
III: No Benefit	B-R	In adults with advanced kidney disease who require dialysis treatment, initiation of a statin is not recommended.

Adults With Chronic Inflammatory Disorders and HIV

Recommendations for Adults With Chronic Inflammatory Disorders and HIV		
COR	**LOE**	**Recommendations**
IIa	B-NR	In adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL (1.7 to 4.8 mmol/L) who have a 10-year ASCVD risk of 7.5% or higher, chronic inflammatory disorders and HIV are risk-enhancing factors and in risk discussion favor moderate-intensity statin therapy or high-intensity statin therapy.
IIa	B-NR	In patients with chronic inflammatory disorders or HIV, a fasting lipid profile and assessment of ASCVD risk factors can be useful as a) a guide to benefit of statin therapy and b) for monitoring or adjusting lipid-lowering drug therapy before and 4 to 12 weeks after starting inflammatory disease–modifying therapy or antiretroviral therapy.
IIa	B-NR	In adults with RA who undergo ASCVD risk assessment with measurement of a lipid profile, it can be useful to recheck lipid values and other major ASCVD risk factors 2 to 4 months after the patient's inflammatory disease has been controlled.

2018 Cholesterol Guideline

Statin Safety and Statin-Associated Side Effects

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	**LOE**	**Recommendations**
I	A	A clinician–patient risk discussion is recommended before initiation of statin therapy to review net clinical benefit, weighing the potential for ASCVD risk reduction against the potential for statin-associated side effects, statin–drug interactions, and safety, while emphasizing that side effects can be addressed successfully.
I	A	In patients with statin-associated muscle symptoms (SAMS), a thorough assessment of symptoms is recommended, in addition to an evaluation for nonstatin causes and predisposing factors.

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	**LOE**	**Recommendations**
I	B-R	In patients with indication for statin therapy, identification of potential predisposing factors for statin-associated side effects, including new-onset diabetes mellitus and SAMS, is recommended before initiation of treatment.
I	B-R	In patients with statin-associated side effects that are not severe, it is recommended to reassess and to rechallenge to achieve a maximal LDL-C lowering by modified dosing regimen, an alternate statin or in combination with nonstatin therapy.

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	**LOE**	**Recommendations**
I	**B-R**	**In patients with increased diabetes mellitus risk or new-onset diabetes mellitus, it is recommended to continue statin therapy, with added emphasis on adherence, net clinical benefit, and the core principles of regular moderate-intensity physical activity, maintaining a healthy dietary pattern, and sustaining modest weight loss.**
I	**C-LD**	**In patients treated with statins, it is recommended to measure creatine kinase levels in individuals with severe statin-associated muscle symptoms, objective muscle weakness, and to measure liver transaminases (aspartate aminotransferase, alanine aminotransferase) as well as total bilirubin and alkaline phosphatase (hepatic panel) if there are symptoms suggesting hepatotoxicity.**

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	**LOE**	**Recommendations**
I	**B-R**	**In patients at increased ASCVD risk with chronic, stable liver disease (including non-alcoholic fatty liver disease) when appropriately indicated, it is reasonable to use statins after obtaining baseline measurements and determining a schedule of monitoring and safety checks.**
IIa	**B-R**	**In patients at increased ASCVD risk with severe statin-associated muscle symptoms or recurrent statin-associated muscle symptoms despite appropriate statin rechallenge, it is reasonable to use RCT proven nonstatin therapy that is likely to provide net clinical benefit.**

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	**LOE**	**Recommendations**
III: No Benefit	**B-R**	**Coenzyme Q10 is not recommended for routine use in patients treated with statins or for the treatment of SAMS.**
III: No Benefit	**C-LD**	**In patients treated with statins, routine measurements of creatine kinase and transaminase levels are not useful.**

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

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

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		

2018 Cholesterol Guideline

Implementation

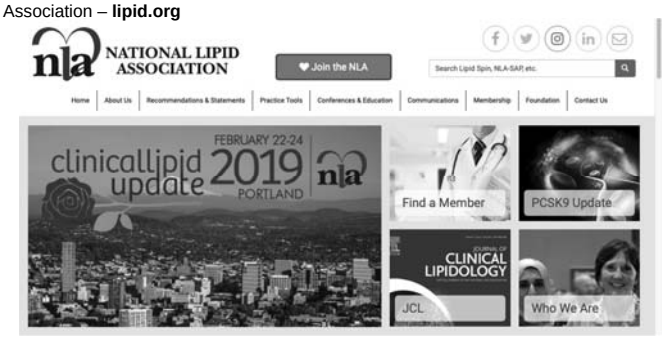
Implementation

Recommendations for Implementation		
COR	**LOE**	**Recommendations**
I	A	Interventions focused on improving adherence to prescribed therapy are recommended for management of adults with elevated cholesterol levels, including telephone reminders, calendar reminders, integrated multidisciplinary educational activities, and pharmacist-led interventions, such as simplification of the drug regimen to once-daily dosing.
I	B-NR	Clinicians, health systems, and health plans should identify patients who are not receiving guideline-directed medical therapy and should facilitate the initiation of appropriate guideline-directed medical therapy, using multifaceted strategies to improve guideline implementation.
I	B-NR	Before therapy is prescribed, a patient-clinician discussion should take place to promote shared decision-making and should include the potential for ASCVD risk-reduction benefit, adverse effects, drug-drug interactions, and patient preferences.

Thank you for your attention!

Please e-mail me with questions at wojcikc@ohsu.edu

If you want to learn more about lipid management consider joining the National Lipid Association – **lipid.org**



Helping People Change Using Motivational Interviewing

Carol DeFrancesco, MALS, RDN

Faculty, Graduate Programs in Human Nutrition
Researcher, Health Promotion & Sports Medicine,
Oregon Health & Science University

Member of Motivational Interviewing Network of Trainers (MINT) since 2000

Special thanks to: Denise Ernst, Steve Berg-Smith, Stephen Andrews and Bill Miller

Objectives

1. Understand **characteristics** of a motivational interviewing approach.
2. Appreciate the role of **active listening** to build rapport.
3. Focus on the "**why**" of change BEFORE the "do" of change.
4. **Evoke** motivation to change from patients rather than supplying reasons.
5. **Five** ready-to-use strategies

Lipid Clinic

Least desirable situation

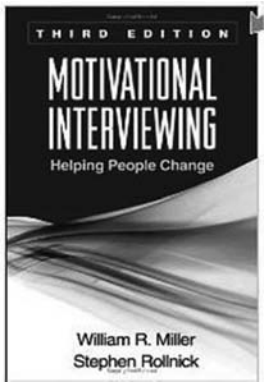
when the health professional advocates for change while the patient argues against it

Righting Reflex

- **Because we are RIGHT!**
- **Patients are on the fence**
  - normal
  - not a sign of denial

Our own ideas about change are more persuasive than what other people tell us.

Bem's Self-perception theory



A collaborative conversation style for

strengthening a person's own motivation and

commitment to change.

PubMed: 3855 articles
>530 Randomized Controlled Trials

Why use Motivational Interviewing

Efficacious

Broad range of behaviors

Broad range of professionals

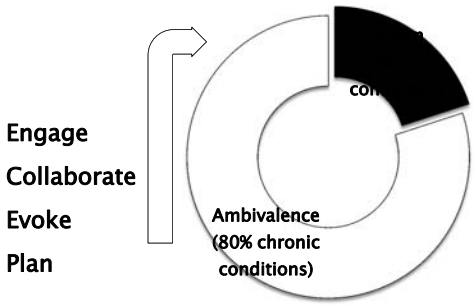
Minority Populations

Improves Patient Satisfaction

Listening

Respect

We need two languages

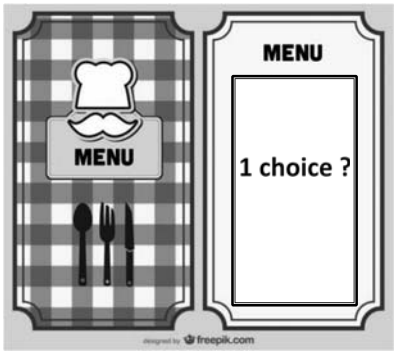


Middle Ground

Directing <=> **Guiding** <=> Following

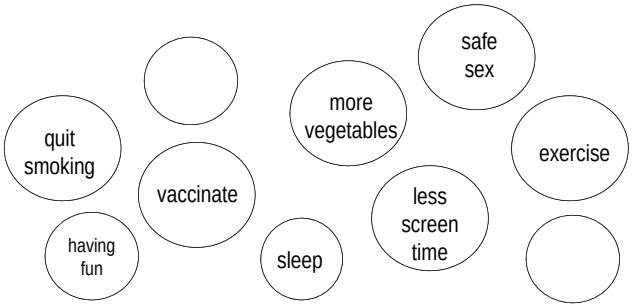
Ready-to-use Strategy #1
Provide Options

People like options



Ready-to-use Strategy #1
Provide Options

"A number of things support health . . .
Where would you like to focus?"



Profound Positive Influence

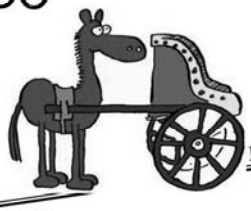
Big Picture

"Dogs and kids know everything."

Be genuine in your patient-centeredness

Long Haul Trucker

Big Picture
The "WHY" comes before the "DO"



JGIM

FROM THE EDITORS' DESK

Getting to the 'Why' of Behavior Change

Mitchell D. Feldman, MD, MPhil

Division of General Internal Medicine, Department of Medicine, University of California, San Francisco, San Francisco, CA, USA.

J Gen Intern Med 31(8):819-20
DOI: 10.1007/s11606-016-3752-9

Change Talk

Sustain Talk

Ready-to-use Strategy #2: Open ended Questions

Evoking Reason Why

- If you decided to, why would you do it?
- What would be the good things about . . .
- What would be the downsides of not making any changes?
- When you did exercise regularly, what were the benefits?

OARS

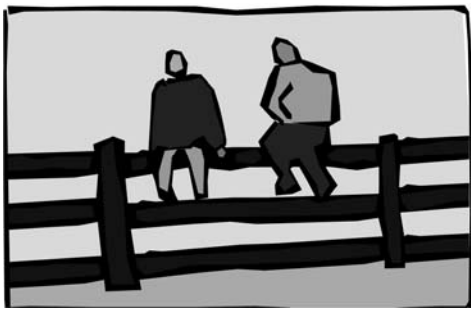
OPEN Questions
AFFIRMATIONS
REFLECTIONS
SUMMARIES

OPEN ENDED QUESTIONS

Choose your questions wisely

(see handout)

Big Picture Evoking rather than Supplying



Affirmations & Self-affirmations

- Affirm
  - effort
  - attempts
  - commitment
  - even without success

Ready-to-use Strategy #3: Evoke Self-Affirmations

- What are you already doing to stay healthy?
- What are you proud of?
- If you decide to make a change, what would you do to be successful?
- When else in your life have you made a significant change like this? How did you do it?
- What personal strengths do you have that will help you succeed?

BUILDING AFFIRMATIONS

Affirmation Activity

(see handout)

1. Write down 2 characteristics or traits of that person.
2. Think about what strengths underlie that characteristic or trait. (what is behind it, what strength supports it?)
3. Then, from that strength (and perhaps a little creativity in adding some context), write an affirmative statement.

Demonstrate Understanding

Big Picture

When a patient feels understood, they are freed up to change.

Open Qs, Affirmations, Reflective Statements, Summaries

Motivation for change is primarily a by-product of being understood

Reflective Statements

- Hint: Begin with the word "You _____ ."
  (end in a period)
- Pt says:
  "I wish my mom would stop nagging me about video games. I don't know why it is such a big deal. I get good grades!"
- Clinician reflects:
  "You are tired of being nagged and you are committed to your school work." (OR)
  "You like to have a balance between school work and fun."

Reflective Statements

- Patient says:

  "_____"

- Clinician reflects:

Bummer.

Reflective statements have value in acute situations too.

Why Not Simply Ask Questions?

Don't believe me; check it out with your own experience

Ready-to-use Strategy #4:

Evoke & Reflect Change Talk SELECTIVELY!

trucker opening line

Ignore other stuff

Giving Information & Advice

Patients forget half . . . .

Giving Information & Advice

- Patient must be receptive
- Eye dropper
- Not shovel
- Too much information undermines change

Ready-to-use Strategy #5: Ask-Provide-Ask

Patients forget half . . . .

ASK **What do they know or want to know about**	• **"What would you most like to know about?"** • **"What have you already learned about….?"**
Provide **State information clearly and in small "chunks"**	• Need-to-know information • Focus on one or two key messages • Use plain language • Use pictures and figures • Emphasize options.
ASK **Ask for feedback or check understanding**	For feedback, ask: • What do you think of that? • How does that sound to you? Teach back for understanding, ask: "I'd like to make sure I did a good job explaining. Would you mind describing what you will do so I know I was clear?

https://www.youtube.com/watch?v=d702HIZfVWs

Summary

1. Be genuine in your patient-centeredness
2. Provide options
3. Open ended questions
4. Affirmations
5. Reflect change talk
6. Before giving information, ask
7. Summarize

Express Hope & Optimism Build Self-efficacy

References and Resources

Compassion

Have compassion for everyone you meet
even if they don't want it. What seems like conceit,
bad manners, or cynicism is always a sign
of things no ears have heard, no eyes have seen.
You do not know what wars are going on
down there where the spirit meets the bone.

– Miller Williams

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Resources

- Motivationalinterviewing.org
  - Provides a listing of trainers around the world
  - Lists trainings that are offered by MINTies (members of the Motivational Interviewing Network of Trainers) in various locations and using different modalities
- DVD set designed to accompany Motivational Interviewing book: www.changecompanies.net/motivational_interviewing.php

Quick Radic:

Efficient and Effective Assessment for Radiating Upper Extremity Pain

OHSU 50th Annual Primary Care Review
190211

Erik Ensrud, MD
Associate Professor, Orthopaedics and Rehabilitation, OHSU
Board Certified in PM&R/EMG/Neurology/Neuromuscular Disease

What is the percentage of your patients are complaining of radiating arm or leg pain?

A. < 5%

B. 5-10%

C. 10-15%

D. 15-20%

E. > 20%

Ms.K, a 38 yo new pt, c/o 2 months right arm pain that shoots down arm just past elbow. You decide to…

A. Order a cervical MRI

B. Order an EMG

C. Examine 8 muscles for strength

D. Examine 6 muscles, one neck test, and 3 shoulder tests

E. Examine 4 muscles, 2 MSK tests, and 3 sensory points…and do this in < 60 sec

PAIN THAT TRAVELS ALONG A LIMB

Radiating (vs radicular) pain is a very common clinical complaint

Often assumed to be radicular

radicular pain-pain "radiated along a dermatome of a nerve due to inflammation or irriation of a nerve root"

But radiating pain is often *not* due to nerve irritation-*muddles* the workup

So sometimes radiating pain can be MSK

But many DO have radicular pain from pinching of nerve roots…how to effectively find that ?

Let's start with what we are looking at…

Let's back up…what Do Normal Peripheral Nerves Do?

3 Functions

1. Carry a signal to muscle to contract
2. Carry normal sensation such as light touch for skin
3. *Carry pain messages from non-nerve tissues (skin, bone, joints, soft tissue). *This message does not mean that the nerve is injured or abnormal.*

Such as, a fire alarm going off may mean the fire alarm is injured/malfunctioning (injured nerve), or…
that the fire alarm is working as designed to carry a message that there is a fire-in this case the fire alarm/NERVE is functioning normally.

Ordering an MRI as First Step

- BENEFITS
  - Time saver-few clicks…"Smart" Set
  - Likely to be abnormal-confirmation bias
  - Pts are always worried about their spine, want to know
  - Very sensitive test
  - Picture for the Instagram Age
- Drawbacks
  - High likelihood of normal abnormalities
  - Often requires pre-auth, denials
  - Much explanation needed in f/u about disc bulges, foraminal stenosis on wrong side
  - Often low specificity test

Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW. Abnormal magnetic resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg Am 1990;72(3):403–8.
Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 1994;331(2):69–73.

Exam?? We're going somewhere, but it's foggy and old-fashioned….

Amish community outside of Champaign-Urbana, IL

Is the exam relevant today?

Sun setting on that way back when windmill thing…

MOTOR EXAMINATION

- Advantages
  - FEE-Fast, Easy, Effective in clinic
  - QUICK-much faster than even rapid CT
  - Can provide valuable info regarding the longest tracks throughout the central and peripheral nervous system
  - Pattern recognition allows for rapid diagnosis
- Disadvantages
  - Relies on pt effort/level of alertness/cooperation
  - Relies on examiner's interpretation of muscle force
  - Difficult to learn this on the web or in a book-it's a learned motor skill, like riding a bike

Basic Principles of Muscle Force Testing 1

- Each muscle crosses a joint and causes changes in that joint ROM with contraction
- Try to STABILIZE the joint the muscle crosses whenever possible, to help isolate the muscle action

Basic Principles of Muscle Force Testing 2

- Use your similar-sized muscles only in hand muscles
- You will use your perception of the force you deliver and your experience of what is "normal"-this is a learned motor skill and takes time to learn-*try to do a focused exam on pts with known diagnoses so that you know what to expect*
- In motor testing, the EXAMINER has the subjective sensation being judged-c/w sensory where the PATIENT has the subjective sensation
- In non-hand muscles, use your additional muscles/body weight as needed-this is not a force competition (i.e., I am stronger and therefore the pt is "weak" or vice-versa)

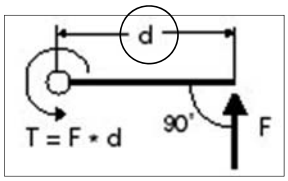
Basic Principles of Muscle Force Testing 3

- Muscle Strength testing =
  - = Force (M x A)
    - Measured in Pounds/Kilograms/Newtons
    - Not time dependent
- Work =
  - = Force x Distance
  - Units are joules

- Power =
  - = Work/time
  - Units are units of energy divided by time,
  - i.e watt = one joule/second

TORQUE !

- The tendency of a force to rotate an object about an axis (aka joint in MST)
  - Physics = Torque
  - Mechanical Engineering = Moment

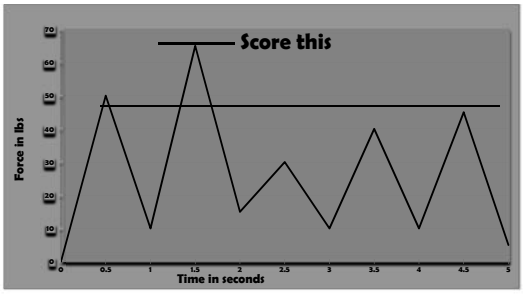


Maximize d !!

Basic Principles of Muscle Force Testing 4

- The score assigned to the muscle is the maximum force generated at any point in time during the testing of that muscle
- Rapid decreases in force do not represent weakness; rather, almost without exception they represent variability in lower motor neuron drive (exception-severe myasthenia)
- * Do not report the average when intermittent activation occurs-report the **PEAK** force

Score Peak force



Another look at peak strength testing

Intermittent Activation (IA): The Great Strength Confounder

"The Chicken Dance"

- Three Reasons for IA
  - Pain in joint crossed-contraction of muscle compresses joint
  - Poor proprioception -cannot sense the contraction of muscle/joint position well
  - "Enhancement" of weakness (somatic vs. malingering)

Back to MsK…consensus is examine first…

What nerve roots might be affected with radiating pain down an arm? C6>C7>C5>C8

Surgical detail	Primaries	Revisions
No. of procedures	1,305	115
Levels	2,811	198
Average levels/procedure	2.2	1.7
Levels affected		
C2	20 (1.5)	0
C3	96 (7.4)	8 (7.0)
C4	285 (22)	31 (27)
C5	493 (38)	35 (30)
C6	855 (66)	31 (27)
C7	803 (62)	49 (43)
C8	195 (15)	33 (29)
T1	64 (4.9)	11 (9.6)

We know that C6 is the most common cervical radiculopathy, what is the best muscle to check strength for C6?

A. Deltoid

B. Biceps

C. Pronator teres

D. Triceps

E. Wrist Extension

Pronator Teres-most sensitive muscle for C6

* the most distal C6-innervated muscle

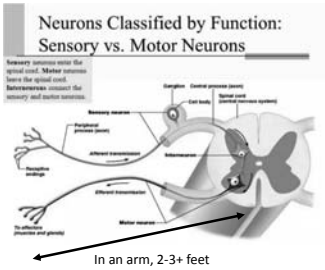
Assessment of Forearm Pronation Strength in C6 and C7 Radiculopathies

James Rainville, MD,*† Damon J. Soto, MD,† Cristie Jouve, MD,*† and Iouis Jenis, MD*‡§

Results. In C6 radiculopathy subjects, forearm pronation weakness was present in 72%, was twice as common as wrist extension weakness, was present in all case where elbow flexion or wrist extension weakness was noted, and was found in all but 2 subjects where elbow extension weakness was present. In C7 radiculopathy subjects, forearm pronation weakness accompanies elbow extension weakness in 23% of subjects and was the only weakness in 10% of subjects. Manual muscle testing demonstrated adequate interrater reliability.

Conclusions. Forearm pronation weakness is the most frequent motor finding in C6 radiculopathies and may be noted is some cases of C7 nerve root compression.

Why is that?
Unique nature of structure of peripheral neurons-the LONGEST cells in the body, very length-dependent transport along the length of the very long cell

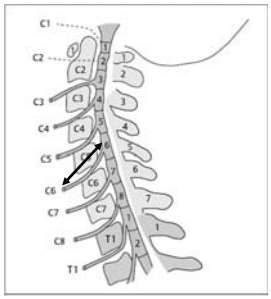


In an arm, 2-3+ feet

Nerve root compression is similar to a dam at the origin of a creek…where does the creek start to run dry? Near the origin or downstream?
Pronator teres is the most "downstream" C6 muscle

Why was this missed? What about ASIA (American Spinal Injury Association) scales? What about wrist extension?

- ASIA motor levels are based on SPINAL CORD levels
- Motor neurons in the spinal cord are always <u>superior/above</u> their <u>nerve root exit</u> from the spinal cord
- Because of this, spinal cord and nerve root levels <u>do not</u> correlate well

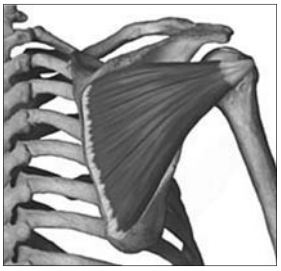


4 Muscle, Side to Side Comparison, C5-8 Screen

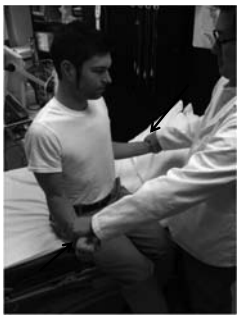
- Infraspinatus C5
- Pronator teres C6
- Extensor Digitorum Communis (EDC) C7
- Extensor Indicis Proprius (EIP) C8

Infraspinatus force testing-C5

side to side immediate comparison (also upper motor neuron advantages)



Extends and laterally rotates the humerus



Pronator Teres-most sensitive muscle for C6

* the most distal C6-innervated muscle

Assessment of Forearm Pronation Strength in C6 and C7 Radiculopathies

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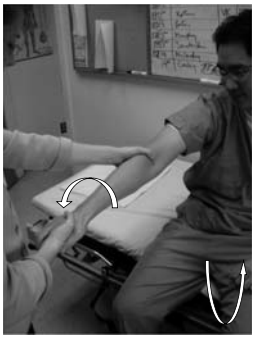
Pronator teres-C6



- Shake pts hand, ask them to keep the thumb DOWN
- Pts elbow must be fully extended (if flexed test pronator quadratus)
- Weak in ~2/3 of C6 radics
- check side-to-side
- Bend your trunk sideways prn for additional force

EDC (Extensor digitorum communis) highly C7

- Have pt grasp knees with all fingers, then lift up the 2 middle fingers
- "flip the bird"
- Minimal force muscle, like all finger extensors
- Don't push too hard too fast-marshmallow analogy
- Check force side-to-side

Extensor indicis propius (EIP) radial nerve, highly C8

- Have pt grasp knees with all fingers, then lift up the 2 index fingers
- Slight force muscle, like all finger extensors-finger flexors much stronger (cause of trigger fingers)
- Check force side-to-side
- Great advantage of not being involved in ulnar neuropathy or CTS

SENSORY EXAM

- "CAN YOU FEEL IT" IS A…
  - A. Good question to ask during the usual sensory exam
  - B. 1980 epic hit single/video by The Jacksons
  - C. Poor question to ask a pt with an acute spinal cord injury
  - D. Album by the innovative 1980's Australian band, Hunters and Collectors (best known for their single, "Throw Your Arms Around Me")

CAN YOU FEEL IT

DST-double simultaneous testing

- Use to test
  - Distal to proximal gradients for length-dependent neuropathy.
    Light touch is best-subserved by both systems
  - Side-to-side distal dermatomes for radiculopathy
  - Different peripheral nerve distributions for focal neuropathies

Side to side distal aspect of dermatomes for radiculopathy

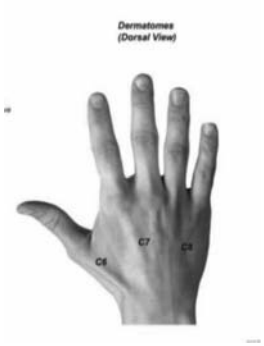
Simultaneously touch
Back of Left and Right hand

Thumb C6

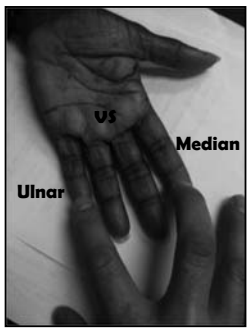
Middle Finger C7

Pinky C8

10 sec



Different peripheral nerve distributions for focal neuropathies



Back to MsK…cervical radic muscle screen negative…

What else might be affected with radiating pain down an arm?

MSK Mimic-definition

A musculoskeletal condition that presents with pain or discomfort suggestive of a nerve injury/neuropathic etiology

Reasons to care about MSK Mimics

Common causes of limb pain

Frequent reason for clinic referral

Pts may have radiculopathy AND mimics

Your extremity skeleton and spinal nerve roots don't coordinate their pain-like 2 kids crying at the same time

"Pain in limb-? radiculopathy, ? CTS"

Treatable conditions

Musculoskeletal Exam Tests: Advantages

FAST/EASY/EFFECTIVE

Ability to diagnose quickly at bedside or exam room with appropriate physical exam

Timesavers for the Provider…keep up your clinic flow

Fewer unnecessary MRIs ordered with time-consuming follow-up

Musculoskeletal Exam Tests: Pearls

Check bilateral limbs for side-to-side comparison: non-involved side first when possible

Ask, "Is that the same pain you have been experiencing?"

* Patients can have more than one condition-i.e. radiculopathy *and* rotator cuff tendinitis

Musculoskeletal Exam Tests Pearls: Wince sign

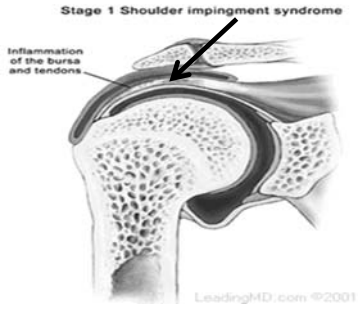
Look for the "Wince" sign for positive test

- **Eye blink/face grimace**
- **Not just mild discomfort**

2 High-Yield MSK Mimic Tests for Radiating/? Radic Exam

- Hawkins Sign
- Lateral epicondyle tenderness

Supraspinatus/Rotator Cuff Tendonitis



Supraspinatus tendonitis mimics

C3-7 radiculopathy*

Supraspinatus tendonitis Symptoms/risk factors

Pain with arm movement, esp. overhead

*Difficulty sleeping when lying on affected side

Pain may radiate up towards neck and down arm, even beyond elbow

Repetitive movements-esp. overhead, acromion anatomy (hooked)

Especially in people with underlying neurologic disease, due to periscapular muscle imbalance leading to instability of glenohumeral joint

Supraspinatus Tendonitis: Hawkins Shoulder Test most sensitive at 92%

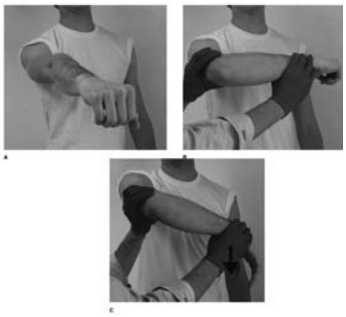
Humerus flexed 90 deg

Elbow flexed 90 deg

Examiner's hand stabilizes pt's shoulder

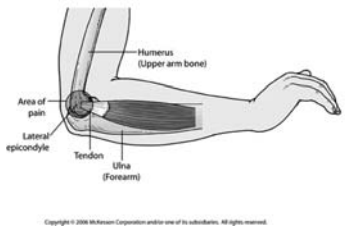
Examiner pulls down on pt's forearm WITH RAPID JERK to internally rotate humerus…forceful enough to knock over a full pint glass on a tabletop

Head of humerus pinches tendon under acromion → PAIN when inflamed



Lateral epicondylitis

Tennis Elbow



Lateral epicondylitis mimics

Lower cervical radiculopathy-pain can radiate distally along forearm/ulna

Ulnar neuropathy*-pain around elbow, radiates from elbow

**Ulnar nerve will go into pinky and ring finger…usually different from radiculopathy

Lateral epicondylitis-exam test

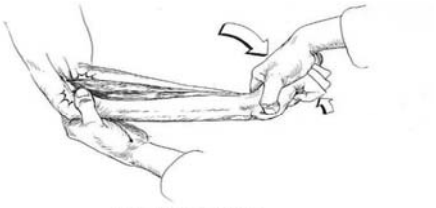


Fig. 49. The tennis elbow test.

- Palpate 0.5-1cm distal to the epicondyle (max . tenderness to palpation)

Practice with another participant

4 Muscle, Side to Side Comparison, C5-8 Screen

- Infraspinatus C5
- Pronator teres C6
- Extensor Digitorum Communis (EDC) C7
- Extensor Indicis Proprius (EIP) C8

L/R Light Touch-C6/7/8

Hawkins and Lateral epicondyle Tests

Back to MsK…cervical radic muscle screen negative, light touch C6/7/8 L/R equal…

Markedly positive R Hawkins Test, negative lateral epicondyle TTP

Now you have options…

1. Home rotator cuff exercises
2. PT Referral
3. Subacromial steroid injection
4. Some combination of the above

RTC 2 months…MUCH better ☺

Review-Quick Radic, Upper Extremity

- 4 muscle force screen 30 sec
- L/R light touch comparison 10 sec
- Hawkins and Lateral Epicondyle MSK Tests 20 sec

Fishing for radiating upper extremity pain…

Cervical Spine MRI

Quick Radic Exam

THE END

Larry Kanfer
Champaign-Urbana, IL

Travel Medicine for the Primary Care Provider

February 11, 2019; Portland, Oregon

Presented by: Timothy Herrick, MD, MS Dept. of Family Medicine

Billing problems

- Activities that are obviously travel-related but coded as part of a regular visit will not be paid for by most insurance.
- The patient will be billed
- At times, the entire visit will be disallowed.

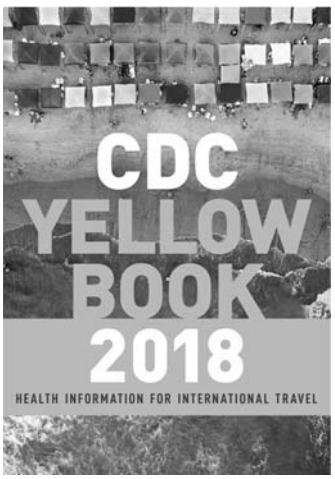
When providing travel services:

- Don't try to bill insurance [cash, non-covered forms] unless BCBS
- Attach vaccines and medications to phone encounters and nurse visits
- First do no harm [understand the indications, contraindications and schedules of any proposed preventive measures]

Alternatives to travel clinics

- Vaccines are available on demand [for adults] at large pharmacies. [call ahead.]
  - Oral medications, including vaccines, are not .[requires an Rx]
  - Some pharmacies provide a consultation where non-licensed providers send a letter back to the PCP with suggested medicines that need a prescription.

Learning travel?



CDC Country-Specific Recommendations

A CDC alternative: Travel Health Pro

Distinctives

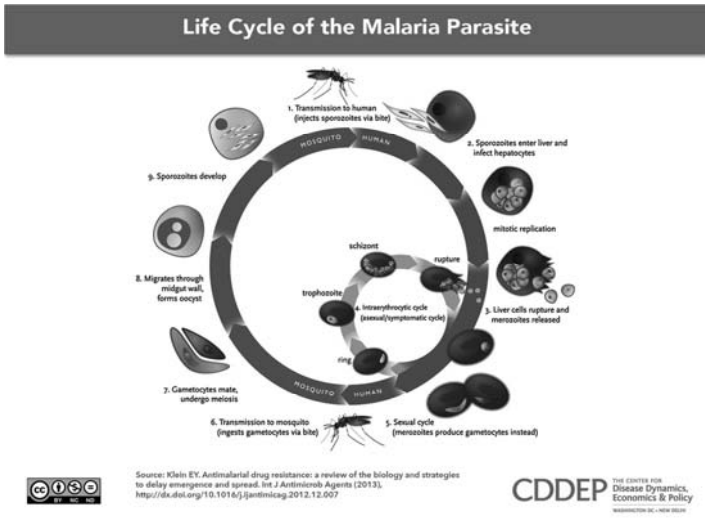
- British website
- More and Better Maps
  - More granular recommendations
- Less intensive recommendations
- Useful to reference both for shared decision-making with the patient.
- Areas where they agree make for stronger recommendations

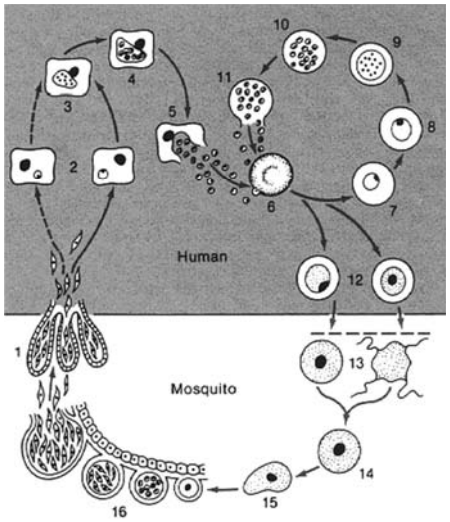
Topics

- Malaria
- Vaccinations
- Other concerns
  - Including altitude medication

Malaria

- Even within countries, extremely itinerary-dependent.
- Special considerations for VFR
- Pharmacological prevention
- Standard Warning about post-visit fever for virtually all travellers.





Prophylaxis in travellers

- Atovaquone/Proguanil; one pill daily
- Mefloquine 250mg/wk
- Doxycycline 100mg/d

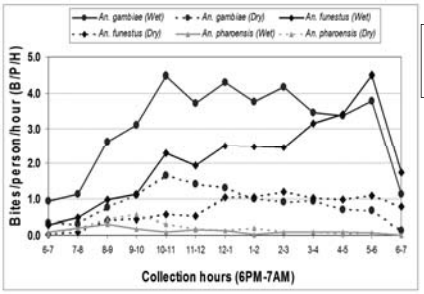
Notes on prophylaxis

- Does not obviate the need for non-pharmacological preventive measures
- Don't forget the tail [depends on product]
- None are fool-proof [hence, post-visit messaging]

Other preventive approaches

- Permethrin-impregnated mosquito nets
  - evidence-based mortality reduction!
- Other Entomological Approaches
- Vaccine trials

Hourly profile of *Anopheles* biting: Comparison by species & season in the Kassena-Nakana District of Ghana



Vector-human contact greatest during the second half of the night Early morning biting habit.

Sleep under an ITN

Stay under bednet In the morning until ready to move about actively

Presumptive Anti-relapse Treatment [PART]

- Vivax and ovale have a stage called hypnozoites
- Liver form, can reactivate after months to years
- Wintering mechanism
- Primaquine; exquisitely sensitivizes G6pd so must do an assay first.

A new product

- Tafenoquine [Arakoda] similar to primaquine.
- Affects the liver stage of all species [this is called causal prophylaxis, and allows for a shorter « tail »]
- Also affects hypnozoites, so useful for PART
- Must do a G6PD quantitative assay.

Tafenoquine

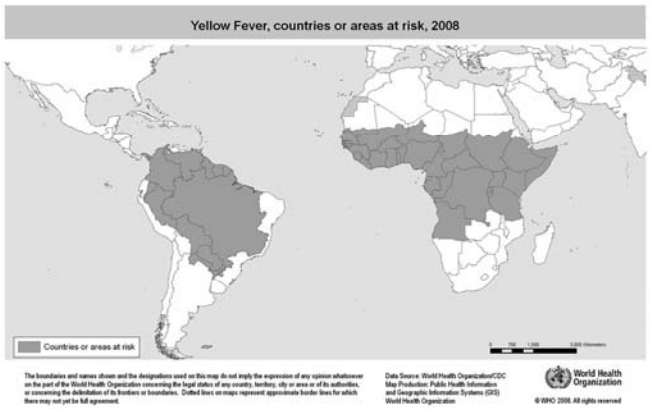
- Of interest because
  - It is causal prophylaxis
  - It will eliminate vivax relapse and vivax is a more significant player than has been realized
  - Long half-life allows for weekly dosage
  - 3 days of 200mg prior to or at start of travel, then 200 weekly, with last dose one week after the last exposure dose
  - Pricing may be competitive with Malarone

Obligatory exotic animal picture

Travel vaccinations

- All routine vaccinations should be updated [polio*]
- Sometimes Required: Yellow Fever,
- Recommended: Hep A+B
  - Typhoid
  - Rabies
  - Meningitis
  - Japanese encephalitis
  - Oral Cholera vaccine

Yellow fever



Yellow fever

- Careful attention to contra-indications:
  - Immunosuppression
  - Thymus disorders
  - Age <9 months; >60

Lifetime immunization
Current outbreaks
Current issues with vaccine availability

Clinics with Yellow Fever Available

Meningitis belt

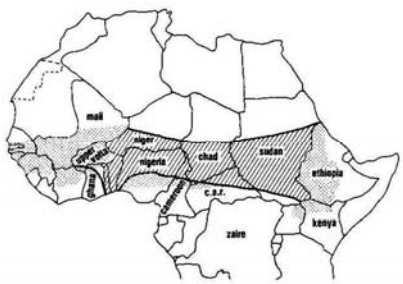


Figure 74–1. The African meningitis belt. The shaded area indicates the area of the belt as originally defined by Lapeyssonnie. Dotted areas indicate regions where outbreaks of meningococcal disease with epidemiologic features characteristic of the African meningitis belt have sometimes been recorded. (Adapted from Lapeyssonnie L: Bull WHO 28(Suppl 3):3, 1963.)

Meningitis

– Quadrivalent conjugate vaccine
– Same as in our vaccination program
– A+C+Y+W-135, conjugate: Menactra
– Every 5 years [as long as risk persists]

Meningococcal B is not a travel issue.

Rabies

- Recommended, depending on risk
- Pre-exposure shots; 3 active
- post-exposure: active plus passive and passive not always available overseas

Pre-Exposure Rabies Vaccination

- Three doses of rabies vaccine
- Given at days 0, 7 and 21-28
- Produces antibodies against rabies
- Simplifies treatment of a bite or other potential rabies exposure
  - Get 2 more doses of rabies vaccine at 0 and 3 days
  - Avoids need to get painful, expensive and often unavailable rabies hyperimmune globulin

Typhoid Fever

- More important given MDR; XDR
- Two choices:
- Oral; attenuated; four qod doses; q5y
  - Very specific instructions;
  - No antibiotics
  - Allow plenty of time, plan on being near a fridge.

  Injectable; killed; q2y

Live vs. Killed Vaccines

- In general, live vaccines are contraindicated for immunosuppressed, and, less stringently, pregnancy.
- Live vaccine include yellow fever; routine vaccines that are live: oral polio, [not given in US now], MMR, rotavirus, HZV/varicella, nasal influenza, and BCG.
- Interval is significant. Live vaccines can be given same day or one month from other vaccines.
- Oral typhoid and cholera are exceptions

Japanese encephalitis

- Range: all of Asia
- CDC says for stays > 30 days
- Arbovirus with reservoirs in birds, pigs
- Our vaccine: two shots one month apart
- Expensive!
- Rare but devastating
- After one year; Booster needed
- other cheaper vaccines available locally

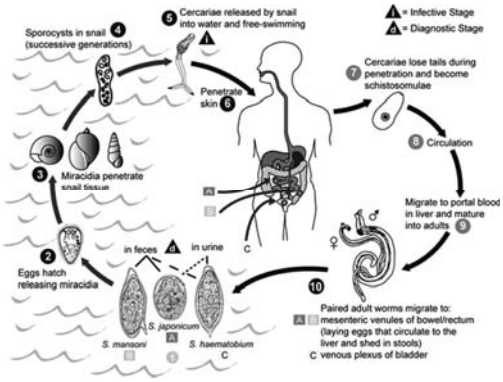
Oral cholera vaccine

- New vaccine [to the US]: Vaxchora
- Live oral vaccine with novel workflow
- Indications actually somewhat narrow
  - Many countries list Cholera
  - All countries that have Cholera anywhere are listed;
  - Mainly indicated for those who will be in proximity to known outbreaks

Traveler's Diarrhea

- Unlike US a large percentage of acute diarrhea is bacterial, therefore amenable to antibiotic therapy.
- Usually given in the case of diarrhea complicated by fever, bleeding, cramps or long duration [>3d]
- azithromycin is DOC [Cipro out of favor, given adverse effects, resistance patterns]
- Rifaximin, expensive alternative

Schistosomiasis



Schistosomiasis

- Risk present in any natural fresh-water bathing situation in Africa and elsewhere, including bucket baths.
- Frequent cause of unexplained eosinophilia in returned travellers
- Rx: Praziquantel

Altitude sickness medicine

- Indicated for those sleeping above 9000 ft.
- Pay attention to itinerary, eg overnight in Quito.
- Diamox 125 mg bid, starting two days before ascent, and first three days at altitude.

Sun protection

- Related to skin type and heredity
- Use of sunblock is a very good idea.

A word about Zika

- Some perspective: At the worst point in the epidemic, in Brazil, the hardest hit country, less than 1% of pregnancies were impacted.

Countries with Active Zika Transmission, CDC

Waiting period for unprotected intercourse

Waiting period of six months after a visit to an endemic country if non-symptomatic.

- If symptomatic, six months after resolution of symptoms
- Based on experimental data, CDC has downshifted to 3 months.

Questions?

- ?
- ?
- ?

UNDERSTANDING AND TREATING POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS) IN PRIMARY CARE

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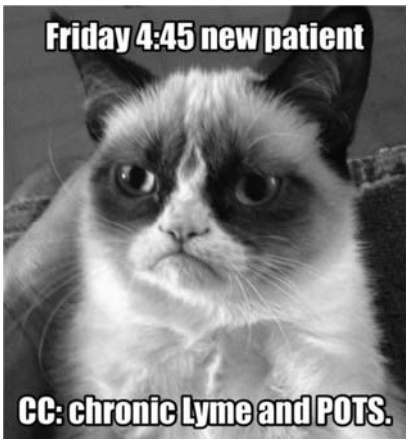
DISCLOSURES

- I HAVE NO FINANCIAL DISCLOSURES
- I WILL BE DISCUSSING OFF-LABEL USE OF FLUDROCORTISONE, MIDODRINE, IVABRADINE, BETA-BLOCKERS, AND PYRIDOSTIGMINE FOR THE TREATMENT OF POTS DURING THIS PRESENTATION.

LEARNING OBJECTIVES

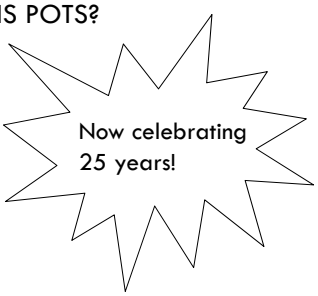
- LIST AT LEAST 5 COMMON SYMPTOMS THAT MAY POINT TO AUTONOMIC DYSFUNCTION AS A CAUSE
- UNDERSTAND ETIOLOGIES FOR POTS
- DESCRIBE THE 3 MAIN LIFESTYLE MODIFICATIONS THAT SHOULD BE STARTED FOR POTS
- UNDERSTAND THE GENERAL CLASSES OF MEDICATIONS USED AND BACKGROUND ON TREATMENT CONTROVERSIES
- KNOW WHEN TO REFER A PATIENT FOR MORE WORKUP OR TREATMENT



POTS AS A SYNDROME WITH CLASSIC AND RECOGNIZABLE SYMPTOMS, FOR WHICH THERE IS A SET TREATMENT APPROACH

WHAT IS POTS?

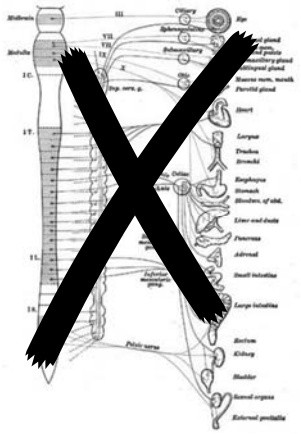
- **P**OSTURAL
- **O**RTHOSTATIC
- **T**ACHYCARDIA
- **S**YNDROME



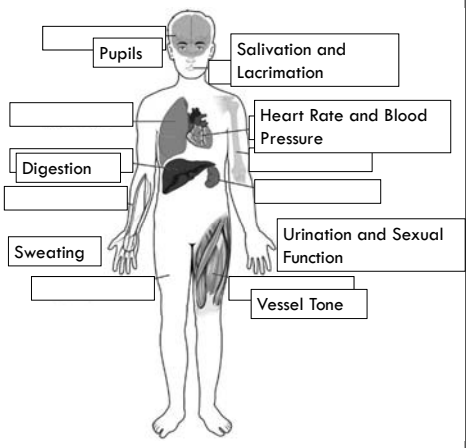
WHAT IS POTS?

DYSFUNCTION OF THE AUTONOMIC NERVOUS SYSTEM

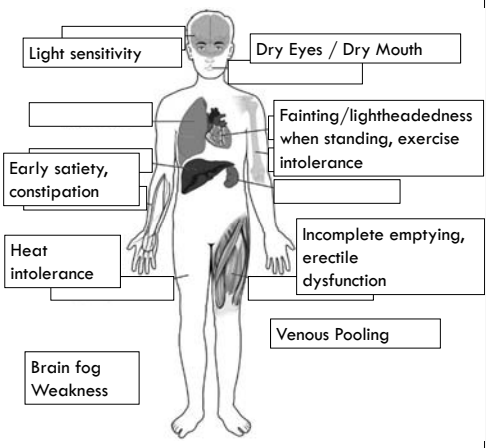
Anatomy of the Autonomic (Sympathetic and Parasympathetic) Nervous System



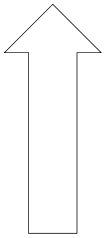
THE AUTONOMIC NERVOUS SYSTEM CONTROLS 'AUTOMATIC' BODY FUNCTIONS



WHAT SHOULD MAKE YOU SUSPECT DYSAUTONOMIA?



POTS: THE BASICS

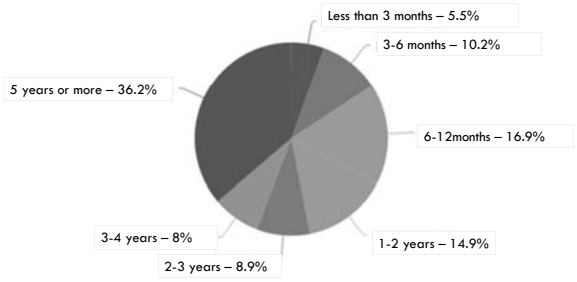


HEART RATE INCREASES BY 30 BPM (OR GOES ABOVE 120) BY 10 MINUTES WITH STABLE BLOOD PRESSURE AND + SYMPTOMS

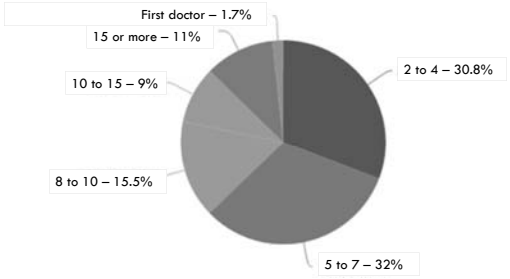
POTS: THE COMPLICATED

- ORTHOSTATIC LIGHTHEADEDNESS
- FAINTING
- FATIGUE
- GENERALIZED WEAKNESS
- HEAT INTOLERANCE
- COLD INTOLERANCE
- CHRONIC DIARRHEA
- CHRONIC CONSTIPATION
- IBS
- HEADACHES
- PAIN
- TREMULOUSNESS
- PALPITATIONS
- POOR SLEEP
- ANXIETY / HYPERVIGILANCE
- BRAIN FOG
- TROUBLE INITIATING URINATION
- URINARY FREQUENCY
- CHEST PAIN
- SHORTNESS OF BREATH
- EXERCISE INTOLERANCE
- NAUSEA

How long were you experiencing symptoms before you were officially diagnosed with POTS?

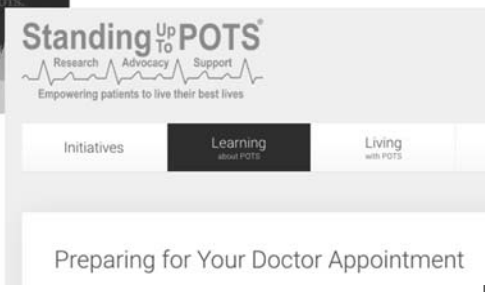


After the onset of POTS symptoms, how many doctor's did you see before receiving a diagnosis of POTS?



ROBUST ONLINE PRESENCE

Oregon EDS Facebook Support Group



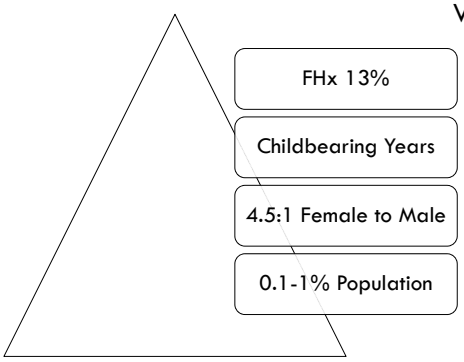
"I found out about POTS on my own through internet research."

LET'S GET TO SOME SOLID FACTS:

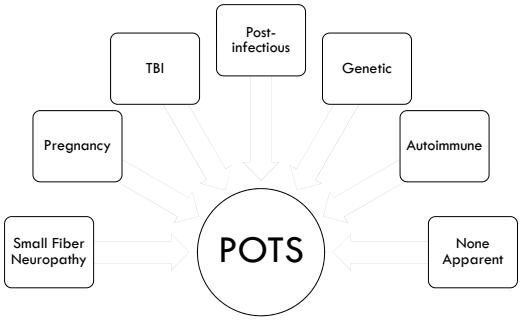
WHO, WHY, HOW, AND THEN WHAT

WHO GETS POTS… AND WHY?

WHO GETS POTS?

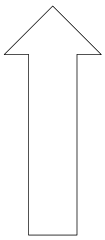


WHAT CAUSES POTS?



HOW TO DIAGNOSE POTS

DIAGNOSTIC CRITERIA



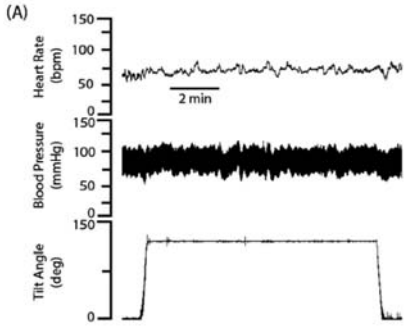
SUSTAINED HEART RATE INCREASE BY 30 BPM (OR GOES ABOVE 120) BY 10 MINUTES WITH STABLE BLOOD PRESSURE AND + SYMPTOMS

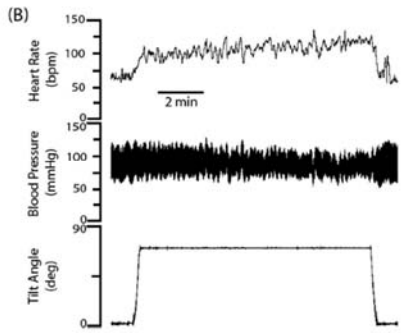
IN OFFICE TESTING

- LAY DOWN FOR 5 MINS
- STANDING 1 MINUTE
- STANDING 3 MINUTES
- STANDING 5 MINUTES
- STANDING 10 MINUTES

FORMAL AUTONOMIC TESTING

- TILT TABLE TEST
- HEART RATE VARIABILITY
- QSART (SWEAT RESPONSE TEST)





CARDIOLOGY WORKUP

- MINIMUM: EKG NORMAL
- HOLTER MONITOR
- ECHO

LABORATORY TESTING

- CBC AND IRON STUDIES
- THYROID STUDIES
- FURTHER TESTING IF HISTORY/EXAM CONCERNING FOR COMORBID CONDITION

THEN WHAT?

"LIFESTYLE MODIFICATIONS"

THE ABC'S OF TREATMENT[1]

- ABDOMINAL COMPRESSION
- BOLUSES OF WATER
- BED UP
- COUNTERMANEUVERS
- DRUGS
- EDUCATION
- EXERCISE
- FLUID AND SALT

EXERCISE

- MARKED EXERCISE INTOLERANCE
- FIGHT OR FLIGHT RESPONSE
- DECONDITIONING IS NOT THE CAUSE, BUT IT IS A RESULT
- THIS IS THE CORNERSTONE OF POTS THERAPY

SPECIFIC PROTOCOLS

- LEVINE PROTOCOL (TEXAS)
- CHOP PROTOCOL

FLUIDS AND SALT

- INCREASE WATER AS TOLERATED TO 3L PER DAY (100 OZ)
- INCREASE SALT TO UP TO 10G PER DAY (2 TSP)
  - CONSIDER GLUCOSE-SALT REHYDRATION

PHARMACOLOGIC OPTIONS

THE CORE TREATMENTS

Midodrine*	Fludrocortisone*	Beta Blockers*	Pyridostigmine*
2.5mg BID	0.1mg/day	Propranolol 10mg	30mg BID-TID
10mg TID max	Potassium	Hypotension	GI upset
Supine Hypertension	Supine Hypertension		Transient Fasciculations

*= off label use

PHARMACOLOGIC OPTIONS

NEW AND CONTROVERSIAL

IVABRADINE

- AN ALTERNATIVE TO BETA BLOCKERS?
- DIRECT SINOATRIAL NOTE INHIBITION
- TYPICAL STARTING DOSE 5 MG BID
- NO DATA

- $$$

IV SALINE – A CONTROVERSIAL APPROACH

- ACUTE VS CHRONIC
- WANING EFFECT OVER TIME
- INVASIVE PROCEDURES
- CHRONIC USE DISCOURAGED BY CONSENSUS STATEMENTS

IMMUNOTHERAPY

- POTS AS AN AUTOIMMUNE DISORDER?

- IVIG, PLASMAPHERESIS/PLASMA EXCHANGE, IMMUNOSUPPRESANTS

- NO DATA, SIGNIFICANT RISK
- INSURANCE COVERAGE ONLY FOR TREATMENT OF OTHER DISORDER

WHEN TO REFER TO A SPECIALIST?

- CLARIFY DIAGNOSIS
- RAPID / SUBACUTE SYMPTOMS
- REFRACTORY
- UNDERLYING NEUROLOGIC ETIOLOGY

DYSAUTONOMIA INTERNATIONAL

AWARENESS ADVOCACY ADVANCEMENT

www.dysautonomiainternational.org

POTS AS A SYNDROME WITH CLASSIC AND RECOGNIZABLE SYMPTOMS, FOR WHICH THERE IS A SET TREATMENT APPROACH

QUESTIONS?

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Assessing and Treating Pediatric Anxiety

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Disclosures

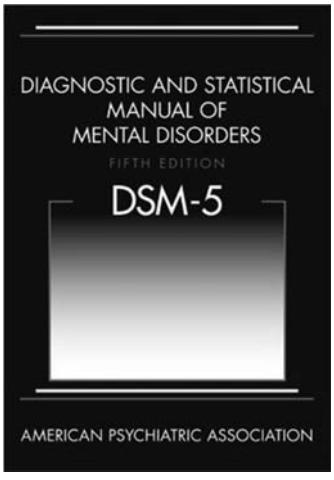
- No honorarium for this talk
- No funding from industry

Definition of Anxiety

"an abnormal and overwhelming sense of apprehension and fear often marked by physiological signs, by doubt concerning reality and nature of the threat, and by self-doubt about one's capacity to cope with it"

–Merriam Webster Dictionary

Broad Categories of Anxiety

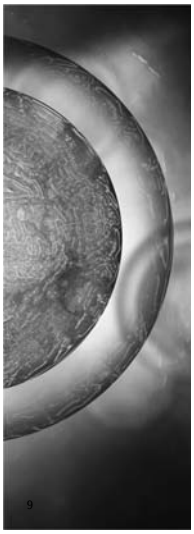


Broad Categories of Anxiety

- Trauma-Related
  - Acute Stress Disorder
  - Posttraumatic Stress Disorder
- Obsessive Compulsive Disorder
- Non-Trauma or OCD Related Anxiety Disorders

Non-Trauma or OCD Related Anxiety Disorders

- Separation Anxiety Disorder
- Social Phobia
  - Selective Mutism
- Generalized Anxiety Disorder
- Specific Phobia
- Panic Disorder with or without Agoraphobia



Pediatric Anxiety Disorders

- Most common class of psychiatric disorders
- Comorbidity is common
- A higher risk of anxiety disorders and major depressive disorder as adults

Pediatric Anxiety Disorders

- Separation anxiety disorder is more prevalent in childhood
- Generalized anxiety disorder, social phobia, and panic disorder are more prevalent during adolescence

Causative Factors

- Biological Factors
  - Genetic predisposition
- Environmental Factors
  - Modeling and competition in the family
  - Critical and over-controlling parenting

Psychological Factors

- Overachiever
- Cognitive Biases
  - Preferential attention to perceived threatening cues

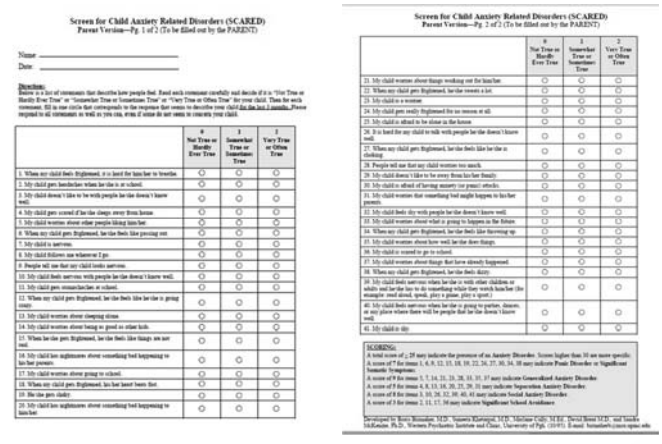
Conditioning Happens!

Assessment

- Interview of parents
- Interview of child
- Collateral information from teachers
- Consider co-morbid psychiatric conditions

Assessment

- Consider medical conditions
  - Substance use disorder in teenagers
  - Eating disorder
  - Endocrine disorder
- Ask about trauma <u>early</u> in the assessment



Screen for Child Anxiety Related Disorders (SCARED)
Parent Version—Pg. 1 of 2 (To be filled out by the PARENT)

Name _____
Date: _____

Directions:
Below is a list of statements that describe how people feel. Read each statement carefully and decide if it is "Not True or Hardly Ever True" or "Somewhat True or Sometimes True" or "Very True or Often True" for your child. Then for each statement, fill in one circle that corresponds to the response that seems to describe your child for the last 3 months. Please respond to all statements as well as you can, even if some do not seem to concern your child.

	0 Not True or Hardly Ever True	1 Somewhat True or Sometimes True	2 Very True or Often True
1. When my child feels frightened, it is hard for him/her to breathe.	○	○	○
2. My child gets headaches when he/she is at school.	○	○	○
3. My child doesn't like to be with people he/she doesn't know well.	○	○	○
4. My child gets scared if he/she sleeps away from home.	○	○	○
5. My child worries about other people liking him/her.	○	○	○
6. When my child gets frightened, he/she feels like passing out.	○	○	○
7. My child is nervous.	○	○	○
8. My child follows me wherever I go.	○	○	○
9. People tell me that my child looks nervous.	○	○	○
10. My child feels nervous with people he/she doesn't know well.	○	○	○
11. My child gets stomachaches at school.	○	○	○
12. When my child gets frightened, he/she feels like he/she is going crazy.	○	○	○
13. My child worries about sleeping alone.	○	○	○
14. My child worries about being as good as other kids.	○	○	○
15. When he/she gets frightened, he/she feels like things are not real.	○	○	○
16. My child has nightmares about something bad happening to his/her parents.	○	○	○
17. My child worries about going to school.	○	○	○
18. When my child gets frightened, his/her heart beats fast.	○	○	○
19. He/she gets shaky.	○	○	○
20. My child has nightmares about something bad happening to him/her.	○	○	○

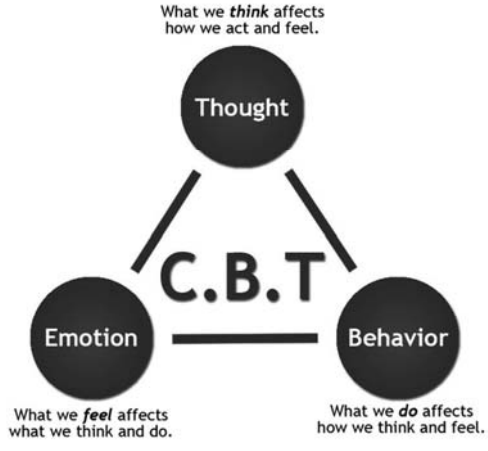
Screen for Child Anxiety Related Disorders (SCARED)
Parent Version—Pg. 2 of 2 (To be filled out by the PARENT)

	0 Not True or Hardly Ever True	1 Somewhat True or Sometimes True	2 Very True or Often True
21. My child worries about things working out for him/her.	○	○	○
22. When my child gets frightened, he/she sweats a lot.	○	○	○
23. My child is a worrier.	○	○	○
24. My child gets really frightened for no reason at all.	○	○	○
25. My child is afraid to be alone in the house.	○	○	○
26. It is hard for my child to talk with people he/she doesn't know well.	○	○	○
27. When my child gets frightened, he/she feels like he/she is choking.	○	○	○
28. People tell me that my child worries too much.	○	○	○
29. My child doesn't like to be away from his/her family.	○	○	○
30. My child is afraid of having anxiety (or panic) attacks.	○	○	○
31. My child worries that something bad might happen to his/her parents.	○	○	○
32. My child feels shy with people he/she doesn't know well.	○	○	○
33. My child worries about what is going to happen in the future.	○	○	○
34. When my child gets frightened, he/she feels like throwing up.	○	○	○
35. My child worries about how well he/she does things.	○	○	○
36. My child is scared to go to school.	○	○	○
37. My child worries about things that have already happened.	○	○	○
38. When my child gets frightened, he/she feels dizzy.	○	○	○
39. My child feels nervous when he/she is with other children or adults and he/she has to do something while they watch him/her (for example: read aloud, speak, play a game, play a sport.)	○	○	○
40. My child feels nervous when he/she is going to parties, dances, or any place where there will be people that he/she doesn't know well.	○	○	○
41. My child is shy.	○	○	○

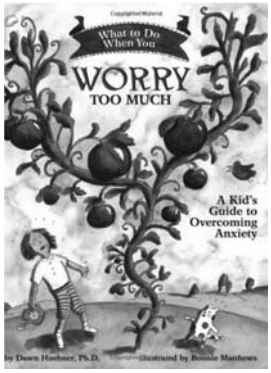
SCORING:
A total score of ≥ 25 may indicate the presence of an Anxiety Disorder. Scores higher than 30 are more specific.
A score of 7 for items 1, 6, 9, 12, 15, 18, 19, 22, 24, 27, 30, 34, 38 may indicate Panic Disorder or Significant Somatic Symptoms.
A score of 9 for items 5, 7, 14, 21, 33, 28, 35, 37, 39 may indicate Generalized Anxiety Disorder.
A score of 8 for items 4, 8, 13, 16, 20, 25, 29, 31 may indicate Separation Anxiety Disorder.
A score of 8 for items 3, 10, 26, 32, 36, 40, 41 may indicate Social Anxiety Disorder.
A score of 3 for items 2, 11, 17, 39 may indicate Significant School Avoidance.

Developed by Boris Birmaher, M.D., Suneeta Khetarpal, M.D., Christine Cully, M.Ed., David Brent M.D., and Sandra McKenzie, Ph.D., Western Psychiatric Institute and Clinic, University of Pgh. (10/95). E-mail: birmaherb@upmc.edu

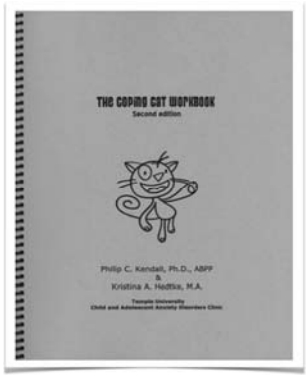
http://www.neurotransmitter.net/anxietyscales.html



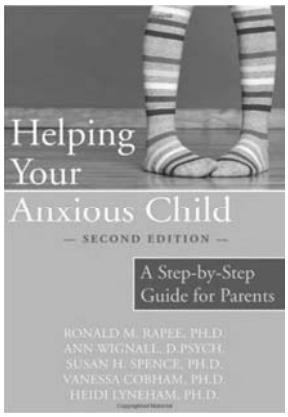
Handbook for Parents to Use

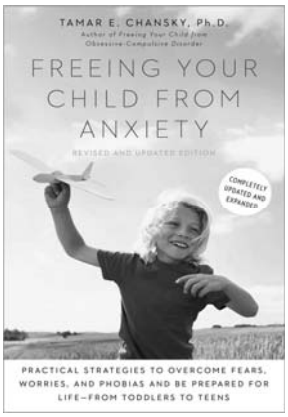


Workbooks Used by CBT Therapists



Books for Parents



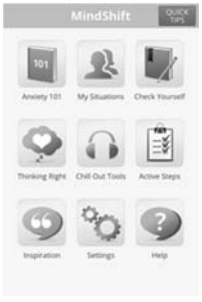


Other Resources

youth.anxietybc.com

www.childmind.org

Smartphone Apps

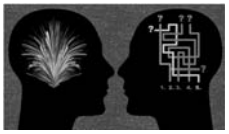


Education

- "Fight, flight, or freeze"
- Anxiety Thermometer
  - Daily log of anxiety level, physical symptoms, triggers

Externalizing the Problem

- The power of language
  - "the dragon or the worry bully"
  - Older children and adolescents
    - Thinking brain and emotional brain



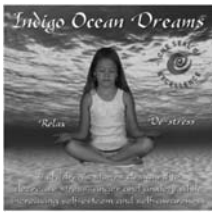
Worry Time

- Set aside 15 minutes each day
- Protected time from siblings
- Review worries
- Leftover time is "Talk Time"

Worry Box

Lowering Stress Level

- Exercise
- Relaxation strategies
  - Progressive muscle relaxation
  - "Belly breathing"
  - Guided imagery



Challenging Unhelpful Thoughts

- Cognitive restructuring
  - Changing thoughts rather than feelings

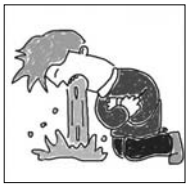
Anxiety Hierarchy

- Build a "fear ladder"
- Approach feared situations rather than avoid
  - "Being brave"
  - Earn rewards

Exposure

- Help child discover that the feared situation is not dangerous
- Different forms of exposure
  - Imaginal
  - In vivo

Specific Phobia to Vomit/Vomiting



How to Find a CBT Therapist

- www.abct.org lists cognitive behavioral therapists by state
- www.opa.org lists psychologists and their specialty

Pharmacotherapy for Pediatric Anxiety Disorders

Duloxetine

- Only medicine FDA approved for non-OCD anxiety disorders in children and adolescents
  - Patients with GAD who are 7 years and older

Duloxetine

- Dosing per Micromedex
  - "Initial, 30 mg orally once daily for 2 weeks, and may then increase to 60 mg orally once daily; may increase further by increments of 30 mg once daily; MAX 120 mg once daily"

NEW RESEARCH

A Randomized, Placebo-Controlled Study of Duloxetine for the Treatment of Children and Adolescents With Generalized Anxiety Disorder

Jeffrey R. Strawn, MD, Apurva Prakash, BA, Qi Zhang, PhD, Beth A. Pangallo, BS, Chad E. Stroud, BS, Na Cai, PhD, Robert L. Findling, MD, MBA

- Youth aged 7-17 years with primary diagnosis of GAD
- Flexible dose duloxetine or placebo for 10 weeks followed by open-label duloxetine for 18 weeks

 Strawn JR, et al. J Am Acad Child Adolesc Psychiatry 2015;54(4):283-293

NEW RESEARCH

A Randomized, Placebo-Controlled Study of Duloxetine for the Treatment of Children and Adolescents With Generalized Anxiety Disorder

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- Mean duloxetine dose was 53.6 mg
- Last prescribed dose for duloxetine patients during acute phase treatment was:
  - 30 mg (27.4%)
  - 60 mg (30.4%)
  - 90 mg (29.6%)
  - 120 mg (12.6%)

 Strawn JR, et al. J Am Acad Child Adolesc Psychiatry 2015;54(4):283-293

FLUVOXAMINE FOR THE TREATMENT OF ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS

THE RESEARCH UNIT ON PEDIATRIC PSYCHOPHARMACOLOGY ANXIETY STUDY GROUP*

- 8 week, DB PCT
- N=128, ages 6-17 years
  - Social anxiety disorder, GAD, separation anxiety disorder
- Flexible dosing used with max dose of 250 mg in < 12 y/o's and 300 mg in 12-17 y/o's

 NEJM, 2001, 344(17):1279-1285

FLUVOXAMINE FOR THE TREATMENT OF ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS

THE RESEARCH UNIT ON PEDIATRIC PSYCHOPHARMACOLOGY ANXIETY STUDY GROUP*

- Outcome measures: Pediatric Anxiety Rating Scale (PARS) and Clinical Global Improvement Scale (CGI)
- Results:
  - Fluvoxamine > placebo (76% vs 29%)
  - Generally well-tolerated
  - Significant side effects: abdominal discomfort and increased motor activity

 NEJM, 2001, 344(17):1279-1285

Fluoxetine

- Single site, 12 week study, double blind
  - Fluoxetine 20 mg or placebo
- N=64, ages 7-17 years
- Outcomes: CGI, PARS, SCARED
- Results:
  - Fluoxetine > placebo (61% vs 35%)
  - Did not separate until 9th week of trial

 Birmaher, J Am Acad Child Adolesc Psychiatry 2003, 42(4)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 25, 2008 VOL. 359 NO. 26

Cognitive Behavioral Therapy, Sertraline, or a Combination in Childhood Anxiety

John T. Walkup, M.D., Anne Marie Albano, Ph.D., John Piacentini, Ph.D., Boris Birmaher, M.D., Scott N. Compton, Ph.D., Joel T. Sherrill, Ph.D., Golda S. Ginsburg, Ph.D., Moira A. Rynn, M.D., James McCracken, M.D., Bruce Waslick, M.D., Satish Iyengar, Ph.D., John S. March, M.D., M.P.H., and Philip C. Kendall, Ph.D.*

Methodology

- 12 week, multi-site, DB PCT
- N=488, ages 7-17 years (mean age 10.7 +/- 2.8)
- GAD, separation anxiety disorder, social anxiety disorder or combination
- Comorbidities allowed including ADHD on stimulant medications

 Walkup et al, NEJM 2008, 359(26):2754-2766

Randomized to One of 4 Arms

- Sertraline (N=133)
  - Fixed-flexible dosing schedule (25 to 200 mg)
- Medication placebo (N=76)
- CBT (N=139)
  - 14 one hour sessions using Coping Cat
- CBT and sertraline (N=140)
  - Subjects knew they were receiving active sertraline in this group

 Walkup et al, NEJM 2008, 359(26):2754-2766

Outcome Measures

- Categorical and dimensional ratings of anxiety severity and impairment at baseline and at 4, 8, and 12 weeks
  - CGI, PARS, and the Children's Global Assessment Scale (CGAS)

 Walkup et al, NEJM 2008, 359(26):2754-2766

Results

- Very much or much improved on CGI
  - Combination therapy – 80.7%
  - CBT – 59.7%
  - Sertraline – 54.9%
  - Placebo – 23.7%
- Combination was superior to either monotherapy (P<0.001)
- Similar outcomes as measured by PARS

 Walkup et al, NEJM 2008, 359(26):2754-2766

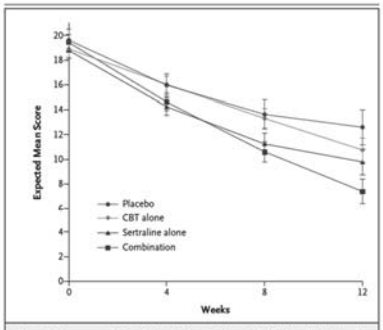


Figure 2. Scores on the Pediatric Anxiety Rating Scale during the 12-Week Study.

Scores on the Pediatric Anxiety Rating Scale range from 0 to 30, with scores higher than 13 consistent with moderate levels of anxiety and a diagnosis of an anxiety disorder. The expected mean score is the mean of the sampling distribution of the mean. The I bars represent standard errors.

Adverse Events

- No increase in suicidal or homicidal ideation when sertraline used
- No child attempted suicide
- Among children in CBT group, there were fewer reports of insomnia, fatigue, sedation, and restlessness or fidgeting than in the sertraline group

 Walkup et al, NEJM 2008, 359(26):2754-2766

Duloxetine

- Duloxetine is the only FDA approved medicine for non-OCD pediatric anxiety disorders (GAD only though)
- Approved for ages 7 y/o and above
- Generic comes in 20 mg, 30 mg, 40 mg, and 60 mg capsules

Duloxetine

- Dosing recommendations (Micromedex)
  - 30 mg a day for 2 weeks, then increase to 60 mg daily; may increase further by increments of 30 mg once daily; Max 120 mg a day
- 10 week research study, last prescribed dose was:
  - 30 mg (27.4% of patients)
  - 60 mg (30.4% of patients)
  - 90 mg (20.7% of patients)
  - 120 mg (8.9% of patients)
  - Similar dosing during 16 week, open label trial

 Strawn et al, J Am Acad Child Adolesc Psychiatry. 2015;54(4):283-93

NEW RESEARCH

The Impact of Antidepressant Dose and Class on Treatment Response in Pediatric Anxiety Disorders: A Meta-Analysis

Jeffrey R. Strawn, MD, Jeffrey A. Mills, PhD, Beau A. Sauley, MA, Jeffrey A. Welge, PhD

J Am Acad Child Adolesc Psychiatry 2018;57(4):235–244.

SSRIs and SSNRIs

- Data from 9 trials (SSRIs: n=5; SSNRIs: n=4)
- Evaluating 7 medications in 1,673 youth
- Statistically significant treatment effects emerged within 2 weeks of treatment and by 6 weeks, clinically significant differences emerged

 Strawn JR, et al. The impact of Antidepressant Dose and Class on Treatment Response in Pediatric Anxiety Disorders: A Meta-Analysis, J Am Academy of Child Adolesc Psychiatry 2018

"In pediatric patients with generalized, separation and/or social anxiety disorders, antidepressant-related improvement occurs early in the course of treatment and SSRIs are associated with more rapid and greater improvement compared to SSNRIs".

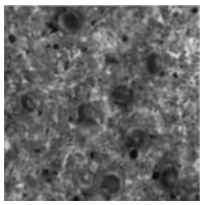
 Strawn JR, et al. The impact of Antidepressant Dose and Class on Treatment Response in Pediatric Anxiety Disorders: A Meta-Analysis, J Am Academy of Child Adolesc Psychiatry 2018

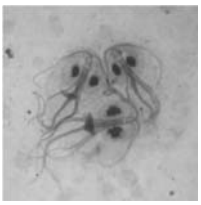
Summary

- Anxiety disorders are the most common class of psychiatric disorders in children and adolescents
- CBT is a very effective form of treatment
- Duloxetine is the only FDA approved medicine for non-OCD pediatric anxiety disorders (GAD only though)
- Strong support for use of sertraline

Cheers!

johnsoky@ohsu.edu





Infectious Diarrhea

February 11, 2019 Ellie Sukerman, MD

Disclosures

I have no disclosures.

Outline

- Epidemiology and ddx of gastroenteritis
- Clinical approach, diagnostics and treatment
- *Clostridioides difficile*
- Traveler's diarrhea

U.S. Epidemiology

- Approximately 179 million cases of acute gastroenteritis (AGE) each year
- Monthly prevalence ~8%
- ~600k AGE hospitalizations/year
- ~5000 AGE deaths/year

Kim, et al. J Clin Gastroenterol. 2017.

DDx: >250 pathogens

Bacterial:
- *Bacillus cereus*
- *Campylobacter*
- *Clostridium difficile*
- *Escherichia coli*
  - Shiga toxin-producing (STEC)
  - ETEC, EPEC, EIEC, EAEC
- *Listeria monocytogenes*
- *Plesiomonas shigelloides* (formerly *Aeromonas shigelloides)*
- *Salmonella*
- *Shigella* spp
- *Staphylococcus aureus*
- *Vibrio cholerae*
- *Vibrio parahemolyticus*
- *Yersinia* spp

Viral:
- Adenovirus
- Astrovirus
- Enterovirus
- Hepatitis A
- Norovirus
- Rotavirus
- Sapovirus

Algae/Toxins:
- Ciguatera toxin
- Neurotoxic shellfish poisoning (brevetoxin)
- Diarrheic shellfish poisoning
- Amnestic shellfish poisoning (domoic acid)

Parasitic:
- *Cryptosporidium parvum*
- *Cyclospora cayetanensis*
- *Cystoisospora belli* (previously *Isospora belli*)
- *Entamoeba histolytica*
- *Giardia lamblia*
- Microsporidia (now classified as a fungus)
- *Ancylostoma duodenale*
- *Diphyllobothrium latum*
- Schistosomiasis
- *Strongyloides stercoralis*
- *Trichinella spiralis*

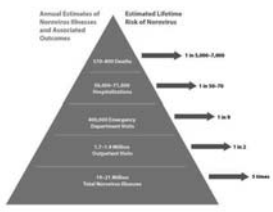
Unknown

wwwn.cdc.gov/nndss/conditions/notifiable/2018. Accessed 04/20/2018.

Causes of AGE

Of the cases where we obtain a diagnosis, what is the leading cause of acute gastroenteritis in the U.S.?

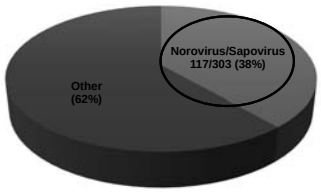
A. Escherichia coli
B. Salmonella
C. Clostridium difficile
D. Norovirus
E. Campylobacter



https://www.cdc.gov/norovirus/php/illness-outbreaks-figure.html (Accessed 5/23/18).

Local Epidemiology

Disease Outbreaks by Etiology: Oregon 2016



Selected Cases of Notifiable Diseases: OR, 2016

Pathogen/Disease	# cases
Campylobacteriosis	994
Cryptosporidiosis	327
E. Coli O157 (STEC)	191
Giardiasis	338
Listeriosis	16
Salmonellosis	448
Shigellosis	101
Vibriosis	21
Yersiniosis	34

www.oregon.gov/OHA/PH/DISEASESCONDITIONS/COMMUNICABLEDISEASE/DISEASESURVEILLANCEDATA/ANNUALREPORTS

Adapted from: http://www.oregon.gov/OHA/PH/DISEASESCONDITIONS/COMMUNICABLEDISEASE/DISEASESURVEILLANCEDATA/ANNUALREPORTS/Documents/2016/2016-DiseaseYear.pdf

How do I begin to narrow the ddx?

SMALL VS. LARGE BOWEL SYMPTOMS?

ACUTE VS. CHRONIC DIARRHEA?

WATERY DIARRHEA VS. DYSENTERY?

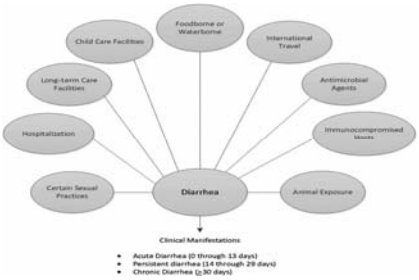
FREQUENCY OF DIARRHEA?

EMESIS VS. DIARRHEA PREDOMINANT?

SEVERITY?

Medical History

- Assess symptoms
  - Type of symptoms
  - Duration
  - Severity
  - Onset in relation to potential exposure
- Exposure history
- Host immune status
- Prevent additional cases
- Recognize potential outbreaks



Shane et al., CID. 2017.

Watery Diarrhea	
Pathogen	**Epidemiologic Clues**
Clostridium difficile	Antibiotic use, hospitalization, gastric acid suppression
Cryptosporidium parvum	Produce, daycare, swimming, AIDS
Enterotoxigenic *E. coli*	Travel to resource-limited settings
Giardia lamblia	Travel/hiking/camping, swimming pools, daycare
Listeria monocytogenes	Pregnancy, immune compromise, extremes of age
Norovirus	Outbreaks in restaurants, health care and childcare facilities, cruise ships
Other viral pathogens (adenovirus, astrovirus, rotavirus, sapovirus)	Daycare, children, immunocompromised adults
Cyclospora cayetanensis	Chronic diarrhea in HIV/AIDS

Inflammatory/Bloody Diarrhea	
Pathogen	**Epidemiologic Clues**
Campylobacter spp.	Poultry, meat, unpasteurized milk; animal contact (puppies, kittens), travel
Entamoeba histolytica	Travel, MSM
Enterohemorrhagic *E. coli*	Ground beef, fresh produce, unpasteurized milk and juice, nursing homes, extremes of age
Nontyphoidal *Salmonella*	Poultry, eggs/egg products, nut butters, spices, reptiles, petting zoos, travel
Shigella spp.	Raw vegetables, daycare, MSM, travel
Vibrio parahemolyticus	Raw seafood and shellfish, cirrhosis
Yersinia spp.	Pork or pork products, untreated water, abnormal iron metabolism

UpToDate. Causes of acute infectious diarrhea in adults in resource-rich settings (Accessed 5/21/18).

Physical Exam

- Assess severity of illness:
  - Vital signs
  - Evaluate for dehydration
  - Abdominal exam findings
- Extra-intestinal manifestations associated with enteric infections

Diagnostic Evaluation

Parasite job hunting

When should stool testing be performed?

- Patients with diarrhea accompanied by fever, bloody or mucoid stools, severe abdominal tenderness or signs of sepsis
- Immunocompromised patients
- If you plan to start empiric antibiotics
- In the context of a possible outbreak with guidance from your public health department

Stool Cultures

- Routine stool cx: *Salmonella, Shigella* and *Campylobacter*
- Many labs require specific request for STEC O157 testing as well as other specific bacteria of concern
- **Generally not useful in patients hospitalized >3 days**

Le Guern, et al., Diagnostic Microbiology and Infectious Disease (2013).

Stool Ova & Parasites

- Not cost effective in most cases of acute diarrhea
- Not indicated for hospital onset diarrhea
- Reasonable if: persistent diarrhea (>14 days), immunocompromised patients and in the context of possible outbreak
- Need to specify certain organisms which may not be detected on routine O&P (e.g., *Cryptosporidium, Cyclospora, Cystoisospora*)
- Consider EIA assay or molecular testing

Shane et al., CID. 2017.

Diagnostic Testing

Which testing method are you using for diagnosis of gastroenteritis?

A. Stool culture
B. Culture-independent diagnostic testing
C. Both
D. Unsure

Stool Culture vs. CIDT

	Culture-Dependent Testing	Culture–Independent Testing
Requires patient specimens	✓	✓
Accuracy	High	Variable
Time to Results	Slow	Rapid
Requires special knowledge to perform	✓	✕
Produces culture for subtyping and susceptibility testing	✓	✕
May test for bacterial, viral and parasitic infections simultaneously	✕	✓

Pathogen	FilmArray	Verigene	Luminex	BDMax	Prodesse
Campylobacter	✓	✓	✓	✓	✓
Salmonella	✓	✓	✓	✓	✓
Shigella	✓	✓	✓	✓	✓
Shiga-like toxin 1 and 2	✓	✓	✓	✓	✓
Enterotoxigenic *Escherichia coli*	✓				
Enteropathogenic *E. coli*	✓				
Enteroaggregative *E. coli*	✓				
E. coli O157	✓		✓		
Vibrio	✓	✓			
Yersinia enterocolitica	✓	✓			
Pleisiomonas shigelloides	✓				
Clostridium difficile	✓		✓		
Norovirus GI and GII	✓	✓	✓		
Adenovirus	✓		✓		
Rotavirus	✓	✓	✓		
Astrovirus	✓				
Sapovirus	✓				
Giardia	✓		✓	✓	
Cryptosporidium	✓		✓	✓	
Cyclospora cayetanensis	✓				
Entamoeba histolytica	✓		✓	✓	

Reporting

Immediately	Within One Working Day
Vibrio cholerae	Campylobacteriosis
Marine intoxications[1]	Cryptosporidiosis
Any outbreak of disease[2]	Cyclosporosis
Any uncommon illness of potential public health significance	*Escherichia coli* (enterotoxigenic, Shiga-toxigenic including E. coli O157 and other serogroups)
	Gromontia spp.
	Hemolytic uremic syndrome (HUS)
	Listeriosis
	Salmonellosis (including typhoid)
	Shigellosis
	Vibriosis (other than *V. cholerae*)
	Yersiniosis (other than plague)

[1]Paralytic shellfish poisoning (saxitoxin), scombroid, domoic acid intoxication, ciguatera etc.
[2]Outbreaks are ≥2 cases from separate households associated with a suspected common source

Adapted from Oregon Health Authority. http://www.oregon.gov/oha/PH/diseasesconditions/communicablediseasereportingcommunicablediseasepages/reportable.aspx#timeframes

How do I Report?

Contact your local health department – you can do this online!

http://www.oregon.gov/oha/PH/DISEASESCONDITIONS/COMMUNICABLEDISEASE/REPORTINGCOMMUNICABLEDISEASE/Pages/counties.aspx

Empiric Therapy

In which of the following scenarios is empiric therapy warranted for cases of bloody diarrhea?

A. Empiric antibiotics should be initiated for all cases of bloody diarrhea until stool test results are available
B. Patients requiring hospitalization related to gastroenteritis
C. Close contacts of those with bloody diarrhea
D. Patient with bloody diarrhea without systemic symptoms in the setting of recent foreign travel

Empiric Therapy for Bloody Diarrhea

- In immunocompetent adults and children, empiric antibiotics while awaiting results of lab investigation is **not** recommended with the following exceptions:
  - Severe illness
  - Infants <3 months of age with suspected bacterial etiology
  - Those who have recently traveled with temp ≥ 38.5C and/or signs of sepsis
- Consider empiric therapy in immunocompromised persons with severe illness and bloody diarrhea

Empiric therapy for adults = fluoroquinolone or azithromycin

Shane et al., CID. 2017.

Directed Therapy

A 42yo woman with a history of htn and diabetes presents with bloody diarrhea. Her vitals are within normal limits. She has poorly localized abdominal tenderness. Her CIDT stool testing is positive for Shiga Toxin-Producing *E. coli* (STEC).

What is the most appropriate next step?

A. Start a fluoroquinolone
B. Contact your local health department
C. Supportive care including anti-diarrheal medication
D. Send stool culture
E. B and D

STEC

- Antibiotics **NOT** recommended for patients with suspected or proven STEC infection
- Benefit of treatment not clearly demonstrated **AND**
- Antibiotic therapy may increase the risk of hemolytic uremic syndrome (HUS)

www.cdc.gov/ecoli/clinicians.html (Accessed 5/21/18).

Directed Therapy

Salmonella, Shigella, Campylobacter, Yersinia

- Order stool cultures with susceptibility testing in patients with suspected infection or those with positive CIDT
  - Antibiotic resistance is not uncommon
- Antibiotic treatment generally limited to those with severe disease and/or immune compromise

Directed Therapy - Bacterial

Indication	1st Line	Alternative	Comments
Campylobacter	Azithromycin	Ciprofloxacin	Per CDC, antibiotics needed only for those with severe illness or at high risk of severe disease
Nontyphoidal *Salmonella enterica**	Usually not indicated	NA	Antimicrobial therapy should be considered for groups at increased risk of invasive infection. If susceptible, treat with ceftriaxone, ciprofloxacin, tmp-smx or amoxicillin. Ceftriaxone preferred over ciprofloxacin if invasive disease suspected or confirmed.
Shigella	Azithromycin, cipro or ceftriaxone	Tmp-smx or ampicillin if susceptible	CDC recommends targeted treatment with antibiotics (severe illness or high risk of severe illness). Avoid prescribing fluoroquinolones if cipro MIC is 0.12 ug/mL or higher even if laboratory identifies isolate as susceptible
Vibrio cholerae	Doxycycline	Ciprofloxacin, azithromycin or ceftriaxone	Primary therapy is aggressive rehydration; antibiotics are adjunctive
Non-*Vibrio cholerae*	Usually not indicated for non-invasive disease Invasive disease = ceftriaxone plus doxycycline	Invasive disease = tmp-smx plus aminoglycoside	
Yersinia enterocolitica	Tmp-smx	Cefotaxime or ciprofloxacin	Reserve antibiotics for severe or complicated infections.

Adapted from Shane et al., CID. 2017.; www.cdc.gov (Accessed 2/5/19).

Directed Therapy - Parasites

Indication	1st Line	Alternative	Comments
Cryptosporidium spp	Nitazoxanide (in combination with effective cART if HIV+)	Effective cART	
Giardia lamblia	Tinidazole Nitazoxanide	Metronidazole	Tinidazole approved for children ≥3yo
Cyclospora cayetanensis	Tmp-smx	Nitazoxanide (limited data)	
Cystoisospora belli	Tmp-smx	Pyrimethamine	Potential 2nd line alternatives: • Ciprofloxacin • Nitazoxanide
Trichinella spp	Albendazole	Mebendazole	

Adapted from Shane et al., CID. 2017.

Clostridioides difficile

- Most commonly identified cause of healthcare-associated infection in adults in the U.S.
- 2011 Data:
  - ~500k cases of *C. difficile*
  - ~1 in 5 patients experienced at least one recurrence
  - 29k died within 30d of diagnosis

https://www.cdc.gov/hai/organisms/cdiff/cdiff_clinicians.html
https://www.cdc.gov/hai/pdfs/cdiff/CDIff-One-Pager.pdf (Accessed 5/23/18).

C. difficile Case

A 62yo man is diagnosed with his first episode of *C. difficile* infection. He is afebrile and his WBC and creatinine are normal. Which treatment option is the most appropriate?

A. Vancomycin 125mg PO QID plus IV flagyl
B. Metronidazole 500mg PO TID
C. Vancomycin 125mg PO QID
D. Fecal transplant

2018 *C. difficile* Guidelines

- **Initial episode, non-severe**
  - Vancomycin (VAN) 125mg PO QID x 10d **OR**
  - Fidaxomicin (FDX) 200mg BID x 10 days
  - Metronidazole is an alternative if other therapies unavailable or contraindicated
- **Initial episode, severe***
  - VAN 125mg QID x 10d **OR**
  - FDX 200mg BID x 10 days
- **Initial episode, fulminant† (severe, complicated CDI)**
  - VAN 500mg PO QID PLUS
  - IV metronidazole 500mg Q8h
  - Consider rectal VAN if ileus present

*WBC ≥15 or serum creatinine >1.5mg/dL
†Hypotension or shock, ileus, megacolon

McDonald et al., CID. 2018.

Recurrent *C. difficile* Treatment

- **First recurrence**
  - VAN x 10d if metronidazole was used for initial episode
  - Prolonged tapered pulsed VAN if standard regimen used for 1st episode
    - 125mg PO QID x 10-14d -> BID x 7d -> daily x 7d -> Q2-3d x 2-8 weeks
  - FDX x 10d if VAN used for initial episode
- **Second or subsequent recurrence**
  - Tapered pulsed VAN **OR**
  - VAN x 10d followed by rifaximin 400mg TID x 20d **OR**
  - FDX x 10d **OR**
  - Fecal microbiota transplant*

McDonald et al., CID. 2018.

Follow-up

Your patient has now completed his course of oral vancomycin. You should now send a repeat stool sample to confirm that his *C. difficile* infection has been treated successfully, true or false?

A. True
B. False

Stewardship of *C. difficile* Testing

- Submit stool specimens only from patients with unexplained and new onset of ≥3 unformed stools in a 24h period
- Do not perform repeat testing (within 7d) during the same episode of diarrhea
- Do not send repeat testing for test of cure
- Do not test stool from asymptomatic patients
- Do not routinely test in patients ≤2 years of age

McDonald et al., CID. 2018.

C. difficile Testing

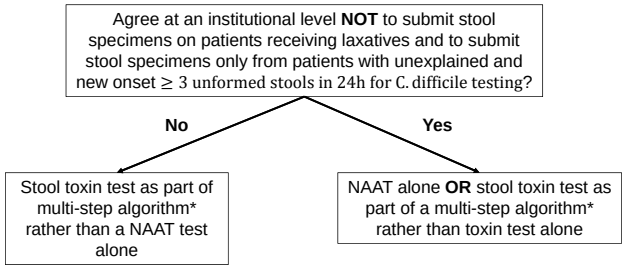
The Brecher Guidelines

Observation	Response
Look at the stool specimen	If it ain't loose, it's of no use
Put a thin lab grade stick in the specimen	If the stick stands, the test is banned
	If the stick falls, test them all [a]

[a] Refers to a single stool specimen.

Brecher, et al. CID. 2013.

C. difficile Testing



*Multi-step algorithm, (GDH plus toxin; GDH plus toxin arbitrated by NAAT; NAAT plus toxin)

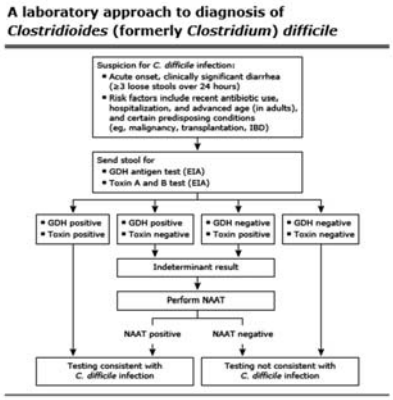
McDonald, et al. CID. 2018.

C. Difficile Testing

Test	Sensitivity	Specificity	Substance Detected
Toxigenic culture	High	Low*	*C. difficile* vegetative cells or spores
Nucleic acid amplification tests	High	Low/moderate	*C. difficile* nucleic acid (toxin genes)
Glutamate dehydrogenase (GDH)	High	Low*	*C. difficile* common antigen
Cell culture cytotoxicity neutralization assay	High	High	Free toxins
Toxin A and B enzyme immunoassays	Low	Moderate	Free toxins

*Must be combined with a toxin test

Adapted from McDonald, et al. CID. 2018.



www.uptodate.com. (Accessed 2/5/19).

Your patient returns…

He now has recurrent diarrhea 6x/day after being treated for a "UTI." In weighing your treatment options, which of the following is correct?

A. Fidaxomicin is more likely to result in resolution of his symptoms at the end of treatment
B. He is less likely to have a subsequent recurrence if treated with fidaxomicin rather than vancomycin
C. He should be treated with fecal microbiota transplantation (FMT) based on clinical guidelines
D. Cholestyramine (an anion-binding resin) should be added to vancomycin to optimize therapy

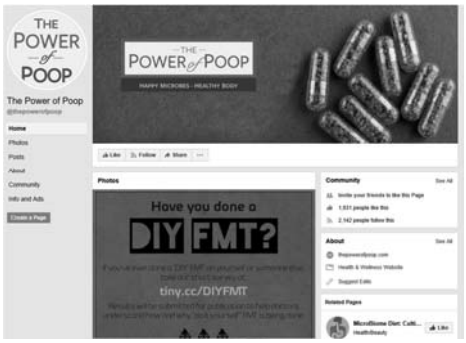
Fidaxomicin vs. Vancomycin

- Sustained clinical response superior for fidaxomicin vs vancomycin
  - Less efficacious response to fidaxomicin is likely in pts with multiple recurrences
- Cost is an important consideration
  - Vancomycin capsules $$$$
  - Compounded IV vancomycin $
  - Fidaxomicin $$$$

McDonald, et al. CID. 2018.

Fecal Microbiota Transplant (FMT)

Current guidelines recommend appropriate antibiotic treatment for at least 2 recurrences (3 CDI episodes) before FMT should be tried.



McDonald, et al. CID. 2018.

Probiotics

- Not recommended in current guidelines
- Moderate quality evidence suggesting a protective effect in preventing *C. difficile* associated diarrhea (CDAD)
  - May be more effective in those with a high baseline risk of CDAD

McDonald, et al. CID. 2018.
Goldenberg, et al. Cochrane Database. 2017.

Traveler's Diarrhea

Traveler's Diarrhea (TD) Case

A 47yo man with a hx of htn, CRI and asthma presents to your office prior to a trip to Mexico. He reports a hx of aspirin allergy but no antibiotic allergies. He asks you for a prescription for an antibiotic to prevent Travelers' Diarrhea (TD) while on vacation. What do you tell him?

A. Recommend that he take cipro as fluoroquinolones have been the most effective antibiotics for the prophylaxis of bacterial TD
B. Recommend that he take bismuth subsalicylate as opposed to an antibiotic to prevent TD
C. Advise him that you do not recommend prophylactic antibiotics for TD
D. Recommend that he use probiotics because of the strong evidence that probiotics are effective in preventing TD

Traveler's Diarrhea Prophylaxis

- TD rates have been shown to be reduced by the use of antibiotics however, prophylactic antibiotics for TD should not be routinely recommended:
  - Increasing antibiotic resistance to commonly used agents
  - Increases the risk of infection with resistant bacteria
  - May limit therapeutic options if TD did develop despite prophylactic antibiotic use
  - Risk of C. difficile infection
  - Potential for allergic or adverse reactions
  - Do not protect against non-bacterial pathogens

https://wwwnc.cdc.gov/travel/yellowbook/2018/the-pre-travel-consultation/travelers-diarrhea

TD Case Continued

You provide him with an antibiotic to use if he does develop TD. He develops diarrhea while on vacation and sends you a message to ask if he should take it. He reports 3-5 episodes of diarrhea per day x 2 days with mild abdominal cramping. He denies fever. He has noted some blood on the toilet paper. He has been able to continue with planned sight-seeing activities.

What do you advise him to do?

A. Take the antibiotic because he is having moderate TD with 3-5 BMs/day
B. Do not take the antibiotic because he has been able to continue his usual activities and has mild TD
C. He should take the antibiotic because he may have dysentery and avoid anti-diarrheal medications
D. Take a short 5d course of antibiotic

TD Definitions

- **Mild (acute)**: diarrhea that is tolerable, is not distressing and does not interfere with planned activities
- **Moderate (acute)**: diarrhea that is distressing or interferes with planned activities
- **Severe (acute)**: diarrhea that is incapacitating or completely prevents planned activities; all **dysentery** is considered severe
- **Dysentery** = passage of stools with gross blood admixed with stool, often accompanied by constitutional symptoms such as fever

https://wwwnc.cdc.gov/travel/yellowbook/2018/the-pre-travel-consultation/travelers-diarrhea

TD Prevention - Vaccines

Pathogen	Vaccination
Typhoid	Oral or injectable vaccine: recommended for travelers going to country that is endemic for typhoid • Administer injectable vaccine at least 2 weeks before travel • Complete 4 doses of oral vaccine (taken 2d apart) at least 10d before travel; contraindicated in immunocompromised patients
Cholera	Vaccination recommended for adults traveling to areas of active cholera transmission • Single dose administered at least 10d before travel Approved for adults 18-64yo. Safety not established in immunocompromised patients.

Something's Fishy

A 24yo woman presents to urgent care with complaint of acute onset nausea/vomiting, watery diarrhea and abdominal cramping x 1 hour. She also c/o tooth pain. She reports eating a meal at a seafood restaurant 2 hours ago. She ate well cooked sea bass at the meal.

Exam: Temp 98.7 P 90 BP 110/70 SpO2 100% RA
Gen: appears uncomfortable but non-toxic
Abd: +BS, soft, nt/nd

What does your patient have?

A. Norovirus
B. Vibrio
C. Ciguatera
D. Hepatitis A
E. Pleisiomonas shigelloides

Clues

- Fish ingestion
  - Especially barracuda, grouper, moray eel, amberjack, sea bass, sturgeon, red snapper, parrot fish
- Rapid onset of symptoms within a few hours -> think toxins
- Heat does not destroy toxins
  - Ciguatera toxin, *S. aureus* enterotoxin, *Bacillus cereus* enterotoxin
- Neurologic symptoms (e.g., tingling sensation, tooth pain, blurred vision)

https://wwwnc.cdc.gov/travel/page/fish-poisoning-ciguatera-scombroid

Summary

- A WIDE variety of pathogens causes gastroenteritis
- Clinical and exposure history gives important clues to diagnosis but signs and symptoms are non-specific
- Use of diagnostic tests is guided by type of syndrome, severity of illness, host immune status and public health considerations
- Judicious use of antibiotics is important to prevent antibiotic resistance and *C. difficile* infection
- New(ish) C. diff guidelines available
- Don't forget about reporting

Thanks!

Exploration and Discussion of POLST Form Completion: Is it as Simple as It Looks?

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Learning Objectives

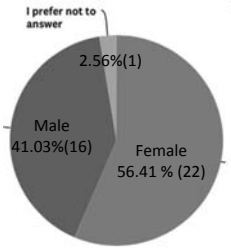
1. Apply the "POLST: Guidance for Oregon's Health Care Professionals" from firsthand knowledge.
2. Predict and recognize confusion and complications that commonly occur in filling out POLST forms and employ advanced problem-solving to remedy them.

POLST Survey

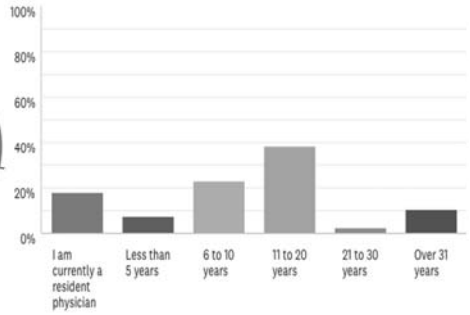
OHSU Family Medicine Providers and Residents

(39 responses)

Gender



How long have you been practicing Medicine?



POLST Survey

1. Overall, POLST forms are a helpful tool during the "goals of care" conversation with my patients and/or their families.

OREGON POLST

Revised December 21, 2018

Guidance for Oregon's Health Care Professionals

What's New in 2019?

Version #13
Effective January 2, 2019

- Changed from a solid pink form to a white form with a pink border.
- Removal of the "Artificially Administered Nutrition" section.
- Under Contact Information, "Heath Care Representative/Surrogate" has been replaced with "Emergency Contact".

POLST: Guidance for Oregon's Health Care Professionals

Introduction

"It is one thing to be able to undertake a medical action, and another thing to know whether or not you should."
Miles J. Edwards, M.D.

MISSION
The Mission of the Oregon POLST Coalition is to improve the quality of life for Oregonians nearing the end of life by providing an evidence-based, patient-centered, voluntary process that elicits, records and honors the treatment goals of those with advanced illness and frailty in a compassionate manner that is respectful of the inherent dignity of the individual.

POLST: Guidance for Oregon's Health Care Professionals

VISION/VALUES

- **The right patient**: The patient will feel empowered
- **The right decision-maker**: The patient's correct legal decision-maker
- **The right time***:* The patient who might die in 1-2 years
- **The right conversation***:* With a trained and experienced health care professional, having a sensitive and meaningful "Goals of Treatment Conversation"
- **The right documentation**: the POLST form → completed→ registered

POLST: Guidance for Oregon's Health Care Professionals

Purpose

- The Oregon POLST® Program is designed to help health care professionals honor the treatment wishes of their patients.
- The POLST form is a **P**ortable* **O**rder for **L**ife-**S**ustaining **T**reatment for people with advanced illness, or who are old and frail ,and may or may not want all possible treatment.

**In April 2018, the Oregon POLST Coalition approved the change of the "P" in POLST from 'physician' to 'portable'.*

POLST: Guidance for Oregon's Health Care Professionals

Purpose

- Promote a **patient's autonomy**, reflecting the patient's **current** treatment preferences.
- Facilitate appropriate treatment in an **emergency.**
- Assist parents of minor children as well as guardians of seriously ill minors and protected persons, to express their wishes and intentions for treatment.
- Be compliant with HIPAA in the transfer of patient records between health care professionals and health care settings.

POLST: Guidance for Oregon's Health Care Professionals

Purpose

- Transforms a patient's treatment plan and goals of care into a "**Medical Order"**

The current standard of care in the United States requires that emergency personnel, in the absence of a medical order, make every attempt to save a person's life.

A POLST form is a medical order that can be used when a patient wishes to AVOID some of these treatments. The POLST form alerts medical personnel about the patient's treatment preferences.

- When a patient is transferred, the POLST Form **should always be sent with the patient.**
- The POLST Form is **always voluntary.**

POLST: Guidance for Oregon's Health Care Professionals

Purpose

Who Should Have a POLST Form?

- Patients with advanced illness or frailty where accurate predictions cannot be made but death is likely in the foreseeable future.
- If the answer is "Yes" to any of these questions; the patient may have a condition that warrants the completion of a POLST form:
  - ❖Does the patient have a disease process (not just their stable disability) that is in an advanced stage?
  - ❖Is the patient experiencing a significant decline in health (such as frequent aspiration pneumonias)?
  - ❖Is the patient in a palliative care or hospice program?
  - ❖Has this patient's level of functioning become more severely impaired as a result of a deteriorating health condition for which intervention will not significantly impact the process of decline?

POLST: Guidance for Oregon's Health Care Professionals

Purpose

Who Should NOT have a POLST Form?

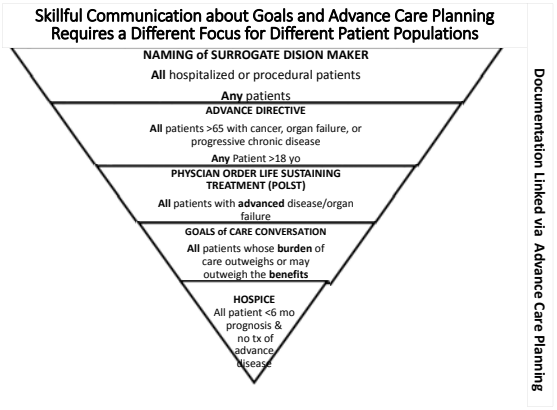
- Patients with stable medical or functionally disabling problems who have many years of life expectancy.
- **Reduce the overuse of POLST in those who are "too healthy."**
  - ❖**Unneeded** for every patient being discharged to a facility.
  - ❖**Should NOT** be completed for healthy patients at Medicare wellness visits.
  - ❖**Inappropriate** for healthy individuals who would want everything done in an emergency.

POLST Survey

2. POLST forms have No meaning if patients and/or their authorized surrogates request "Attempt Resuscitation/CPR" and "Full Treatment" be attempted.

Key Differences Between Oregon's AD and POLST

Advance Directive A **Voluntary** Legal Document	**POLST** A **Voluntary** Medical Order
For all adults regardless of health status at any age, starting at age 18	For those with advanced illness, or frailty, or a limited prognosis at any age, depending on health status
1) Appoints a legal decision-maker 2) Memorializes values and preferences 3) Is signed by the patient	Is a specific medical order and is signed by a Health Care Professional.
Provides for theoretical situations in which a person may not have capacity for decision making. Guidelines for imagined future situations which may arise and for which a person may have preferences for a particular kind of care plan.	Provides for likely events that can be foreseen. Specific medical orders addressing defined medical interventions for situations that are likely to arise given the patient's health status and prognosis.



From OHSU Care Wisely

Pros and Cons of Completing POLST for Patients/SDMs Request "Attempt Resuscitation/CPR" and "Full Treatment" be attempt

Let's discuss our thoughts!

Pros	Cons
Provides an opportunity to discuss medical facts and realities that run contrary to patients' wishes.	Patients/SDMs may feel pressured by the care team.
May empower patient/SDM as to their wishes.	Time-consuming despite the same outcome?!

POLST Survey

3. I have seen patients whose POLST forms were not honored when they sought care at the hospital.

Dealing with POLST Form Disputes

- Follow your organization's policies regarding surrogate decision-making.
  - Does the patient have a AD ?
  - Is the Health Care Representative allowed to change life-support wishes on the AD?
- Some organizations offer ethics consults. Some disputes may require legal advice.

What can we do to prevent this???

- Make sure to have an appropriately qualified SDM who is aware of the patients wishes.
- For CMO orders, have a clear care plan (e.g. Hospice).

Section by Section Review of the POLST Form

CPR on 92 yo Metastatic Malignancy Male

Tracy A. Brader, a third-year resident in Emergency Medicine at Christiana Care in Newark, Delaware, published this painting in the AMA Journal of Ethics. [2018;20(8):E774-775]

POLST Survey

4. Patient's and/or their authorized surrogates' requests to "Attempt Resuscitation/CPR" should always be honored.

POLST Survey

5. Attempted Resuscitation/CPR should only be offered to medically-indicated patients.

Section A: Cardiopulmonary Resuscitation (CPR)

Apply only when the patient is unresponsive, pulseless and not breathing *(Dead!)*

- If the patient **wants** cardiopulmonary resuscitation (CPR) **AND** CPR is ordered, then the "Attempt Resuscitation/CPR" box is checked. Full CPR measures should be carried out and 911 should be called.
- If a patient has indicated that he/she does not want CPR in the event of no pulse or breathing, then the "Do Not Attempt Resuscitation/DNR" box is checked.

Section B:
Medical Interventions

Apply to patients with a pulse and breathing *(Alive!!)*

Comfort Measures Only

- Goals are to **maximize comfort** AND **avoid hospitalization** (unless necessary to ensure meeting comfort needs)
- Consider a palliative care or hospice care referral then **make a treatment plan.**

Limited Treatment

- Desires being hospitalized if needed, **avoid mechanical ventilation** and generally **avoid ICU care**.

Full Treatment

- Desires all life-sustaining treatment: intubation, mechanical ventilation, intensive care (as indicated) with no limits to treatment.

Section B:
Medical Interventions

Additional Orders

- Additional clarifying orders to the patient's preferences can be written under.

  Examples;
  - "Patient wishes to continue blood transfusions if appropriate"
  - "Intubation for 1-2 weeks."
  - "No tracheostomy"
  - "No Feeding Tube"

- What about Dialysis?

POLST Survey

6. On the POLST form, combining "Attempt Resuscitation/CPR" and "Limited Treatment (no intubation)" is a valid option.

Additional Considerations for the Discussion Needed to Complete Section B

- *While the Oregon POLST Registry currently accepts POLST Forms with Section A designating CPR and Section B Limited Treatment, it is controversial at the national level as it is medically problematic. Patients or their surrogate should be aware that for those who survive, intubation and ventilation are standard parts of resuscitation.*

Appropriate Section A and B Combinations in Oregon

Section A / Section B	Comfort Measures Only	Limited Treatment	Full Treatment
CPR	**X**	○	○
DNR	○	○	○

Quotes from the Literature

…Oregon considers the possible, but unlikely, circumstance in which rapid defibrillation results in a prompt return of spontaneous circulation in which intubation and mechanical ventilation are unnecessary; and a number of hospice/ palliative medicine providers prefer to retain the usually physiologically incompatible option as part of a multistep process that a significant number of patients take in their process (as the next to the last POLST form) in moving to a POLST with DNR orders.

A. Moss MD, D. Zive MPH et al;The Quality of POLST Completion to Guide Treatment : A 2-State Study: http://dx.doi.org/10.1016/j.jamda.2017.05.015

…Currently, some states, such as Oregon, accept this combination in their Registry and other states, such as West Virginia and California, do not.

T. Schimidt, D Zive S Tolle et al; Physician Orders for Life-Sustaining Treatment (POLST): Lessons learned form analysis of the Oregon POLST Registry: http://dx.doi.org/10.1016/j.resuscitation.2013.11.027

What are the Cons?

Let's discuss our thoughts!

- It can provide more confusion since not all providers agree upon the treatment.
- May promote "Slow CPR".
- May mislead patients and SDMs regarding treatment.

POLST Form
Ethical Dilemmas and Questions

Let's discuss our thoughts!

- Should I sign a POLST form with which I do not agree, regarding the Care Plan?
- What about my ***autonomy as a clinician?***
- Should we renew the POLST, especially one with a CMO and which has not signed for years?
- What about healthy adults who want to be DNR?

Summary

- Most clinicians believe POLST forms are helpful tools for the Goals of Care conversation and for clarifying patients' preferences for EOL care.
- A POLST form is a medical order; to be a meaningful order, each health care professional and clinician should complete the POLST form carefully and accurately, reflecting patients' preferences.

  → *With the right patients and at the right time*
- It's all about getting the right SDM!
- Consider having clear care plans (e.g. Hospice) when choosing a CMO, so it is likely the plan can be followed without requiring hospitalizations.
- POLST Forms (Medicine in US in general) appear to prioritize patient autonomy, but ideal decision-making should include provider input as well.
- The "CPR with limited treatment" combination is confusing, medically problematic, and *I believe,* will add more confusion. Simplification orders is preferred in EOL care where sending a consistent message from each provider is crucial.

Any thoughts and questions ? onishi@ohsu.edu

Integrative Medicine Approaches for Chronic Pain

Sonia Sosa, MD
Assistant Professor, Department of Family Medicine
American Board of Integrative Health and Medicine Diplomate
OHSU

Disclosures

- I have nothing to disclose

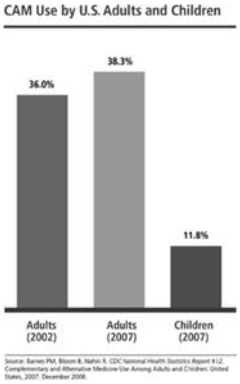
Objectives

- Define Integrative Medicine and explain its relevance in an allopathic medical practice.
- Discuss the origins of chronic pain and the impact of trauma on perception of pain.
- Recognize the magnitude of the opioid epidemic.
- Review non-allopathic methods for the management of chronic pain with a focus on fibromyalgia, osteoarthritis, back pain and neuropathic pain.

Definitions

- **Allopathic medicine:** "western medicine", "conventional medicine"
- **Alternative medicine:** any of various systems of healing or treating disease (as homeopathy, chiropractic, naturopathy, Ayurveda, or faith healing) that are not included in the traditional curricula taught in medical schools of the United States and Britain; used **instead of** conventional medicine
- **Complementary medicine:** generally refers to using a non-mainstream approach **together with** *conventional medicine*.

Who uses Integrative Medicine?



Why?

- In a survey of over 30,000 Americans it was revealed that people most often use CAM because:
  - They **believed that it would help** them when combined with conventional medical treatments.
  - They thought CAM would be interesting to try.
  - A **conventional medical professional suggested they try CAM**.
  - They felt that conventional medicine was too expensive.
- **Patients who have chronic conditions that are difficult to treat effectively may be more likely to pursue CAM methods:** irritable bowel syndrome (IBS), rheumatoid arthritis, autism spectrum disorder, attention deficit hyperactivity disorder (ADHD), fibromyalgia, chronic fatigue, and cancer. In one study, published in the *Journal of Alternative and Complementary Medicine*, cancer patients who received a poor prognosis reported using CAM more often than the better prognosis group. Other studies show that cancer patients experience positive changes and increased spiritual importance as a result of CAM.

Integrative Medicine Modalities

- Natural products: herbal, vitamins, minerals and other natural products
- Mind body medicine: deep breathing, meditation, yoga, acupuncture, guided imagery, tai chi, hypnotism, progressive relaxation, qi gong
- Manipulative and body based practices: massage, manipulation
- Energy medicine: Reiki, healing touch, qi gong
- Chinese medicine
- Ayurvedic medicine
- Functional medicine
- Homeopathy
- Naturopathy
- Traditional healers
- Environmental medicine
- Group Visits

Why practice Integrative Medicine?

Because it's just good medicine.

WHAT ARE THE ORIGINS OF CHRONIC PAIN?

- Chronic Pain: prolonged and persistent pain of at least 3 months in duration
- 2011 report showed > 1.5 billion people worldwide suffer from chronic pain,
- ~ 3-4.5% of the global population suffers from neuropathic pain.
- IOM Report 2011: Costs society at least $560-$635 billion annually, including lost productivity / wages

- 2011, Institute of Medicine Report from the Committee on Advancing Pain Research, Care, and Education: *Relieving Pain in America, A Blueprint for Transforming Prevention, Care, Education and Research*.
- RJ Gatchel et al. The Biopsychosocial Approach to Chronic Pain: Scientific advances and future directions. Psychological Bulletin, Vol 133 (4), Jul 2007, 581-624.

- Multiple systems involved: nervous, musculoskeletal, immune, endocrine, inflammatory
- Many triggers: genetics, environmental, illness, surgery, degenerative changes
- Trauma History- high ACE score is a risk factor for chronic pain such as back pain and even a risk factor for more pain in pregnancy

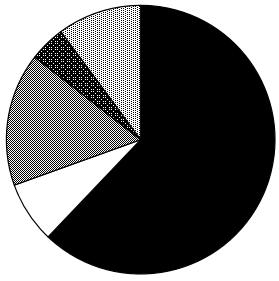
- Drevin J et al. Adverse childhood experiences influence development of pain during pregnancy. Acta Obstet Gynecol Scand. 2015 Aug; 94 (8): 840-846.

- Pain can be a necessary, protective response.
- Chronic pain however is a maladaptive response.
- While the original response to stimuli may have been protective, the prolonged response becomes harmful.

Symptoms of chronic pain

- Physical Stress
- Interrupted sleep
- Poor wound healing
- Decreased immunity
- Depression
- Isolation
- Self-medication
- Spiritual
- Reminder of mortality
- At times perceived as a punishment or evidence of moral wrongdoing
- Causes feelings of powerlessness, hopelessness

Incidence of Chronic Illness



American Academy of Pain Medicine: Facts and Figures on Pain, http://www.painmed.org/patientcenter/facts_on_pain.aspx#incidence

The New England Journal of Medicine

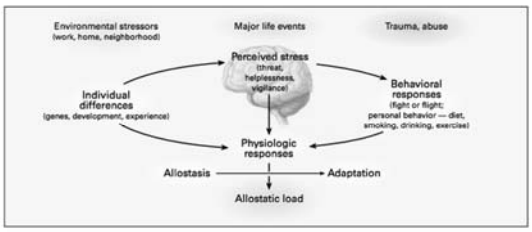


Figure 1. The Stress Response and Development of Allostatic Load.
The perception of stress is influenced by one's experiences, genetics, and behavior. When the brain perceives an experience as stressful, physiologic and behavioral responses are initiated, leading to allostasis and adaptation. Over time, allostatic load can accumulate, and the overexposure to mediators of neural, endocrine, and immune stress can have adverse effects on various organ systems, leading to disease.

From The NEJM, Bruce S. McEwan, PhD. Protective and Damaging Effects of Stress Mediators, 338:171-179. Copyright © 1998 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society

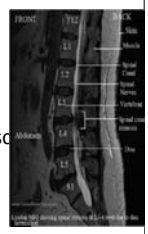
Allostatic Load = Stress or Wear and Tear on the Body

Lorimer Moseley- Why Things Hurt

VS

https://www.youtube.com/watch?v=gwd-wLdIHjs

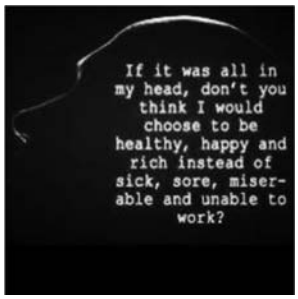
What about that abnormal MRI?



- Forty-six asymptomatic individuals who had a high rate of disc herniations (73%) were observed for an average of 5 years
  - Low back pain was predicted by (P < 0.001): listlessness, job satisfaction and working in shifts
  - **NOT** by abnormal discs
  - Boos et al. Spine. 25(12):1484-1492, June 15, 2000.
- Review of 33 articles including 3000 asymptomatic patients
  - Degenerative disc disease is identified in 37% of 20 year olds and increases to 96% of 80 year olds; disc bulge seen in 30% of 20 year olds and 84% of 80 year olds
  - Brinjikji W, Luetmer PH, Comstock B, et al. Systematic literature review of imaging features of spinal degeneration in asymptomatic populations. *AJNR Am J Neuroradiol*. 2014;36(4):811-6.

So what you're telling me is that you think this is all in my head?
You think that I'm making this up?

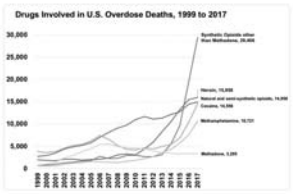
- Why would I choose to:
  - Lose my job
  - Lose my friends
  - Be stuck in bed all day
  - Not be able to play with my grandkids
  - Undergo painful procedures
  - Not be able to do the things I love
  - Be judged
  - ???

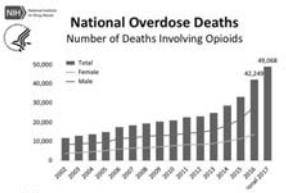


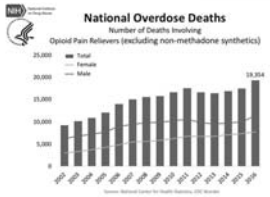
- Survey:
- 50% of CNP patients had inadequate pain relief
- 50% " considered suicide due to feelings of hopelessness associated with their pain"
  - J Pain Symptom Manage. 1994 Jul;9(5):312-8
- Severe pain increases risk of suicide in vets Suicide Life Threat Behav. 2010 Dec;40(6):597-608, Journal of Pain April 2017Volume 18, Issue 4, Supplement, Page S62
- Individuals with physical pain were more likely to report:
  - Lifetime death wish (p = 0.0005)
  - Current and lifetime
    - Suicidal Ideation (both p < 0.00001)
    - Suicide Plan (current: p = 0.0008; lifetime: p < 0.00001
    - Suicide Attempt (current: p < 0.0001; lifetime: p < 0.00001
    - Suicide Deaths (p = 0.02).
    - Journal of Psychiatric Research December 2015 Volume 71, Pages 16–32 The impact of physical pain on suicidal thoughts and behaviors: Meta-analyses Rafaella Calati et al

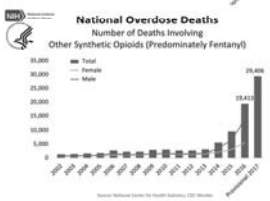
Conventional Treatment of Chronic Pain

- Acetaminophen, ibuprofen, gabapentin, cymbalta…none of these medications are without side effects or 100% effective.
- Injections:
  - Cochrane Review from 2008: There is **insufficient evidence** to support the use of injection therapy in subacute and chronic low-back pain. However, it cannot be ruled out that specific subgroups of patients may respond to a specific type of injection therapy. Staal JB, de Bie R, de Vet HCW, Hildebrandt J, Nelemans P. Injection Therapy for subacute and chronic low back pain. Cochrane. 6 July 2008. http://www.cochrane.org/CD001824/BACK_injection-therapy-for-subacute-and-chronic-low-back-pain
  - Some evidence that they **may be helpful for short term pain relief**. PM R. 2009 Jul;1(7):657-68.









Risks of chronic opiate use

- Opioid-induced hyperalgesia documented in animals and humans
  - A number of case reports document decreases in pain with stopping opioids
  - Mechanism may be NMDA receptor-mediated central sensitization
- Opioid-related Endocrinopathy
  - Up to 90% of patients treated with opioids!
  - More pronounced in doses > 100 mg morphine per day
  - Symptoms: fatigue, irregular menses, hot flashes, reduced libido, low testosterone, night sweats
    The American Journal of Medicine Volume 126, Issue 3, Supplement 1, March 2013, P S12–S18
- Respiratory depression, constipation, sedation, nausea…

Additional risks

- Preoperative opioid use was determined to be a negative predictor of return to work rates after lumbar discectomy in worker's comp patients.
- Long-term preoperative opioid use was associated with higher medical costs, psychiatric illness and postoperative opioid use. Even a short, or moderate course of preoperative opioids was associated with worse outcomes compared to no use.
- O'Donnell JA et al. Preoperative Opioid Use is a Predictor of Poor Return to Work in Worker's Compensation Patients after Lumbar Diskectomy. Spine (Philla Pa 1976). 2017 Aug 23

SO, HOW CAN WE USE INTEGRATIVE MEDICINE FOR CHRONIC PAIN?

Tack rules

- If you are sitting on a tack it takes a lot of _____ to make the pain go away. (acetaminophen, ibuprofen, oxycodone, turmeric)
  - The proper treatment for tack-sitting is tack removal.
- If you are sitting on two tacks taking one away does not reduce the pain by 50%.
- If morphine makes the pain of the tack go away, you may stop trying to remove the tack

True Treatment of Chronic Pain

- Accurate diagnosis is important: Do not rush to control symptoms and ignore the message about an underlying health problem
- Remove tacks where possible, i.e. treat underlying causes
  - Surgical treatment
  - Physical therapies- chiropractic, osteopathic manipulation, massage, physical therapy
  - Specific medical treatment for neuropathy, systemic inflammation- dietary causes
  - Sleep, nutritional influences on tissue healing
  - Hypothyroidism
  - Counseling/Mind body - History of trauma
- Utilize benefits of neuroplasticity in order to "rewire" pain channels

Manual therapy (MT)

- Combining different forms of MT with exercise is better than MT or exercise alone
  - Hidalgo B, Detrembleur C, Hall T, Mahaudens P, Nielens H. The efficacy of manual therapy and exercise for different stages of non-specific low back pain: an update of systematic reviews. *J Man Manip Ther*. 2014;22(2):59-74.
- Mobilization does not need to be applied to the symptomatic level(s) for improvements of neck pain patients (helps with risk reduction of some higher risk manipulation techniques)
  - Hidalgo B et al. The efficacy of manual therapy and exercise for treating non-specific neck pain: A systematic review. J Back Musculoskelet Rehabil. 2017 Aug 2. doi: 10.3233/BMR-169615
- A systematic review and meta-analysis concluded that early evidence shows that manual therapy might be effective for relieving pain, stiffness and dysfunction in osteoarthritis of the knees
  - Xu et al. The effectiveness of manual therapy for relieving pain, stiffness and dysfunction in knee osteoarthritis. Pain Physician. 2017 May; 20 (4): 229-243

Acupuncture

- Acupuncture is one of the most widely used IM modalities for pain management
- Growing fast - in 2002 the NIH showed that an estimated 8.2 million adults had used acupuncture from just 2.1 million the year before.
- Research is still somewhat limited but body of evidence is growing:
  - Moderate evidence that **acupuncture was more effective than sham-acupuncture** in reducing pain immediately post-treatment for CNP, CLB, ALBP
    - 2015: Yuan, QL et al. **TCM for neck pain and LBP: a systematic review & meta-analysis.** 75 RCTs, 11,077 patients
  - 16 Systematic reviews of variable quality (much of it low) showed that acupuncture, either used in isolation or as an adjunct to conventional therapy, **provides short-term improvements in pain and function for chronic LBP.**
    - Liu L, Skinner M, McDonough S, Mabire L, Baxter GD. Acupuncture for Low Back Pain: An overview of systematic views. Evid Based Complement Alternat Med. 2015; 2015: 328196.

Acupuncture

- **Joint Commission** recommends acupuncture as a treatment option for pain management; **American Pain Society** & **American College of Physicians** agree acupuncture is an option for low back pain.
- Based on NIH studies: In 2012, most (60 percent) of the respondents who had chiropractic care had at least some insurance coverage for it, but those rates were much lower for acupuncture (25 percent) and massage (15 percent). Rates of coverage for all three increased from 2002 to 2012.
- More Medicaid plans (including Oregon's) are covering acupuncture

Systemic Inflammation

- Acute increases in C-reactive protein (CRP), IFN-gamma, IL-1, IL-6, and TNF-alpha can become chronic; not always measurable with standard labs
- Systemic inflammation is increased by stress, genetics, lack of exercise We know that it is tied to increases in auto-immune conditions, heart conditions, cancer and Alzheimer's
- It is also a cause of chronic pain: Systemic inflammation results in lowering the pain threshold
  - De Goeij M et al. Systemic Inflammation Decreases Pain Threshold in Humans in Vivo. PLoS One. 2013; 8(12): e84159
  - Wegner A et al. Inflammation-induced hyperalgesia: effects of timing, dosage, and negative affect on somatic pain sensitivity in human experimental endotoxemia. Brain Behav Immun. 2014 Oct. 41; 46-54

Nutrition

- Anti-inflammatory diet: do we have any evidence?
  - Still limited and contradictory
  - Some research states that some foods are pro-inflammatory- among these foods high in saturated fats, added sugars, preservatives and refined carbohydrates
  - Foods shown to decrease inflammation are foods rich in omega-3 fatty acids and antioxidant rich foods
  - Nutrition and Pain. Mayo Clinic. https://www.mayoclinic.org/nutrition-and-pain/art-20208838?p=1
- 2016 study published in the Scandinavian Journal of Pain showed that patients with fibromyalgia who eat a FODMAP diet had a reduction in pain and improved daily life based on pre and post symptom analysis
  - Marum AP et al. A low fermentable oligo-di-mono saccharide and polyols (FODMAP) diet reduced pain and improved daily life in fibromyalgia patients. Scand J Pain. 2016 Oct; 13:166-172.
- Chronic pain and obesity are correlated although the nature of the relationship may not be linear.
  - Weight loss leads to reduction in chronic pain
  - Okifuji A and Hare BD. The association between chronic pain and obesity. J Pain Res. 2015; 8:399-408

https://www.drweil.com/diet-nutrition/anti-inflammatory-diet-pyramid/what-is-dr-weils-anti-inflammatory-food-pyramid/

Turmeric

- Deep yellow root
- Active constituent is curcuminoids
- Anti-inflammatory: COX2 inhibitor; use in place of NSAIDs
- Anti-arthritic: NK-kB activation
- Uses: evidence for OA and HLD; insufficient for: IBD, RA, SLE, lichen planus, gingivitis, joint pain
- Can cause GI irritation
- Dose: 1000mg twice daily=1 tsp twice daily; take with black pepper and fat for better absorption
- Natural Medicine Comprehensive Database

Food Sensitivities

- Remember the tacks
- Gold Standard is the Elimination diet (not IgG, IgE or muscle strength testing)
- Reasons to consider: chronic pain, fibromyalgia, IBS, chronic headaches, GERD, eosinophilic esophagitis
- Go to the basics: lamb or chicken, apple or pear, rice; expand from there after two weeks
- Recommend advanced planning
- University of Wisconsin: Department of Family Medicine, Elimination Diet
- http://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/handout_elimination_diet_patient.pdf

Sleep

- Pain severity was related to fewer hours slept and delayed sleep onset.
  - J Pain Symptom Manage. 1991 Feb;6(2):65-72.
- Low levels of somatomedin C (IGF-1) in patients with the fibromyalgia syndrome
  - Arthritis Rheum. 1992 Oct;35(10):1113-6.
- 55.4% of patients with OSA have chronic widespread pain
  - J Phys Ther Sci. 2015 Sep;27(9):2951-4. doi: 10.1589/jpts.27.2951
- Sleep deprivation lowers the pain threshold

Treatment of sleep disorders

- **Look for sleep apnea-** especially with patients on chronic opiates
- Opioids exacerbate sleep-disordered breathing.
  - Chest. 2016 Jun 1. pii: S0012- 3692(16)49109-9
- Work on sleep hygiene- watch for daytime sleeping
  - Consider low dose melatonin to help reset sleep cycle: start with 0.3mg 3 hours prior to sleep as opposed to the much more common doses of 3-5mg
  - Light box: 10,000 lux for 30 min every morning
- Herbs for sleep: chamomile, **passionflower**, hops, **lemon balm,** valerian
- Treat restless legs with magnesium: titrate to BM except in patients with kidney disease

Mind-body

- Mitigate symptoms
- Improve resilience
- Improve feelings of patient self-efficacy and self-esteem
- Provide insight, understanding, acceptance, forgiveness
- Increase compassion
- Work through emotional trauma

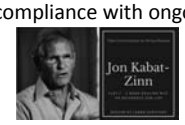
Yoga

- **2016**: Chang et al, Journal of Orthopedics & Rheumatology. **Yoga as a treatment for chronic low back pain: A systematic review of the literature.** Lit search beg. 2015, Pub Med for RCTs - 27 articles
  - Yoga can **reduce pain & disability**, be practiced safely, well received by participants.
  - Some studies indicate yoga may improve psych symptoms, but these effects aren't as well established.
- **2013:** Holtzman et al, Pain Research and Management. **Yoga for chronic low back pain: A meta-analysis of randomized controlled trials.** 8 RCTs, 743 patients
  - Yoga may be an efficacious adjunctive treatment for chronic LBP
  - Recommends more RCTs to include active control groups to determine whether yoga has a) specific treatment effects & b) whether yoga offers any advantages over traditional exercise programs / other alternative treatments

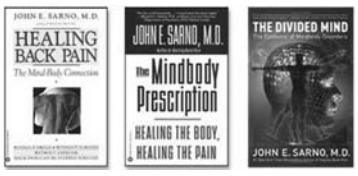
- **2013:** Cramer et al in The Clinical Journal of Pain. **A systematic review and meta-analysis of yoga for low back pain**. 10 RCTs, 967 patients
  - **Strong evidence** for short-term effects on pain, back-specific disability, global improvement & long-term effect on pain.
  - **Moderate evidence** for long-term effect on back–specific disability.
  - No evidence for either short or long term effects on health-related QOL.
  - Yoga can be recommended as an additional, safe therapy to chronic low back pain patients.

Meditation

- Kabat-Zinn, J., L. Lipworth & R. Burney: **The clinical use of mindfulness meditation for the self-regulation of chronic pain.** Journal of Behavioral Medicine. 8: 163– 190. Controlled study.
  - 90 chronic pain patients were trained in mindfulness-based meditation practice.
  - The treatment group decreased pain-related drug use, and activity levels and feelings of self-esteem increased.
- Most improvements were maintained at the 15-month follow-up, and showed a high level of compliance with ongoing meditation practice.



John Sarno



Mindbody Prescription

- Symptoms arise when there is too much rage and not enough counterbalancing soothing elements; the **purpose of pain is to distract from "dangerous feelings**" such as rage, hurt and sadness
- Encourage patients to **write about possible factors contributing to pain-** childhood trauma, current stressors, feelings of inferiority
- Encourage daily writing, repetition is important
- Evidence shows that patients that used more and not less negative words actually had more benefit
- Many patients will need assistance with this process (therapy)

4/7/8

A few specific conditions…

Headaches

- Butterbur: specifically for migraine prophylaxis
  - one study showed reduction in frequency by 48%
  - make sure that it is a pyrrolizidine-free extract
  - Dose: 75-100mg BID, no evidence of use beyond 3 months of ongoing use
  - Grossmann WM, Schmidramsl H. An extract of Petasites hybridus is effective in the prophylaxis of migraine. Int J Clin Pharmacol Ther 2000; 38:430-5.
- Feverfew: reduces frequency of migraines, reduces associated symptoms of pain, nausea, vomiting and light/sound sensitivity
  - Frequently used but studies are mixed
  - Do not use in those with ragweed allergy
  - Does: 50-100 mg daily
  - Wider B, Pittler MH, Ernst E. Feverfew for preventing migraine. Cochrane Database Syst Rev. 2015 Apr 20; 4.

Headaches, cont

- Magnesium: used for migraines and cluster headaches, possibly effective- many studies are in children
  - Appears to be more beneficial in those with hypomagnesemia (long term PPI)
  - Dose: appears to be most helpful at doses around 600mg but these doses can cause diarrhea in some
  - Wang F, Van Den Eeden SK, Ackerson LM, et al. Oral magnesium oxide prophylaxis of frequent migrainous headache in children: a randomized, double-blind, placebo-controlled trial. Headache 2003; 43: 601-10.
- Peppermint oil: may be effective for relieving tension-type headaches when used topically
  - Gobel H, Schmidt G, Soyka D. Effect of peppermint and eucalyptus oil preparations on neurophysiological and experimental algesimetric headache parameters. Cephalalgia 1994; 14:228-34; discussion 182.

Low Back Pain

- 2007 Recommendations from American Pain Society, American College of Physicians which was based on research conducted at OHSU by Roger Chou includes the following:
- Three categories of low-back pain: nonspecific low-back pain, back pain potentially associated with radiculopathy (nerve disorders) or spinal stenosis (narrowing), or back pain associated with another specific cause. **Include assessment of psychosocial risk factors to predict risk for chronic disabling back pain.**
- **Do not routinely obtain imaging** or other diagnostic tests in patients with non-specific low-back pain.
- Obtain diagnostic imaging when severe or progressive neurologic deficits are present
- Evaluate patients with persistent low-back pain with **MRI only** if they are potential candidates for **surgery or epidural steroid injection**.
- Advise patients to **remain active**, and provide information about effective self-care options.
- Use medications with proven benefits in conjunction with back care information and self care. Assess the severity of baseline pain and functional deficits, potential benefits, risks, and relative lack of long-term efficacy and safety data before initiating therapy.
- If no improvements with self-care options, consider non-pharmacologic therapy with proven benefits for low-back pain: **spinal manipulation for acute low-back pain**; and for chronic or sub-acute low-back pain options include: **intensive interdisciplinary rehabilitation, exercise therapy, acupuncture, massage therapy, spinal manipulation, yoga, cognitive-behavioral therapy, or progressive relaxation.**

Fibromyalgia

- Improve sleep: lemon balm, passionflower, hops, chamomile, motherwort and melatonin are all possibly effective and are low risk for harm; valerian has a similar level of evidence but can cause sedation in some
- Decrease "fibro fog":
  - Rhodiola: an adaptogen that has limited evidence for treatment of depression, anxiety and fatigue; low risk for harm (can increase hypoglycemic and hypotensive effects of some medications)
  - Ashwaganda: possibly effective for reduction in stress, anxiety and depression
  - Ginseng: several different types; in order of stimulating effects: siberian ginseng, american ginseng, panax ginseng; insufficient data- systematic reviews have been very challenging because so many different types are used

Natural Medicine Comprehensive Database: Treatment of Fibromyalgia

Low Dose Naltrexone

- **Low-dose naltrexone for the treatment of fibromyalgia: findings of a small, randomized, double-blind, placebo-controlled, counterbalanced, crossover trial assessing daily pain levels.**
- Conclusions: The preliminary evidence continues to show that low-dose naltrexone has a specific and clinically beneficial impact on fibromyalgia pain. The medication is widely available, inexpensive, safe, and well-tolerated. Parallel-group randomized controlled trials are needed to fully determine the efficacy of the medication.
  - Younger J. Arthritis Rheum. 2013 Feb;65(2):529-38. doi: 10.1002/art.37734
- Inexpensive may be a stretch: ~$75/mon at compounding pharmacies in Portland however it is easy to "compound" at home

Osteoarthritis

- Glucosamine sulfate (not hydrochloride): may work by increasing the production of mucopolysaccharides, increasing synovial fluid, repairing eroded tissue and stimulating new cartilage synthesis; reduces pain scores from 28-41% and improves function by 21-46%
  - Poolsup N, Suthisisang C, Channark P, Kittikulsuth W. Glucosamine long-term treatment and the progression of knee osteoarthritis. Ann Pharmacother 2005; 39:1080-7.
- SAMe: more effective than placebo and as effective as NSAIDs for improving symptoms of OA; low risk
  - Many options are poor quality (recommend the butanedisulfonate salt form)
  - $$$

Neuropathic pain

- Alpha-lipoic acid:
  - Evidence for diabetic neuropathy and fibromyalgia
  - Dose: The starting dose is 300 mg at night, then twice daily (BID). The target dose is 300 or 600 mg BID. The onset of pain relief is slow, over the course of a few weeks.
  - Ziegler D. et al. Diabetes Care. 29(11):2365-70, 2006 Nov.
- Acetyl L-carnitine
  - Evidence of efficacy in relieving painful diabetic neuropathy, HIV associated neuropathy, and chemotherapy induced neuropathy.
  - Dose: The oral acetyl L-carnitine dose is 500 to 1,000 mg three to four times a day.
  - Sima AA. et al. Diabetes Care. 28(1):89-94, 2005 Jan; Youle M, CNS Drugs. 21 Suppl 1:25-30; discussion 45-6, 2007; Flatters SJ.et al.Neuroscience Letters. 397(3):219-23, 2006 Apr 24.)

Additional Books

- The Brain's Way of Healing: Remarkable Discoveries and Recoveries from the Frontiers of Neuroplasticity by Norman Doidge, MD
- Unlearn Your Pain by Howard Schubiner, MD
- Joint Hypermobility Handbook by Brad Tinkle, MD
- Managing Your Pain Before it Manages You by Margaret Caudill, MD, PhD, MPH

Questions?

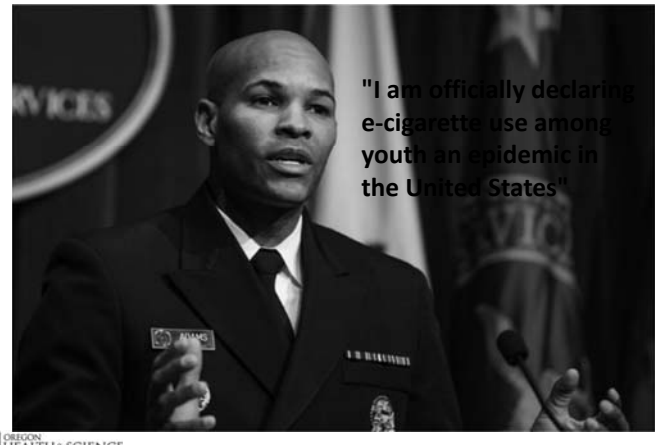
Clearing Away the Smoke and Mirrors: Harmful Effects of E-Cigarettes on Youth

Holger Link, MD

Disclosures and Conflict of Interest

None

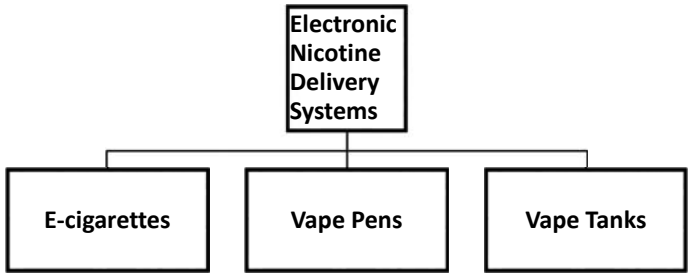
Surgeon General Dr. Jerome Adams on 12-18-2018



Objectives

- Describe state and national data on the trends in E-cigarettes use in youth
- Describe the cycle of nicotine addiction and its effects on the developing brain
- Review evidence that links teenage use of E-cigarettes and smoking as adults
- Review national and state efforts to reduce exposure of youth to electronic cigarettes

* ENDS: Electronic Nicotine Delivery Systems

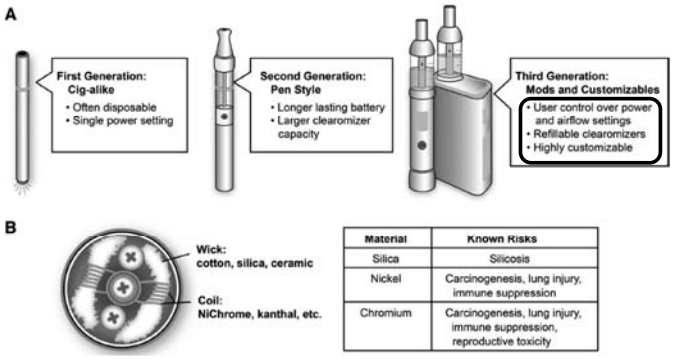


Anatomy of E-Cigarettes

Am J Health-Syst Pharm—Vol 66 Oct 1, 2009

Holger Link, MD ©

Evolution of E-Cigarettes



Material	Known Risks
Silica	Silicosis
Nickel	Carcinogenesis, lung injury, immune suppression
Chromium	Carcinogenesis, lung injury, immune suppression, reproductive toxicity

Am J Physiol Lung Cell Mol Physiol 313: L193–L206, 2017

Holger Link, MD ©

U.S. Department of Health and Human Services. *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*

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Juul

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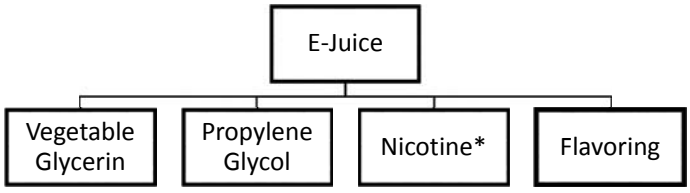
Composition of E-Juice



* Nicotine derived from tobacco plants

Holger Link, MD ©

Vegetable Glycerin and Propylene Glycol

Holger Link, MD ©

Flavoring

- > 7,500 flavors
- No studies on long term effects on lung health
- Note of caution:
  - Diacetyl in 110/159 E-liquids
  - Diacetyl workplace exposure associated with bronchiolitis obliterans (Popcorn Lung)

Am J Physiol Lung Cell Mol Physiol 313: L193–L206, 2017.

A sample station, where customers can try different flavors of vape liquid, are seen at the shop Cloud99 Vapes in Manhattan borough, New York, U.S. September 20, 2018.
REUTERS/Melissa Fares

Am J Physiol Lung Cell Mol Physiol 313: L193–L206, 2017.

Holger Link, MD ©

* ENDS: Electronic Nicotine Delivery Systems

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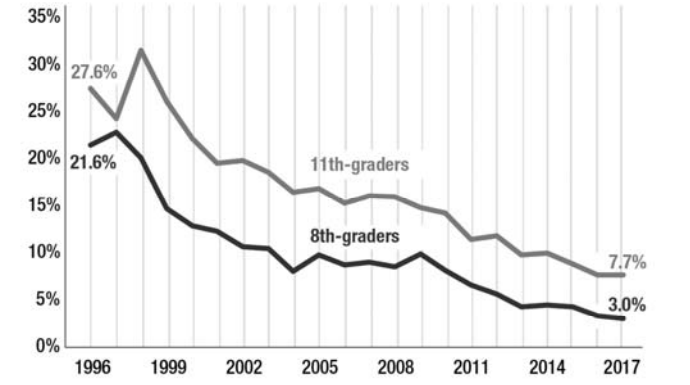
Epidemiology E-Cigarettes

Trends: National and in Oregon

Factors driving adolescent E-cigarette use

Holger Link, MD ©

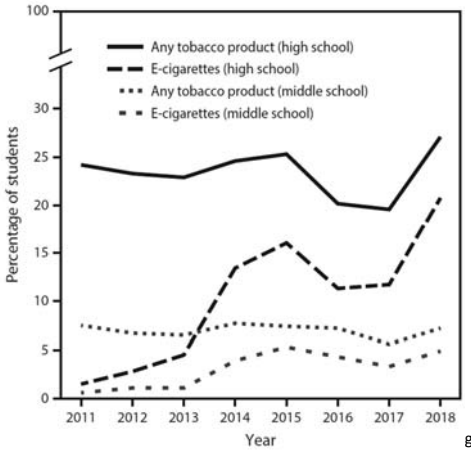
Figure 5.1 Youth cigarette smoking, Oregon, 1996–2017



Sources: *Student Drug Use Survey (1998, 2000); Youth Risk Behavior Survey (1997, 1999); Oregon Healthy Teens (2001–2009, 2011, 2013, 2015,2017); Student Wellness Survey (2010, 2012, 2014, 2016). Unpublished data.*

Holger Link, MD ©

Rapid Increase in E-cigarette Use

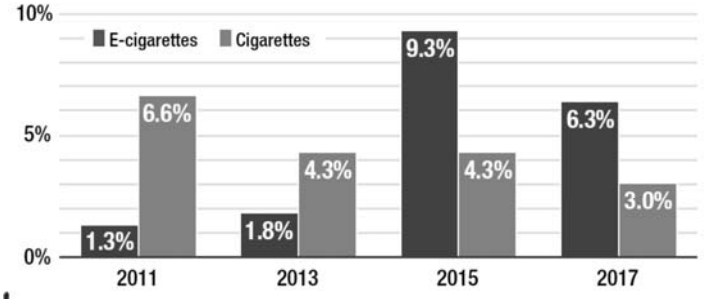


MMWR. November 16, 2018

Holger Link, MD ©

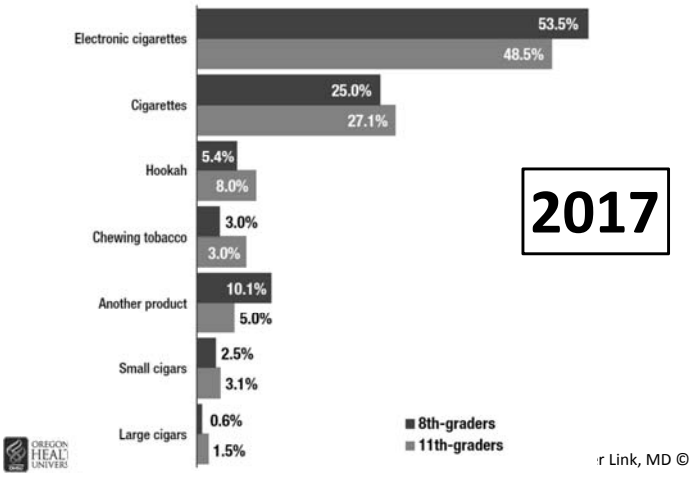
8th Grader's Switch to E-Cigarettes

Figure 5.3 Electronic cigarette and regular cigarette use among 8th-graders, Oregon, 2011, 2013, 2015, 2017



Source: Oregon Healthy Teens. Unpublished data

Oregon: E-cigarettes most popular Nicotine product



2017

r Link, MD ©

Factors Driving Adolescent E-Cigarette Use

Holger Link, MD ©

Marketing Claims

A. Freedom

Source: Esquire (2014).

B. Health

Source: Stanford Research into the Impact of Tobacco Advertising (n.d.b.).

U.S. Department of Health and Human Services. *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*

Holger Link, MD ©

Marketing Claims

C. Romance, sexuality, or sociability

Source: (Left) *Maxim* (2012), (middle) *Men's Journal* (2014), and (right) *Sports Illustrated* (2014).

U.S. Department of Health and Human Services. *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*

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D. Taste

Source: Soap Opera Digest (2013).

E. Smoking cessation

Source: Rolling Stone (2013).

U.S. Department of Health and Human Services. *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*

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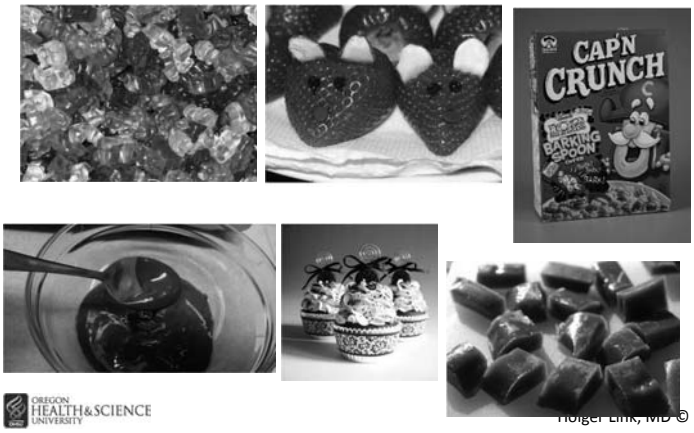
1. Save money

Source: FIN Electronic Cigarettes (n.d.).

Source: Spin (2012).

E-Cigarette Flavors



Flavors Encourage Adolescent E-cigarette Use

Extra Tempting: Fruit. Menthol. Sweet favors.

Source: Photo by Mandie Mills, CDC.

Rizza Colon works at the shop Cloud99 Vapes in Manhattan borough, New York, U.S. September 20, 2018. REUTERS/Melissa Fares

Overview ENDS* **Epidemiology E-cigs** **Nicotine addiction** **E-cigs Safety** **E-cigs and tobacco addiction** **National and state efforts to limit E-cig use**

Jan Hoffman. New York Times. November 16, 2018

JUUL

Started 2015 in San Francisco
Exponential Growth with estimated 70% of total market share in the US in 2018
Valued at 10's of Billions

Special Report: Juul copycats flood e-cig market, despite FDA rule

"Many high schools have resorted to locking bathrooms – jokingly called "Juul rooms" by students. Marcella Bianco, who helps develop school anti-vaping curriculum for the non-profit organization Catch My Breath, said elementary schools have recently started requesting materials"

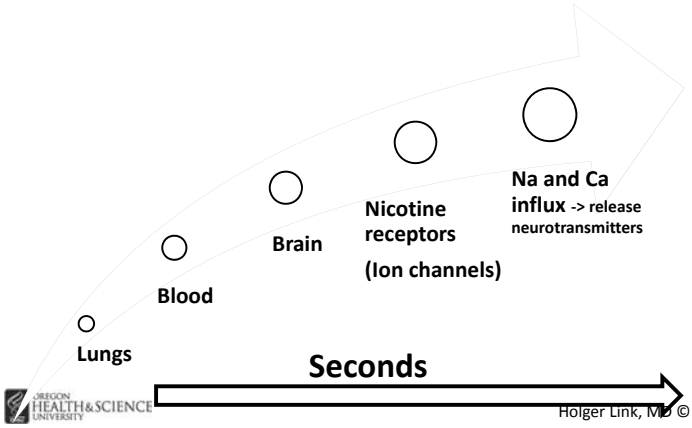
Reuters Health News September 24, 2018 / 4:11 AM

Juul versus Cigarettes

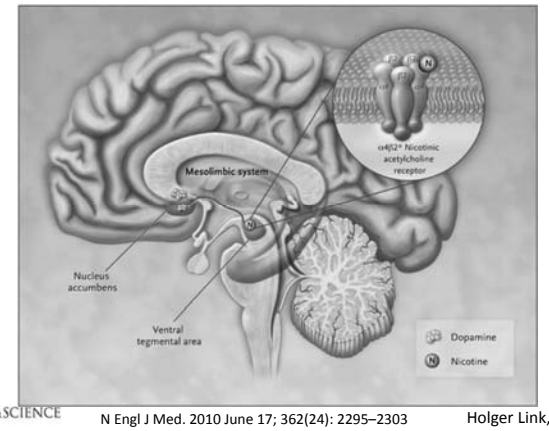
	Juul	Cigarettes
Taste	Yummy	Yuck
Cost	$4/pack equivalent	$5.65/pack*
State Taxes	None	$1.33/pack
Federal Taxes	None	$ 1.01/pack
Image	Cool	Old people
Detection by parents	Easy to hide	Smell of tobacco

*1 pack = 20 cigarettes
Cost and state taxes for Oregon

How Nicotine works

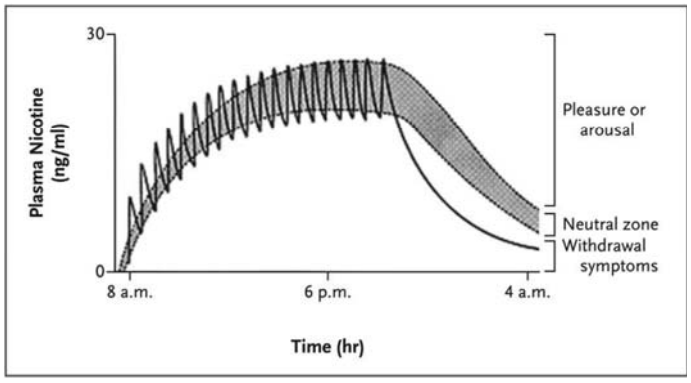


Most abundant Receptor $\alpha 4\beta 2$



N Engl J Med. 2010 June 17; 362(24): 2295–2303

One Day in the Life of a Smoker



N Engl J Med. 2010 June 17; 362(24): 2295–2303

FDA approved Nicotine Replacement Therapy (NRT) for smoking cessation versus E-cigarettes

E-Cigarettes	**Fast release**	**High addiction potential**
NRT	**Slow release**	**Low addiction potential**

Holger Link, MD ©

FDA approved Nicotine Replacement Therapy (NRT) for smoking cessation versus E-cigarettes

E-Cigarettes	**Fast release**	**High addiction potential**
NRT	**Slow release**	**Low addiction potential**

Zero research on how to quit vaping E-cigarettes

Holger Link, MD ©

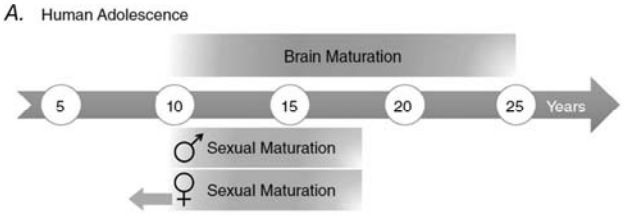
E-Cigarettes and Smoking Cessation

"Due to the low quality of available evidence, it is uncertain whether e-cigarettes are effective for smoking cessation for vulnerable groups"

Literature Review. Nicotine & Tobacco Research, 2018, 1–15

Holger Link, MD ©

Nicotine Effects on Adolescent Brain



"Cholinergic system maturates during adolescence"

"Earlier exposure to nicotine associated with higher rate of addiction"

Am J Prev Med. 2015 August ; 49(2): 286–293
J Physiol 593.16 (2015) pp 3397–3412

Holger Link, MD ©

Nicotine Effects on Adolescent Brain

- Cholinergic system has central role in cognitive maturation, including executive function mediated by the prefrontal cortex

Am J Prev Med. 2015 August ; 49(2): 286–293
J Physiol 593.16 (2015) pp 3397–3412

Holger Link, MD ©

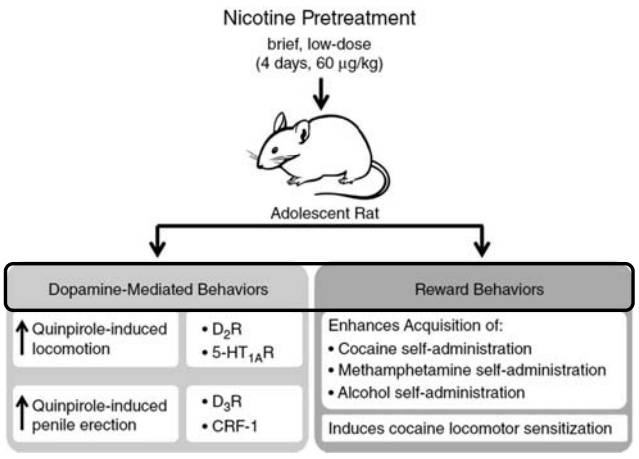
Nicotine Effects on Adolescent Brain

- Cholinergic system has central role in cognitive maturation, including executive function mediated by the prefrontal cortex
- Smoking cigarettes during adolescence has been associated with lasting cognitive and behavioral impairments, including effects on working memory and attention and reduced prefrontal cortex activation

Animal Studies on Nicotine in Adolescents

Structural and functional changes in adolescent animals exposed to nicotine

OREGON HEALTH & SCIENCE UNIVERSITY
Am J Prev Med. 2015 August ; 49(2): 286–293
J Physiol 593.16 (2015) pp 3397–3412
Holger Link, MD ©



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J Physiol 593.16 (2015) pp 3397–3412
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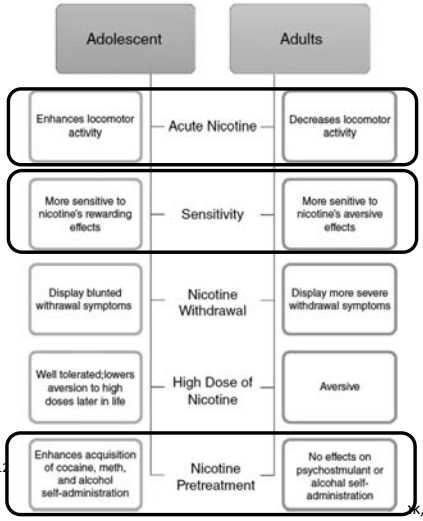
Rodents



J Physiol 593.16 (2015) pp 3397–3412
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How hard is it for teens to get E-Cigarettes?

- Sales through Instagram (# Vape sale)
- Direct order from China at steeply discounted price
- Teenagers make their own Juice

Look up “Vape tricks”, “Vape influencers” on Youtube

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Holger Link, MD ©

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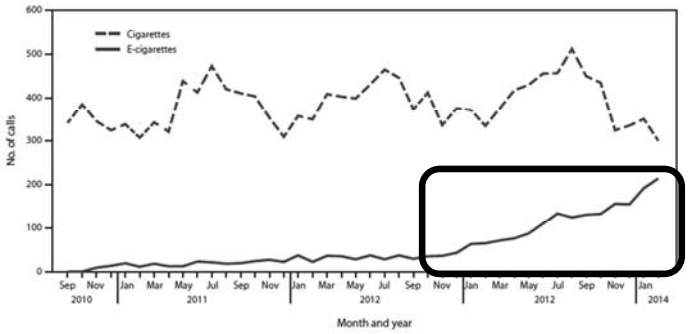
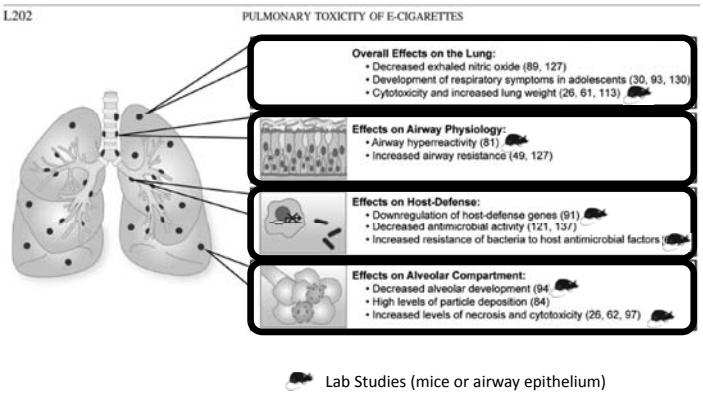
* ENDS: Electronic Nicotine Delivery Systems
Holger Link, MD ©

Increasing Calls to Poison Centers



MMWR. April 4, 2014 / 63(13);292-293

Toxic acute effects E-cigarettes



Lab Studies (mice or airway epithelium)

Am J Physiol Lung Cell Mol Physiol 313: L193–L206, 2017.

Tobacco addiction starts in Adolescence

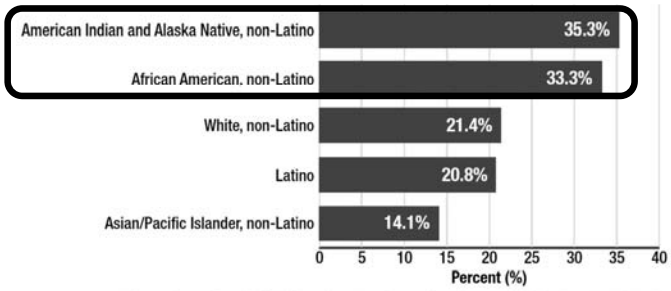
What percentage of adult smokers start before 18 years of age?

A. 30%
B. 40%
C. 60%
D. 80%
E. 90%

Childhood smoking = Adult smoking

High Risk Groups for Smoking

Figure 4.4 Adult cigarette smoking, by race and ethnicity, Oregon, 2010–2011 combined

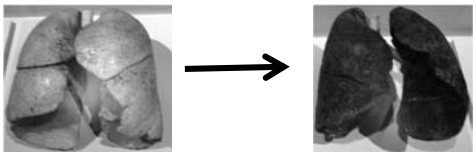


Source: *Oregon Behavioral Risk Factor Surveillance System Race Oversample, 2010–2011. Unpublished data.*
Note: *Estimates are age-adjusted to the 2000 standard population.*

USA: Daily smoking deaths and new smokers

- **1200 deaths**
  - **In 12 days entire OHSU workforce**

- **2400 start smoking**



Source: Surgeon General. 31st tobacco related report

USA: Annual Tobacco Deaths

480,000 Humans

More than in any war the US fought in the 20th Century

What percentage of smokers permanently quit smoking every year?

A. 3%
B. 11%
C. 18%
D. 23%

Only 3% of smokers quit long term

- 45 Million Smokers
- 31.5 Million would like to quit
- 70%
- 13.5 Million quit for at least 1 day
- 30%
- 1.35 Million successfully quit
- 3%

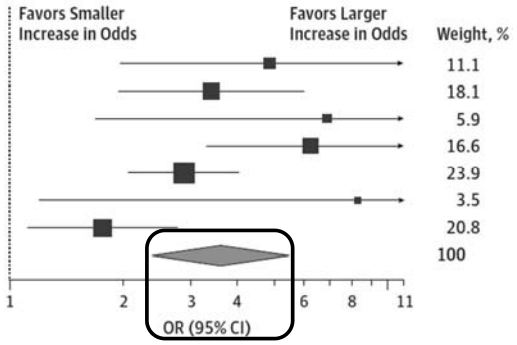
N Engl J Med. 2010 June 17; 362(24): 2295–2303

* ENDS: Electronic Nicotine Delivery Systems

E-cigarette Use and Subsequent Cigarette Smoking

Meta-Analysis

Comparing ever ENDS use to never ENDS user



JAMA Pediatr. 2017;171(8):788-797

E-Cigarette Use and Subsequent Smoking

- Pooled data from 3 prospective teenage cohort studies *
- Baseline 2013-2014. Follow up 2014-2016
- Results:
  - E-cigarette users have increased risk for frequent cigarette use (OR= 3.51)

* Yale Adolescent Survey Study
Happiness and Healthy Study
Southern California Children's Health Study

PEDIATRICS Volume 142, Number 6, December 2018

* ENDS: Electronic Nicotine Delivery Systems

AAP Policy Statement

- Reduce youth access
  - Ban sale < 21 years age
  - Ban internet sale
- Reduce demand
  - Ban flavors
- Ban advertising to youth
- Restrict depiction in movies, TV shows, video games
- Protect youth from harms of involuntary solution or aerosol exposure
  - Prohibit use in public areas
  - Child resistant packaging for e-cigarettes
- Increase cost for youth
  - Tax same as tobacco products

PEDIATRICS Volume 136, number 5, November 2015

Statement FDA Commissioner Scott Gottlieb, MD

"We're announcing the largest ever coordinated initiative against violative sales in the history of the FDA. This is the largest single enforcement action in agency history. It's aimed at retail and online sales of e-cigarettes to minors"

"Let me be clear: Everything is on the table. This includes the resources of our civil and criminal enforcement too"

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm620185.htm

Updated Statement January 18, 2019

"I'll tell you this. If the youth use continues to rise, and we see significant increases in use in 2019, on top of the dramatic rise in 2018, the entire category will face an existential threat," he told a meeting.

"It will be game over for these products until they can successfully traverse the regulatory process."

https://www.nbcnews.com/health/health-news/fda-chief-threatens-take-e-cigarettes-market-n960411

Response Juul to FDA pressure

Juul Labs announced on Tuesday that it would suspend sales of most of its flavored e-cigarette pods in retail stores and would discontinue its social media promotions. In addition, Juul said it would shut down its Facebook and Instagram accounts in the United States that promoted use of the flavored pods. According to its release, the company said it would ask the major social media companies, including Twitter and Snapchat, to help them "police" posts that promote the use of e-cigarettes or cigarettes by underage users.

Mr. Burns, the Juul executive, said that as of Tuesday, the company would stop accepting retail orders for mango, fruit, crème and cucumber Juul pods. Those account for about 45 percent of retail sales for the $16 billion company, according to some estimates

New York Times November 13, 2018

Juul's response to FDA pressure

- Suspend sales of most of its flavored e-cigarette pods in retail stores and would discontinue its social media promotions.
- Shut down its Facebook and Instagram accounts in the United States that promoted use of the flavored pods.
- Ask the major social media companies to help them "police" posts that promote the use of e-cigarettes or cigarettes by underage users.
- Stop accepting retail orders for mango, fruit, crème and cucumber Juul pods that account for about 45 percent of retail sales for the $16 billion company.

New York Times November 13, 2018

Oregon Law E-cigarette devices

- Possession < 18 years prohibited
- No sale or purchase under 21 years
- No use in car with person under 18 years present
- Must be sold in child-resistant package
- No use in hospitals
- Not taxed

https://publichealthlawcenter.org/resources/us-e-cigarette-regulations-50-state-review

Oregon Law E-cigarette devices

- No use in public spaces, placed of employment, within 10 feet of entrances, windows
- No use in DHS child care home or facility
- Public/private schools, college, community college, university career school, technical education school, youth correction and juvenile detention facilities must prohibit possession of inhalant delivery systems by persons under age 21 present at facility or at facility-sponsored event

https://publichealthlawcenter.org/resources/us-e-cigarette-regulations-50-state-review

Tobacco Taxes Oregon versus other states

Oregon ranks 32nd with $1.33

Highest: New York and Connecticut $ 4.35

Lowest: Virginia $0.30

https://www.tobaccofreekids.org

Summary E-cigarettes

- E-Cigarette use in adolescents has reached epidemic proportions
- Nicotine addiction not benign: affects brain structure and mental development
- Teenage vapers are likely the future smokers
- Increasing data regarding *short term* negative health effects
- No data on long term effects of E-cigarettes
- No data on quitting E-cigarettes

Excellent Online Resource

https://e-cigarettes.surgeongeneral.gov

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