From Evidence to Recommendations: the Case of Statins

Mark H. Ebell MD, MS

Professor, University of Georgia and Family Physician

Member of the USPSTF: 2012-2015

Consultant to USPSTF: 2016 - present

Biosketch

- University of Michigan: MD 1987, Family Medicine residency 1990, and MS Public Health 1994

- Professor, College of Public Health, University of Georgia; family physician, Mercy Health Clinic (uninsured pts)

- Research interests: evidence-based practice, meta-analysis of diagnosis, decision support systems, clinical decision rules, acute respiratory infections, primary care.

Today's topics

1. US and Italian lipid guidelines: a brief overview
2. Methodologic standards for guidelines, and how well current guidelines meet them
3. Challenges of implementing the lipid guidelines

Onekama, Michigan

Why do we need guidelines?

1. Medicine is **increasingly complex**, we need good overviews
2. We need help identifying best practices to **improve quality of care**
3. Studies find **too much variation** in preventive medicine decisions
4. Save money by **avoiding low value care**

Goal: provide the right preventive service to the right patients for the right amount of time to maximize benefit and minimize harm.

TEST DESCRIPTION	OUT-OF-RANGE	IN-RANGE	UNITS	EXPECTED	ABNORMAL FLAG

Result Status Key: X - Test canceled or cannot be obtained

Patient is Fasting

303756 - Lipid Panel

Cholesterol, Total:	253		mg/dL	
Triglycerides:	268		mg/dL	
HDL Cholesterol:		66	mg/dL	

According to ATP-III Guidelines, HDL-C >59 mg/dL is considered a negative risk factor for CHD.

VLDL Cholesterol Cal:	54		mg/dL	
LDL Cholesterol Calc:	133		mg/dL	
Comment::		(X)		

Total cholesterol: 253 mg/dl (6.5 mmol/L)
Triglycerides: 268 mg/dl (3.0 mmol/L)
LDL cholesterol: 133 mg/dl (3.4 mmol/L)
HDL cholesterol: 66 mg/dl (1.7 mmol/L)

Patient is a 56 year old man, treated hypertension, no history of heart disease or diabetes, non-smoker, exercises daily. Vote for what you would typically recommend:

a: Do not prescribe a statin
b. Prescribe a moderate intensity statin (simvastatin 20 to 40 mg)
c. Prescribe a high intensity statin (rosuvastatin 10 mg)

Brief overview of current guideline recommendations

- Italian Multi-Society Guidelines (2016)
- American Association of Clinical Endocrinology (2017)
- American College of Cardiology / American Heart Association (2013)
- US Preventive Services Task Force (2016)
- US Veteran’s Administration Guidelines (2014)

Documento di consenso intersocietario ANMCO/ISS/AMD/ANCE/ARCA/FADOI/ GICR-IACPR/SICI-GISE/SIBioC/SIC/SICOA/ SID/SIF/SIMEU/SIMG/SIMI/SISA

Colesterolo e rischio cardiovascolare: percorso diagnostico-terapeutico in Italia

Il Pensiero Scientifico Editore

1. Use SCORE (e.g. the “HeartScore”, www.heartscore.org) to calculate 10 year risk of CV death (hard endpoint).
2. Determine LDL target based on risk score and other risk factors (70 – 115 mg/dl)

Tabella 1. Target di colesterolo LDL secondo le condizioni di rischio.

Rischio	Condizioni	Target C-LDL
Basso	Punteggio secondo le carte del rischio SCORE <1%.	<115 mg/dl
Moderato	Punteggio secondo le carte del rischio SCORE ≥1% e <5%.	<115 mg/dl
Alto	Pazienti con dislipidemie familiari o ipertensione severa, diabetici senza fattori di rischio cardiovascolare e senza danno d’organo e pazienti con insufficienza renale cronica moderata (GFR 30-59 ml/min/1.73 m^2). Punteggio secondo le carte del rischio SCORE ≥5% e <10%.	<100 mg/dl
Molto alto	Pazienti con malattia cardiovascolare documentata (da coronarografia, ecocardiografia da stress, imaging con radionuclidi, evidenza ultrasonografica di placca carotidea), pregresso infarto miocardico, pregressa SCA, pregresso intervento di rivascolarizzazione coronarica (con BPAC o PCI) o periferica, pregresso ictus ischemico e arteriopatie periferiche, diabetici con uno o più fattori di rischio cardiovascolare e/o marker di danno d’organo (es. microalbuminuria) e con insufficienza renale grave (GFR <30 ml/min/1.73 m^2). Punteggio secondo le carte del rischio SCORE >10%.	<70 mg/dl

American Association of Clinical Endocrinology (2017)

Table 6
Atherosclerotic Cardiovascular Disease Risk Categories and LDL-C Treatment Goals

Risk category	Risk factors[a]/10-year risk[b]	Treatment goals		
		LDL-C (mg/dL)	Non-HDL-C (mg/dL)	Apo B (mg/dL)
Extreme risk	– Progressive ASCVD including unstable angina in patients after achieving an LDL-C <70 mg/dL – Established clinical cardiovascular disease in patients with DM, CKD 3/4, or HeFH – History of premature ASCVD (<55 male, <65 female)	<55	<80	<70
Very high risk	– Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease, 10-year risk >20% – Diabetes or CKD 3/4 with 1 or more risk factor(s) – HeFH	<70	<100	<80
High risk	– ≥2 risk factors and 10-year risk 10-20% – Diabetes or CKD 3/4 with no other risk factors	<100	<130	<90
Moderate risk	≤2 risk factors and 10-year risk <10%	<100	<130	<90
Low risk	0 risk factors	<130	<160	NR

Source: Endocrine Practice 2017; 23(Suppl 2): 1

Evolution of Some US Lipid Guidelines

Away from:

- "Treat to target": LDL < 100 mg/dl for high risk, < 130 mg/dl for most others
- Annual monitoring of lipid levels

Toward

- Treatment based on 10 year risk of a CV event (<u>not CV death</u>…)
- Treatment intensity is based on risk
- "Fire and forget": no need to follow lipid levels (?)

Rationale

- Trials did not randomize patients to LDL targets
- Relative benefit is similar regardless of baseline risk, or the amount of LDL lowering

Evolution…

Example of Rationale: Heart Protection Study

- Largest statin trial, compared simvastatin, 40 mg daily, with placebo in 20,536 patients
- 86% secondary prevention, most with total cholesterol >3.5 mMol/L.
- **Simvastatin reduced risk of total myocardial infarction or stroke (RRR 25%)**
- Similar risk reduction across various subgroups (next slide)

Articles

MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial

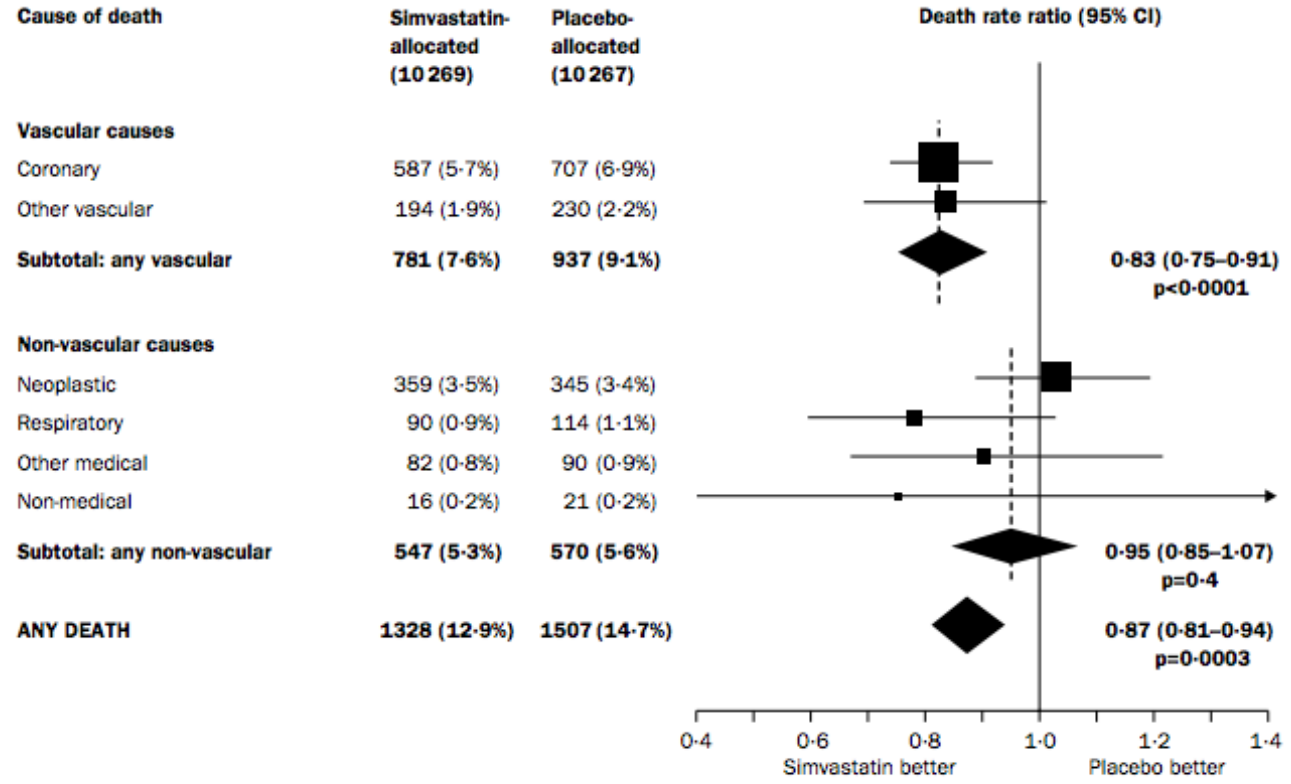
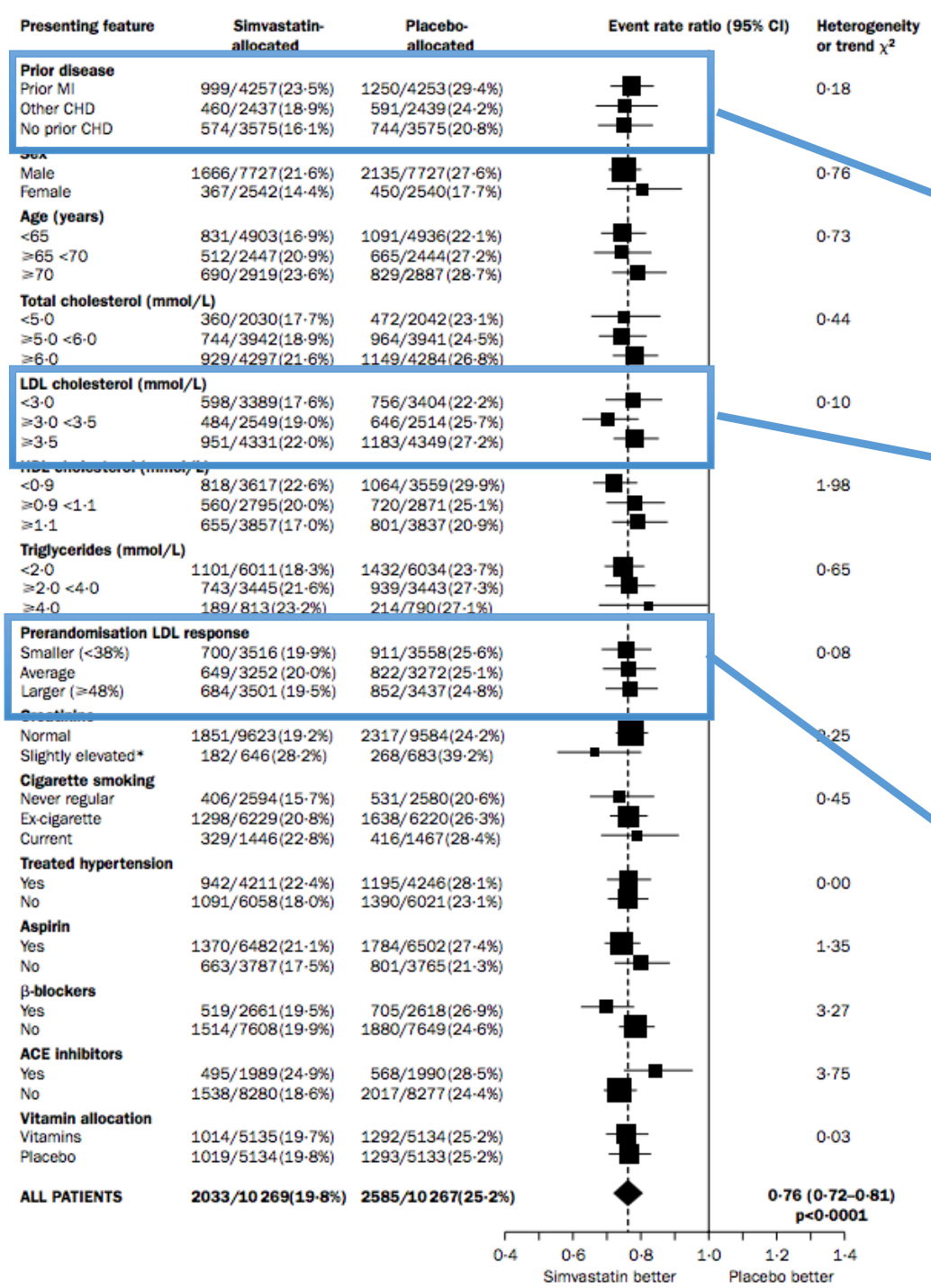


Figure 2: **Effects of simvastatin allocation on cause-specific mortality**
Rate ratios (RRs) are plotted (black squares with area proportional to the amount of statistical information in each subdivision) comparing outcome among participants allocated simvastatin to that among those allocated placebo, along with their 95% CIs (horizontal lines; ending with arrow head when CI extends beyond scale). For particular subtotals and totals, the result and its 95% CI are represented by a diamond, with the RR (95% CI) and its statistical significance given alongside. Squares or diamonds to the left of the solid vertical line indicate benefit with simvastatin, but this is conventionally significant (p<0·05) only if the horizontal line or diamond does not overlap the solid vertical line. A broken vertical line indicates the overall RR for a particular subtotal or total.



Similar relative risk reduction for:

Patient with heart disease: 29% RRR
Primary prevention: 21% RRR

Relative risk reduction by initial LDL cholesterol:

- < 3.0 mmol/L (116 mg/dl): 21%
- 3.0 – 3.5 mmmol/L (116 to 130 mg/dl): 26%
- > 3.5 mmol/L (> 130 mg/dl): 19%

Relative risk reduction by response to statin:

- Smaller response (< 38% LDL reduction): 22%
- Average response (38% - 48% reduction): 20%
- Larger response (> 48% LDL reduction): 21%

So, relative benefit did not depend on initial LDL or how much the LDL was reduced

ACC/AHA Guidelines (2013)

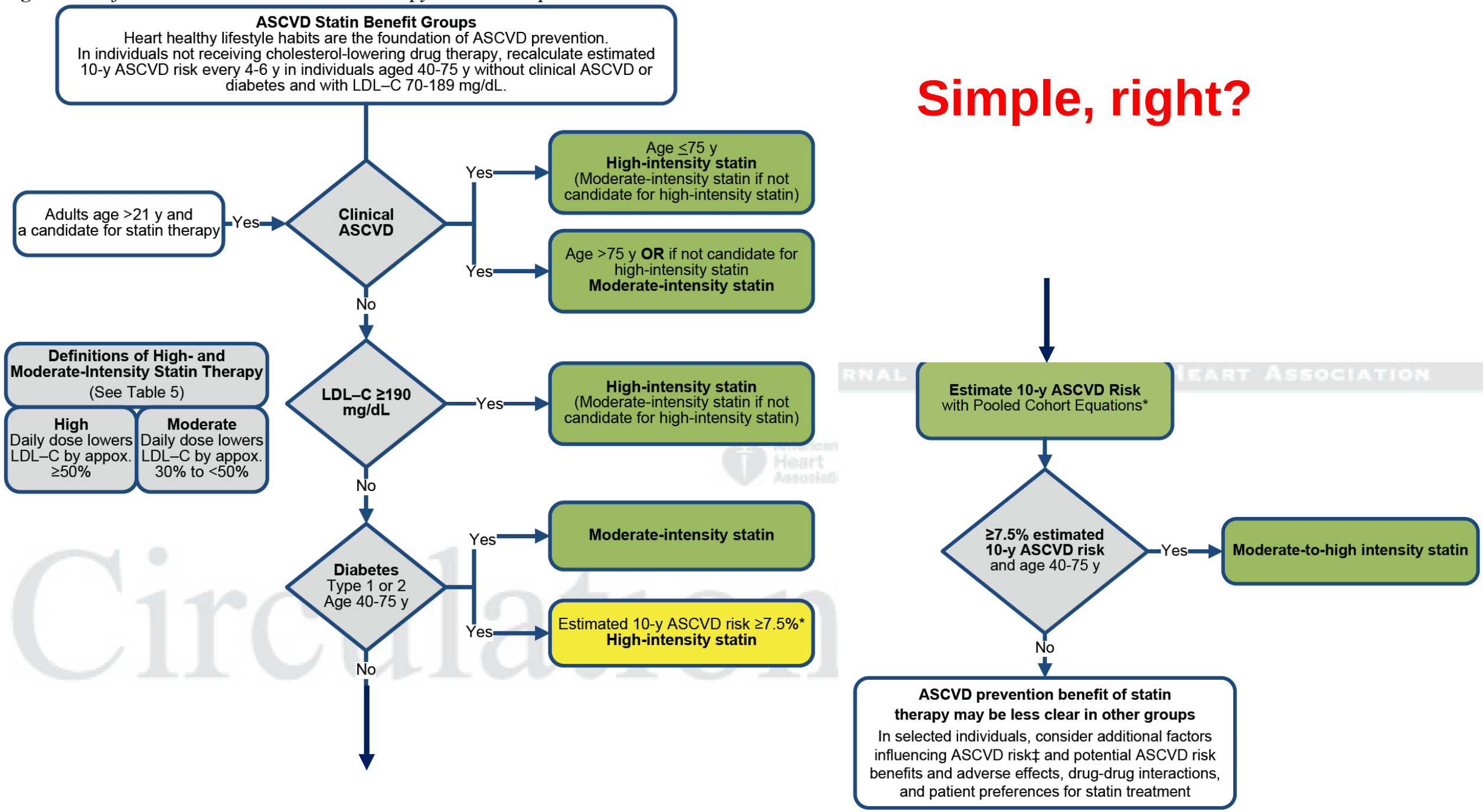
“Therefore, given the absence of data on titration of drug therapy to specific goals, no recommendations are made for or against specific LDL–C or non-HDL–C goals for the primary or secondary prevention of ASCVD.”

Treatment recommendations are now based on 10 year CV event risk and statin dose, not LDL target.

- Anyone <= 75 years with known vascular disease or LDL > 190 mg/dL should receive a **high-intensity statin**.
- Anyone > 75 years with known vascular disease and anyone with diabetes should receive a **moderate-intensity statin**.
- If someone with diabetes has a 10-year risk of at least 7.5%, they should instead be given a **high-intensity statin**.
- If any patient without diabetes has a 10-year risk of at least 7.5%, they should receive a **moderate or high-intensity statin**.
- 10 year risk of 5% to 7.5%, **discuss with patient**

Source: Stone NJ, et al. J Am Coll Cardiol. 2014 Jul 1;63(25 Pt B):2889

Figure 2. Major recommendations for statin therapy for ASCVD prevention



ACC/AHA Guidelines: Statin Intensity

- Statins are divided into moderate intensity (lower LDL by 30% to 50%) and high intensity (reducing LDL by more than 50%).

Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20 *(40)* mg**	**Atorvastatin 10 *(20)* mg** **Rosuvastatin (*5*) 10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40 *(80)* mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*

Specific statins and doses are noted in bold that were evaluated in RCTs (17,18,46-48,64-67,69-78) included in CQ1, CQ2 and the CTT 2010 meta-analysis included in CQ3 (20). All of these RCTs demonstrated a reduction in major cardiovascular events. Statins and doses that are approved by the U.S. FDA but were not tested in the RCTs reviewed are listed in *italics*.

*Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice. There might be a biologic basis for a less-than-average response.

†Evidence from 1 RCT only: down-titration if unable to tolerate atorvastatin 80 mg in IDEAL (47).

‡Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.

bid indicates twice daily; FDA, Food and Drug Administration; IDEAL, Incremental Decrease through Aggressive Lipid Lowering study; LDL–C, low-density lipoprotein cholesterol; and RCTs, randomized controlled trials.

USPSTF Guidelines (2016)

Recommendation Summary

Population	Recommendation	Grade (What's This?)
Adults aged 40 to 75 years with no history of CVD, 1 or more CVD risk factors, and a calculated 10-year CVD event risk of 10% or greater	The USPSTF recommends that adults without a history of cardiovascular disease (CVD) (ie, symptomatic coronary artery disease or ischemic stroke) use a low- to moderate-dose statin for the prevention of CVD events and mortality when all of the following criteria are met: 1) they are aged 40 to 75 years; 2) they have 1 or more CVD risk factors (ie, dyslipidemia, diabetes, hypertension, or smoking); and 3) they have a calculated 10-year risk of a cardiovascular event of 10% or greater. Identification of dyslipidemia and calculation of 10-year CVD event risk requires universal lipids screening in adults aged 40 to 75 years. See the "Clinical Considerations" section for more information on lipids screening and the assessment of cardiovascular risk.	B
Adults aged 40 to 75 years with no history of CVD, 1 or more CVD risk factors, and a calculated 10-year CVD event risk of 7.5% to 10%	Although statin use may be beneficial for the primary prevention of CVD events in some adults with a 10-year CVD event risk of less than 10%, the likelihood of benefit is smaller, because of a lower probability of disease and uncertainty in individual risk prediction. Clinicians may choose to offer a low- to moderate-dose statin to certain adults without a history of CVD when all of the following criteria are met: 1) they are aged 40 to 75 years; 2) they have 1 or more CVD risk factors (ie, dyslipidemia, diabetes, hypertension, or smoking); and 3) they have a calculated 10-year risk of a cardiovascular event of 7.5% to 10%.	C

US Preventive Services Task Force | Recommendation Statement FREE

November 15, 2016

Statin Use for the Primary Prevention of Cardiovascular Disease in Adults

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

» Author Affiliations | Article Information

JAMA. 2016;316(19):1997-2007. doi:10.1001/jama.2016.15450

Recommend a statin if patients is 40 to 75 years old with 1 or more CV risk factors and 10 year CV event risk is 10% or higher (**B recommendation, moderate likelihood of moderate net benefit**).

Consider a statin if patient is 40 to 75 years with 1 or more CV risk factors and 10 year CV event risk is 7.5% to 10%. (**C recommendation, moderate likelihood of small net benefit**)

Insufficient evidence for patients older than 75 years.

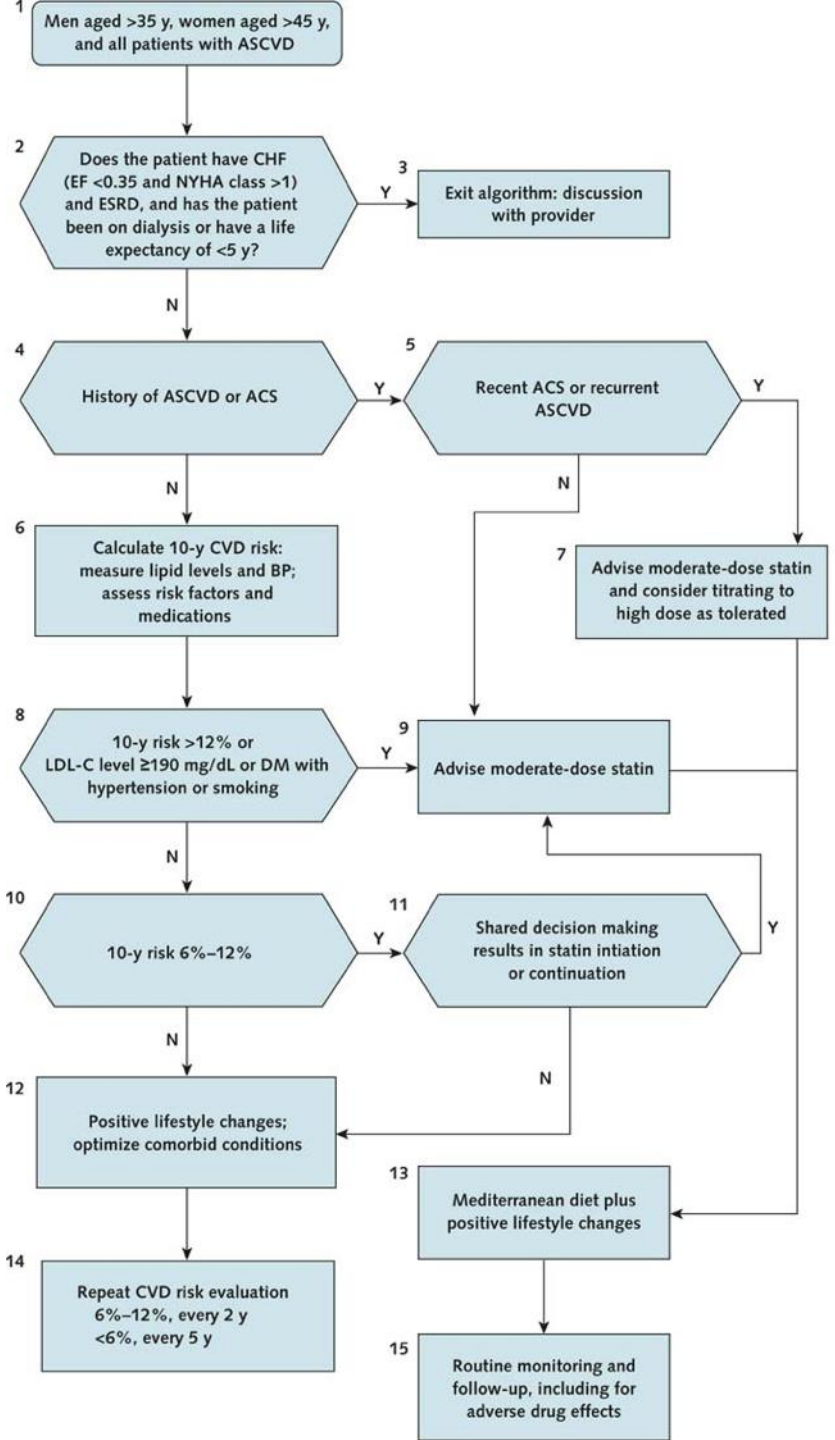
VA Guidelines

Prescribe a moderate (or high) dose statin if:

- Known heart disease
- LDL > 190 mg/dl (4.9 mmol/L)
- 10 year event risk > 12%
- DM + (HTN or smoking)

Do shared decision-making regarding moderate dose statin if:

- 10 year event risk 6 – 12%



ASCVD and Equivalents*

All ACS or MI
CABG or PCI
Stable obstructive CAD (stable symptoms of angina or equivalent)
CVA or TIA
Atherosclerotic PVD (claudication or AAA)

Statin Dose, by 10-Year CVD Risk

10-Year Risk	Statin Dose
ASCVD (second prevention)	Moderate to high
>12%	Moderate
6%–12% (with shared decision making)	Moderate
<6%	None

Drug Doses†

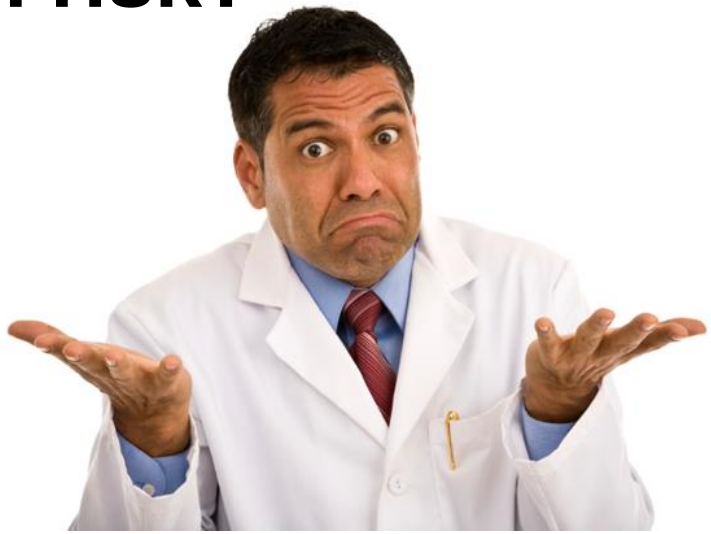
Statin	Moderate, *mg*	High, *mg*
Generics available		
Atorvastatin	10–20	40–80
Simvastatin	20–40	
Pravastatin	40–80	
Lovastatin	40–80	
Fluvastatin	80‡	
Brand formulation only		
Rosuvastatin	5–10	20–40

Summary

Guideline	Recommendation
Italian guidelines	Treat to target based on risk
AACE (endocrinologists)	Treat to target based on risk
ACC/AHA Guidelines	No statin: < 5% Shared decision-making: 5-7.5% Statin: > 7.5%
USPSTF Recommendation	No statin: < 7.5% Shared decision-making: 7.5 – 10% Statin: > 10%
VA Guidelines	No statin: < 6% Shared decision-making: 6-12% Statin: > 12%

What about our 56 year old patient with LDL 133, HDL 66, 7% 10 year CV event risk, 1% CV death risk?

Guideline	Recommendation
Italian guidelines	Prescribe statin, LDL target = 115 mg/dl
AACE (endocrinologists)	Prescribe statin, LDL target = 100 mg/dl
ACC/AHA Guidelines	Prescribe moderate intensity statin
VA Guidelines	Shared decision-making, consider moderate intensity statin
USPSTF Recommendation	Shared decision-making, consider moderate intensity statin



Determining whether you can trust a guideline's methods

Institute of Medicine Definition of an Ideal Practice Guideline (2012)

Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.

IOM Quality Criteria for Guidelines

1. **Transparent process**: the process for developing and funding the guideline should be clearly and transparently described
2. **Conflict of interest**: none or few should have COI; chair or co-chair cannot have COI; financial ties that would create COI are eliminated.
3. **Composition of guideline group**: includes methods experts, clinicians, stakeholders, and patient representatives
4. **Systematic review**: the guideline is based on the results of a good quality systematic review

Source: IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press

IOM Quality Criteria for Guidelines

5. **Strength of recommendation**: this is clearly rated for each recommendation, using a taxonomy that incorporates strength of evidence and confidence in the recommendations

6. **Articulating recommendations**: recommendations are clearly and concisely listed, and can be acted on by physicians

7. **External review**: stakeholders, experts, and others provide external peer review of the guidelines, including opportunity for public comment

8. **Updating**: A process for updating the guideline is stated.

Source: IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press

Red Flags List

Lenzer, et al. BMJ 2013; 347: f5535

Box 1: Red flags that should raise substantial skepticism among guideline readers (and medical journals)

- Sponsor(s) is a professional society that receives substantial industry funding;
- Sponsor is a proprietary company, or is undeclared or hidden
- Committee chair(s) have any financial conflict*
- Multiple panel members have any financial conflict*
- Any suggestion of committee stacking that would pre-ordain a recommendation regarding a controversial topic
- No or limited involvement of an expert in methodology in the evaluation of evidence
- No external review
- No inclusion of non-physician experts/patient representative/community stakeholders

*Includes a panelist with either or both a financial relationship with a proprietary healthcare company and/or whose clinical practice/specialty depends on tests or interventions covered by the guideline

Conflict of interest, panel-stacking, no peer review…

I would add: inclusion of lower quality studies, lack of systematic review or meta-analysis, poor presentation/writing

Guideline methodology in depth: the USPSTF

Established in 1984, makes recommendations on over 70 conditions:

- Screening in asymptomatic persons
- Primary prevention (counseling, medications)

Service must be performed by **primary care physician** or referable from primary care office

USPSTF does not consider financial impact of recommendations (?)

Who is on the USPSTF?

- Independent panel of 16 unpaid experts in primary care medicine: family medicine, general internal medicine, pediatrics, obstetrics/gynecology, nursing
- No financial conflict of interest
- Serve 4 year terms as volunteers: 3 meetings per year + many phone calls + much reading and study.
- Approximately 10% of effort per year.

Sue Curry, PhD (chair)

Death Panel, circa 2014

Our 56 year old patient…

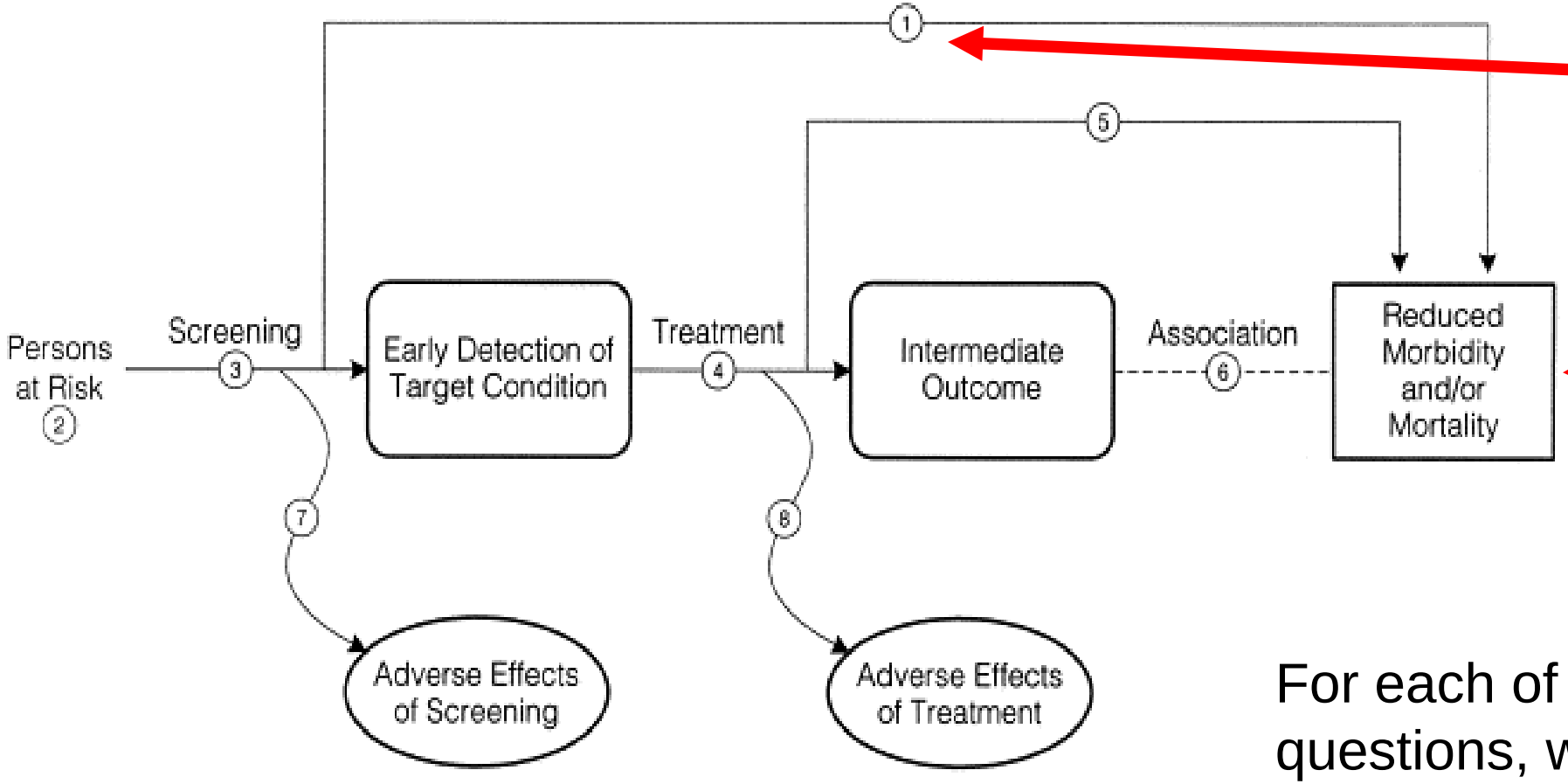
The USPSTF Process

Institute of Medicine recommends the USPSTF as a model for guideline development:

- Recommendations based on systematic reviews of the best available evidence
- Considers benefits and harms, as well as certainty
- Free of conflict of interest
- Methods are transparent
- Obtains public input and input from expert peer reviewers
- Regularly updated (~ every 5 years)

Step 1. Develop a Research Plan

The analytic framework guides which evidence we seek



Direct evidence pathway

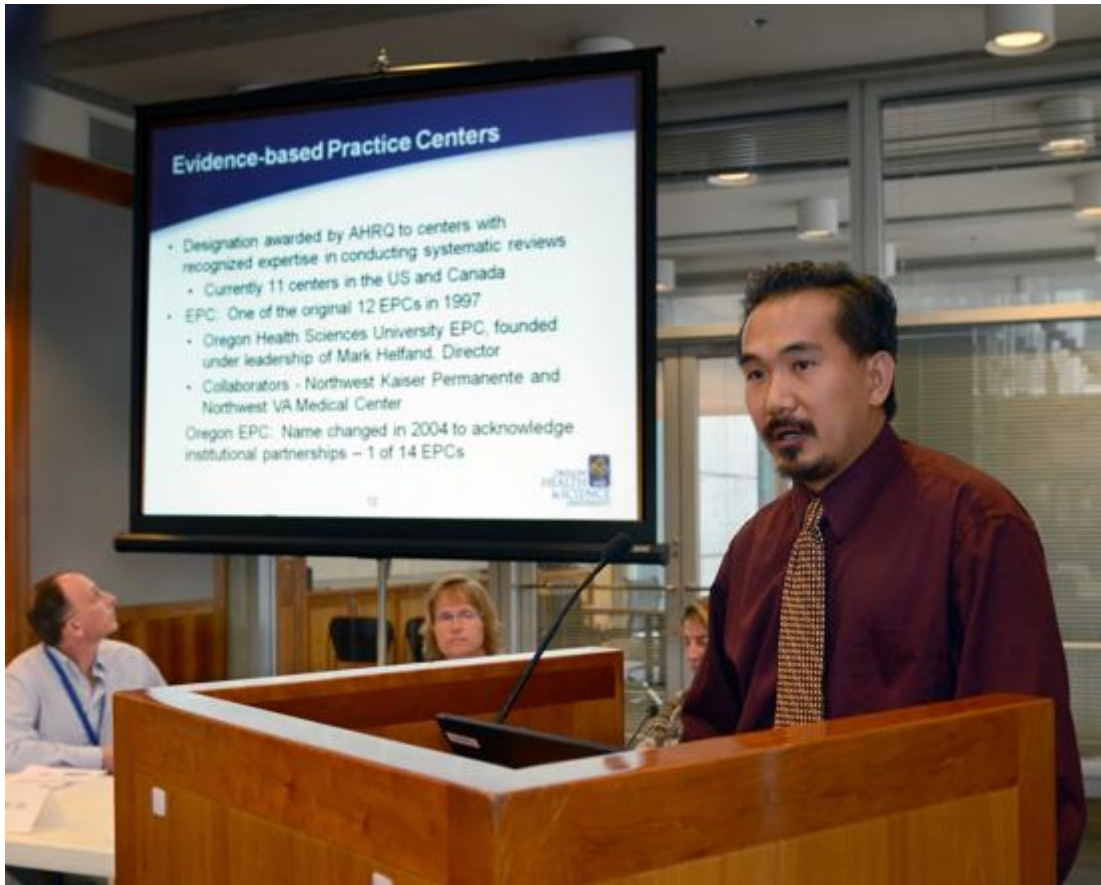
Indirect evidence pathway

For each of the numbered key questions, we will gather the best available evidence.

Step 2. Develop a draft evidence report to answer each of the key questions

- Performed by federally funded “Evidence-Based Practice Centers”
- Team of clinicians and experts in evidence synthesis

- Steps (6 – 12 months)
  - Define and **retrieve** all relevant evidence
  - Evaluate the **quality** of individual studies (Good, Fair or ~~Poor~~)
  - **Systematic review** to synthesize the results, if possible using meta-analysis)



Step 3. Develop a draft recommendation

- Focus is on net benefit

Net Benefit = Benefit - Harm

- Based on the evidence summary, for each key question:
  - How ***certain*** are we about the benefits and harms?
  - What is the ***magnitude (size)*** of both benefits and harms?

Step 4. Assign a grade to the recommendation

	Size of Net Benefit			
Certainty of Net Benefit	**Substantial**	**Moderate**	**Small**	**Zero/negative**
High	**A**	**B**	**C**	**D**
Moderate	**B**	**B**	**C**	**D**
Low	**Insufficient (I Statement)**			

Step 5. Distribute draft recommendation for public comment

- Public comments vary widely in number, content
- Who comments: stakeholder organizations (i.e. American Cancer Society), experts and researchers, disease survivors, and individual citizens
- Some are much more useful than others:

Respondent #: 16 *Role: Consumer or patient* *Organization: Ms.*
Respondent ID: 10568

Question #	Comment
3	**Based on the evidence presented in this draft Recommendation Statement, do you believe that the USPSTF came to the right conclusions? Please provide additional evidence or viewpoints that you think should have been considered.** NO ONE MORE TIME you deny needed services and people will die from your denial of services
6	**Do you have other comments on this draft Recommendation Statement?** You formally and presently cointinually deny medical services and as it gets worse and worse, my family and friends are becoming sick and/or sicker and it is due to your denials of services. You should have a conscience.

Step 6. Create Final Recommendation, Disseminate

- Review public comments
- Discuss, and discuss some more
- Write final recommendation statement

- All Task Force members receive media training and have media expert consultation

How do the guidelines compare: Who is on the guideline panel?

IOM recommendation: includes methods experts, clinicians, stakeholders, and patient representatives.

Guideline	Panel composition
Italian lipid guidelines	Mostly cardiologists, some hospital internists and diabetologists, a pharmacist; many organizations
AACE (endocrinologists)	Mostly endocrinologists, one cardiologist
ACC/AHA Guidelines	Mostly cardiologists
VA Guidelines	Primary care physicians, cardiologist, dietician, methodologists
USPSTF Recommendation	Primary care physicians, methodologists

How do the guidelines compare: Managing Conflict of Interest

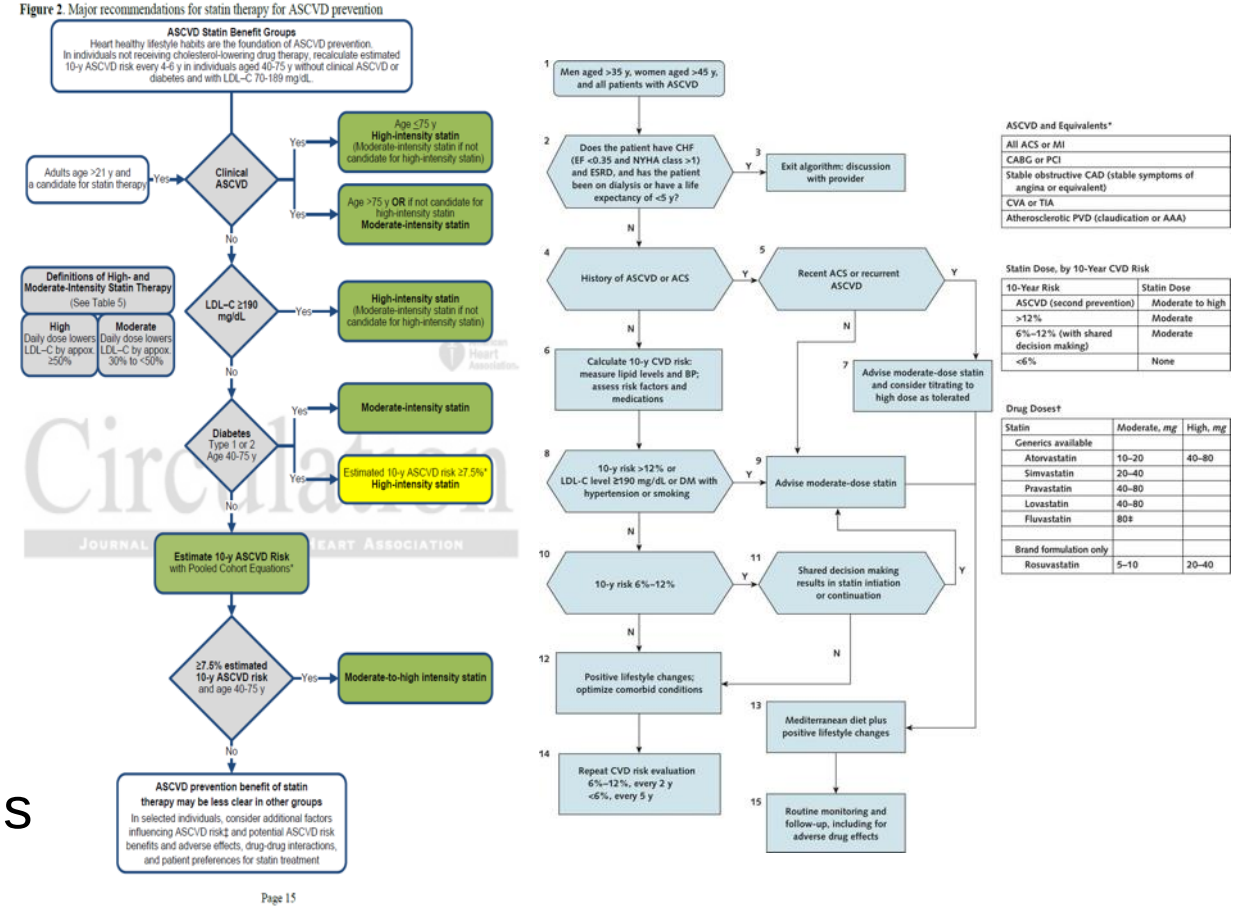
IOM recommends: none or few should have COI; chair or co-chair cannot have COI; financial ties that would create COI are eliminated.

Guideline	Conflict of Interest Policy
Italian guidelines	I wish I could read Italian!
AACE (endocrinologists)	Chair and every member of panel had multiple industry relationships. Disclosure only, no effort to manage COI. 
ACC/AHA Guidelines	Chair had many industry ties, but severed them when he took over; 7 of 16 members continued to accept industry money but recused themselves from votes with COI. 
VA Guidelines	Disclosure and ongoing surveillance for COI; no members had any COI 
USPSTF Recommendation	Disclosure and ongoing surveillance for COI; no members had any COI 

Challenges of implementing lipid guidelines

Guideline Challenges: Increasing complexity as barrier to usage

- Inconsistent adoption and uptake
- More complicated:
  - Old: measure LDL, treat if > 130 mg/dl
  - New: assess risk, follow one of the complicated algorithm at right
- As a result:
  - Most doctors in US still “treat to target”
  - Most do not use Pooled Cohort Equations to assess risk
  - Most continue to check lipid levels after starting statin (“fire and follow”)
- Options:
  - Simplify and give everyone statin (polypill)
  - Shared decision-making apps



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High risk	– ≥2 risk factors and 10-year risk 10-20% – Diabetes or CKD 3/4 with no other risk factors	<100	<130	<90
Moderate risk	≤2 risk factors and 10-year risk <10%	<100	<130	<90
Low risk	0 risk factors	<130	<160	NR

Mayo Clinic decision aid: https://statindecisionaid.mayoclinic.org/index.php

Low(ish) risk patient: 7% 10 year risk of CV event, moderate intensity statin

Current Risk

Select Risk Calculator

ACC/AHA ASCVD | Framingham | Reynolds

Do you have a history of events such as prior heart attack or stroke, acute coronary syndromes, history of angioplasty or stents, etc?

Yes | No

These figures are used to calculate my risk of having a heart attack in the next 10 years:

Age	56
Gender	M / F
Population Group	White or other
Smoker	Yes / No
Diabetes	Yes / No
Treated SBP	Yes / No

Conv. Unit | SI Unit

Systolic Blood Pressure	130	mmHg
HDL Cholesterol	66	mg/dL
Total Cholesterol	250	mg/dL

Select Current Intervention

Statins No | Std Dose | High Dose

Current Risk | Intervention | Issues | Notes | Document

Benefits vs Downsides according to my personal health information

Using ACC/AHA ASCVD Risk Calculator

3. View Issues

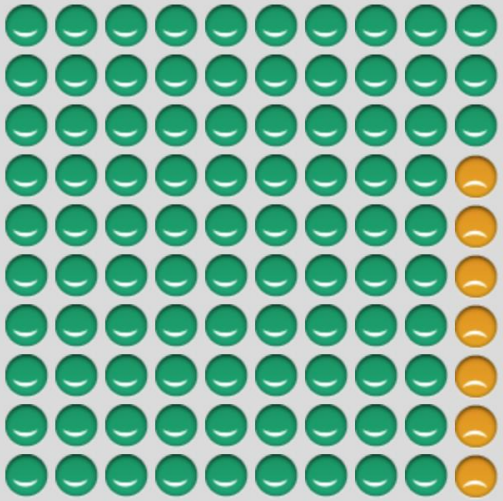
Current Risk of having a heart attack

Risk for 100 people like you who **do not** medicate for heart problems

Over 10 years

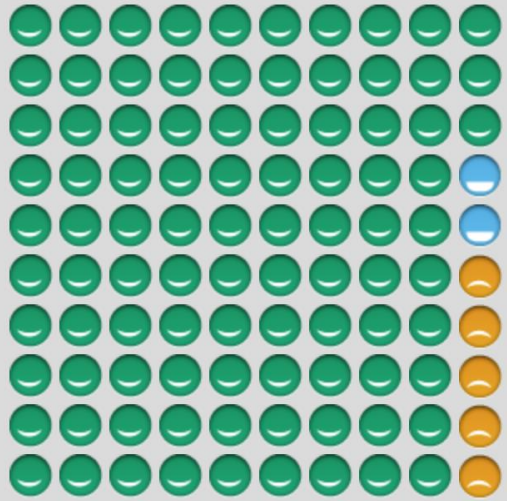
7 people will have a heart attack

93 people will have no heart attack



Future Risk of having a heart attack

Risk for 100 people like you who do take **standard dose statins**



Over 10 years

5 people will have a heart attack

93 people will have no heart attack

2 people will be saved from a heart attack by taking medicine

Mayo Clinic decision aid: https://statindecisionaid.mayoclinic.org/index.php

Higher risk patient: 22% 10 year risk of CV event, moderate intensity statin

Current Risk

Select Risk Calculator

ACC/AHA ASCVD | Framingham | Reynolds

Do you have a history of events such as prior heart attack or stroke, acute coronary syndromes, history of angioplasty or stents, etc?

Yes | No

These figures are used to calculate my risk of having a heart attack in the next 10 years:

Age	60
Gender	M / F
Population Group	White or other
Smoker	Yes / No
Diabetes	Yes / No
Treated SBP	Yes / No

Conv. Unit | SI Unit

Systolic Blood Pressure	130	mmHg
HDL Cholesterol	40	mg/dL
Total Cholesterol	240	mg/dL

Select Current Intervention

Statins No | Std Dose | High Dose

Current Risk | Intervention | Issues | Notes | Document

Benefits vs Downsides according to my personal health information

Using ACC/AHA ASCVD Risk Calculator

3. View Issues

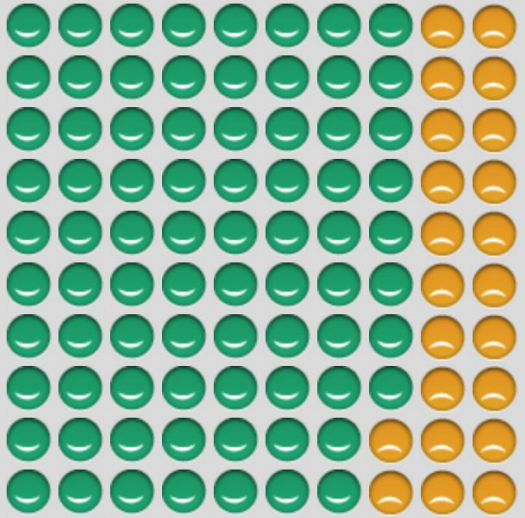
Current Risk of having a heart attack

Risk for 100 people like you who **do not** medicate for heart problems

Over 10 years

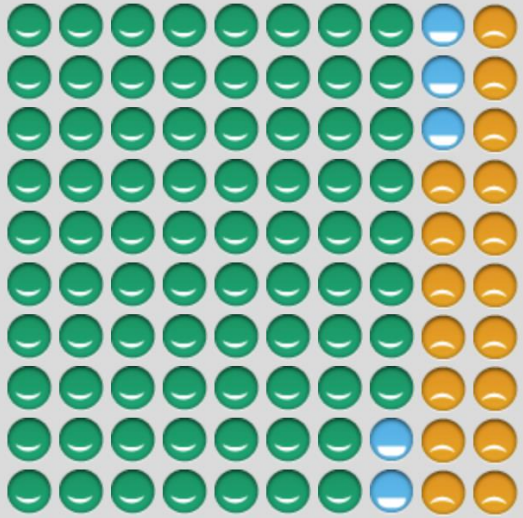
22 people will have a heart attack

78 people will have no heart attack



Future Risk of having a heart attack

Risk for 100 people like you who do take **standard dose statins**



Over 10 years

17 people will have a heart attack

78 people will have no heart attack

5 people will be saved from a heart attack by taking medicine

Mayo Clinic decision aid: https://statindecisionaid.mayoclinic.org/index.php

Higher risk patient: 22% 10 year risk of CV event, high intensity statin

Current Risk

Select Risk Calculator

ACC/AHA ASCVD | Framingham | Reynolds

Do you have a history of events such as prior heart attack or stroke, acute coronary syndromes, history of angioplasty or stents, etc?

Yes | No

These figures are used to calculate my risk of having a heart attack in the next 10 years:

Age	60
Gender	M / F
Population Group	White or other
Smoker	Yes / No
Diabetes	Yes / No
Treated SBP	Yes / No

Conv. Unit | SI Unit

Systolic Blood Pressure	130	mmHg
HDL Cholesterol	40	mg/dL
Total Cholesterol	240	mg/dL

Select Current Intervention

Statins: No | Std Dose | High Dose

Current Risk | Intervention | Issues | Notes | Document

Benefits vs Downsides according to my personal health information

Using ACC/AHA ASCVD Risk Calculator

3. View Issues

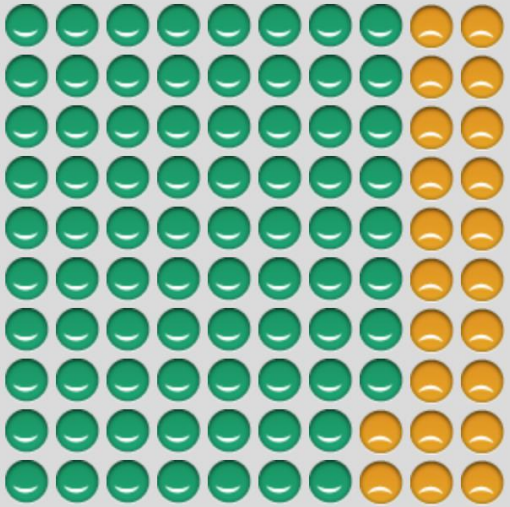
Current Risk of having a heart attack

Risk for 100 people like you who do not medicate for heart problems

Over 10 years

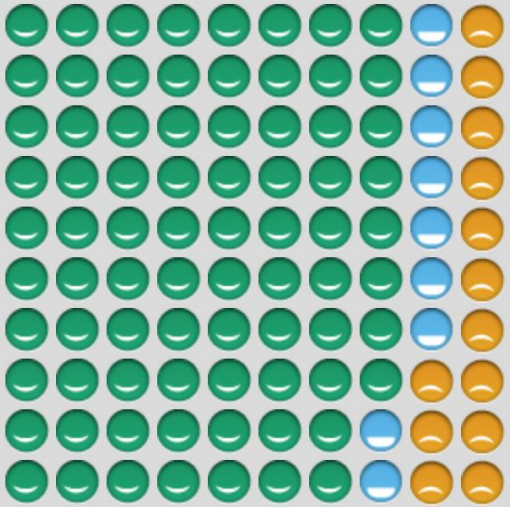
22 people will have a heart attack

78 people will have no heart attack



Future Risk of having a heart attack

Risk for 100 people like you who do take high dose statins



Over 10 years

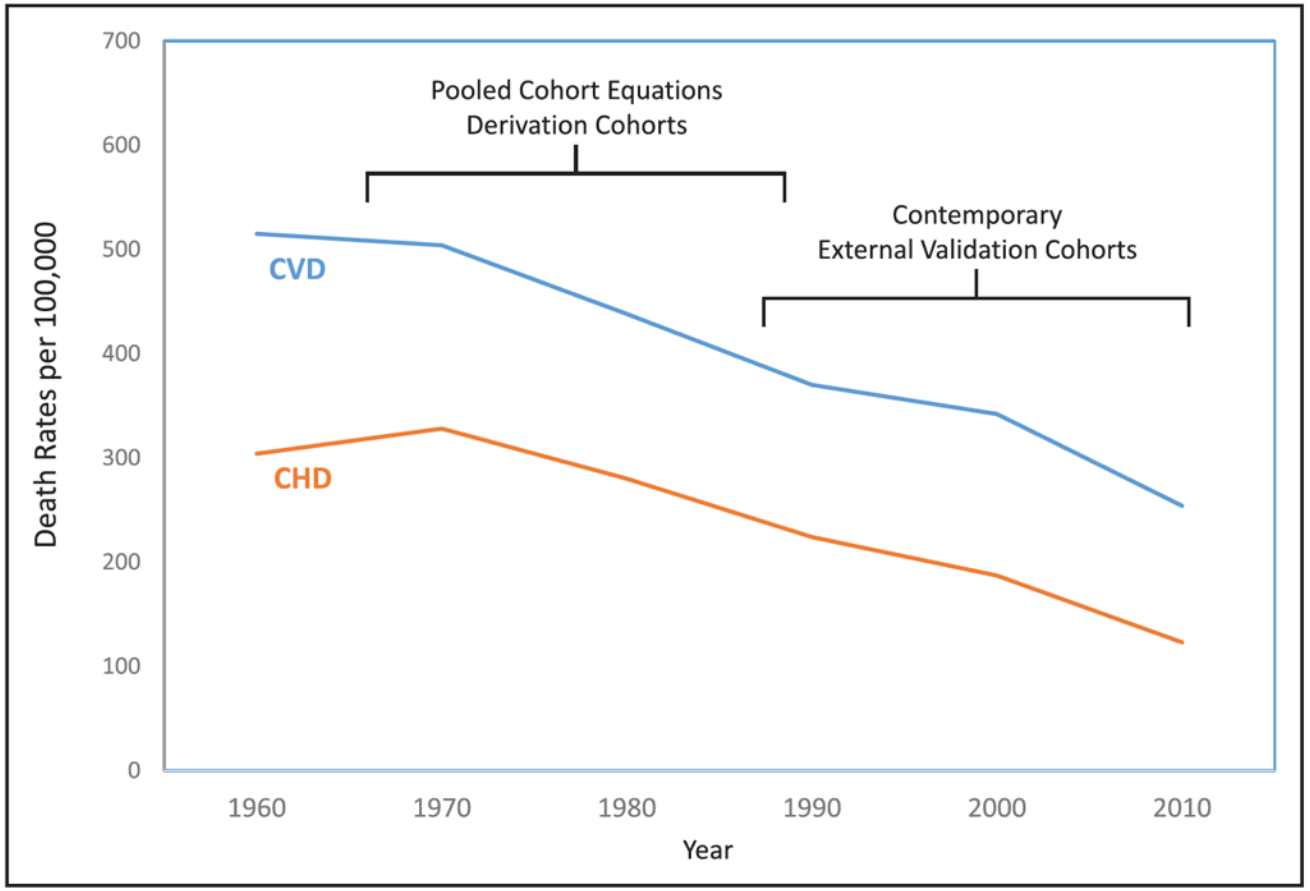
13 people will have a heart attack

78 people will have no heart attack

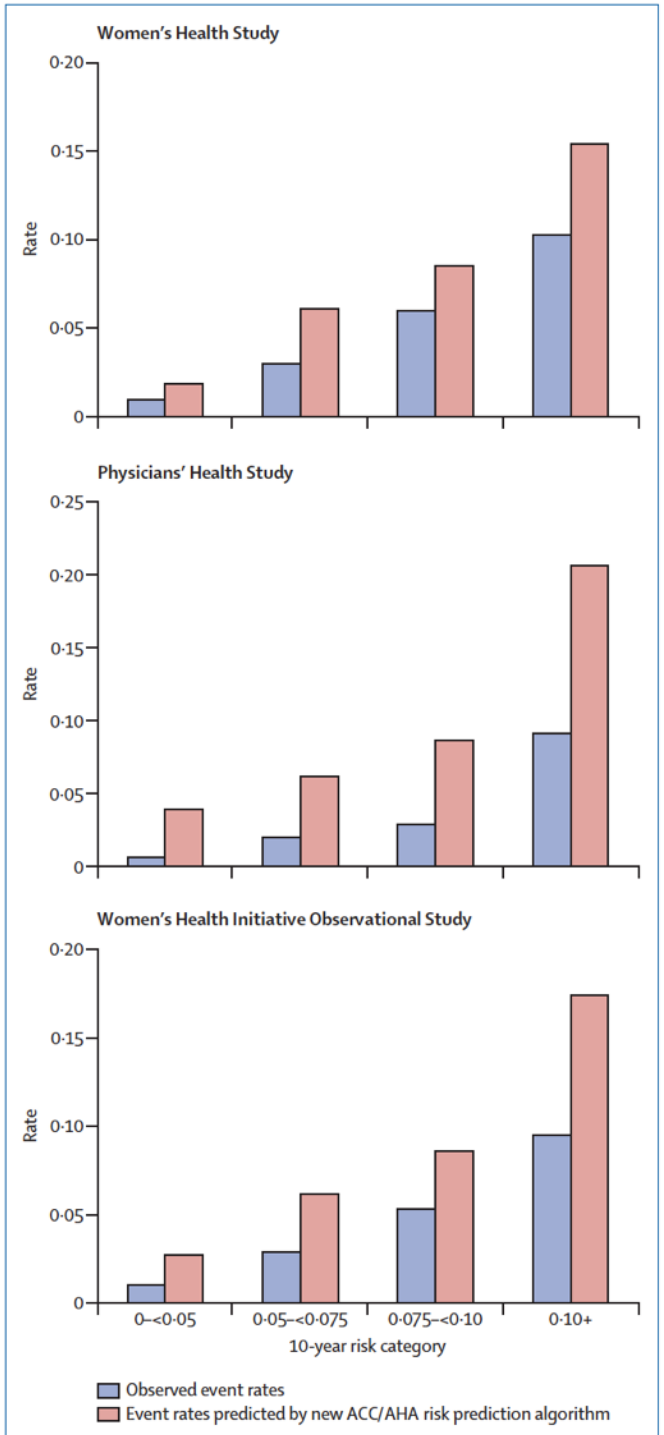
9 people will be saved from a heart attack by taking medicine

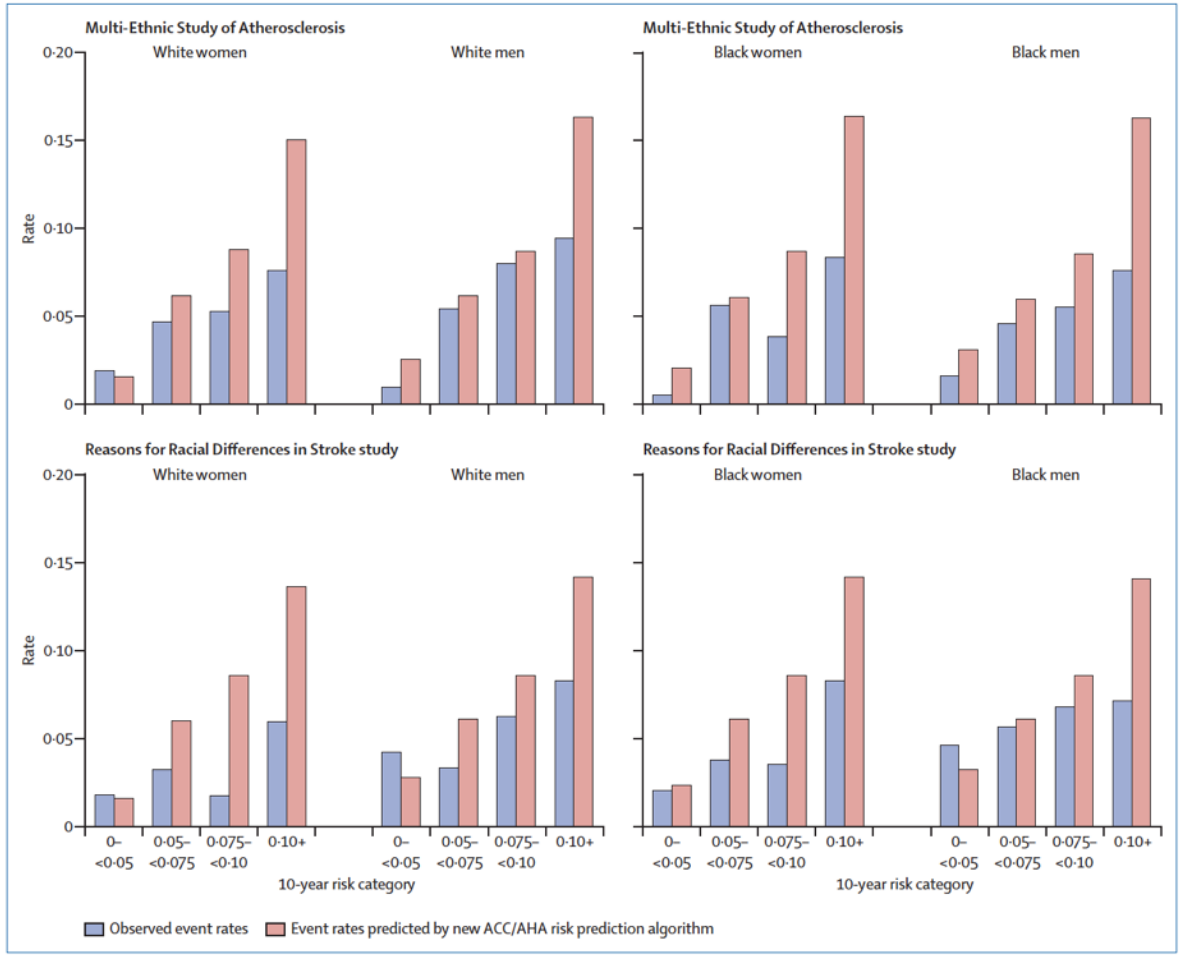
Guideline Challenges: Are Pooled Cohort Equations Accurate?

- Developed using data from 1966 – 1988 when CV risk was higher:
  - Less use of statins
  - Less use of aspirin
  - More tobacco use
  - More untreated hypertension and T2DM
- **USPSTF**: "…the best currently available risk estimation tool, which uses the Pooled Cohort Equations from the 2013 ACC/AHA guidelines on the assessment of cardiovascular risk, has been shown to over-estimate actual risk in multiple external validation cohorts.



Circulation. 2016;134:1789–1791. DOI: 10.1161/CIRCULATIONAHA.116.024246





Graphs show 10 year risk categories from Pooled Cohort Equations (x axis), predicted event rate (red) and observed event rate (blue). PCE overestimates risk by ~40% or more in these 5 cohorts.

Source: Ridker P. Lancet 2013; 382: 1762

Point-of-Care Guides

Estimating Cardiovascular Risk

PRINT COMMENTS SHARE

JONATHON M. FIRNHABER, MD, East Carolina University Brody School of Medicine, Greenville, North Carolina

Am Fam Physician. 2017 May 1;95(9):580-581.

Should we re-calibrate the Pooled Cohort Equations?

Assumes statin reduces risk of CV event by 25%.

Provides NNT to prevent one event over 10 years using PCE, and assuming 50% overestimate.

Table 1.

Reduction in Cardiovascular Events and NNT* with Statin Use

	PREDICTED 10-YEAR RISK OF A CARDIOVASCULAR EVENT (PCR EQUATIONS)	*PREDICTED RISK WITH STATIN USE*	*ABSOLUTE RISK REDUCTION*	*NNT TO PREVENT ONE EVENT*	*NNT TO PREVENT ONE EVENT ASSUMING PCR EQUATIONS OVERESTIMATE RISK BY 50%*
	30.0%	22.5%	7.5%	13	20
High risk	20.0% →	15.0%	5.0%	20 →	30
	15.0%	11.25%	3.75%	27	40
	10.0%	7.5%	2.5%	40	60
Low risk	7.5% →	5.63%	1.87%	53 →	80
	5.0%	3.75%	1.25%	80	120

Challenges: At Which Risk Level Should We Treat?

Agreement!

- **< 5% 10 year risk of CV event is "low risk", do not treat**
- **> 12% 10 year risk of CV event is "high risk", prescribe statin**

Guideline	Recommendation	NNT to prevent 1 CV event/10 yrs*	NNT to prevent 1 CV death/10 yrs*
Italian guidelines	Treat to target based on risk	Varies	Varies
AACE	Treat to target based on risk	Varies	Varies
ACC/AHA	Discuss statin: 5-7.5% Prescribe statin: > 7.5%	80 53	400 265
USPSTF Recommendation	Discuss statin: 7.5 – 10% Prescribe statin: > 10%	53 40	265 200
VA Guidelines	Discuss statin: 6 – 12% Prescribe statin: > 12%	67 33	335 165

* Assumes 25% relative reduction in event rates with statin, and 20% of events are CV death

TEST DESCRIPTION	OUT-OF-RANGE	IN-RANGE	UNITS	EXPECTED	ABNORMAL FLAG

Result Status Key: X - Test canceled or cannot be obtained

Patient is Fasting

303756 - Lipid Panel

Cholesterol, Total:	253		mg/dL	
Triglycerides:	268		mg/dL	
HDL Cholesterol:		66	mg/dL	

According to ATP-III Guidelines, HDL-C >59 mg/dL is considered a negative risk factor for CHD.

VLDL Cholesterol Cal:	54		mg/dL	
LDL Cholesterol Calc:	133		mg/dL	
Comment::		(X)		

Total cholesterol: 253 mg/dl (6.5 mmol/L)
Triglycerides: 268 mg/dl (3.0 mmol/L)
LDL cholesterol: 133 mg/dl (3.4 mmol/L)
HDL cholesterol: 66 mg/dl (1.7 mmol/L)

Patient is a 56 year old man, treated hypertension, no history of heart disease or diabetes, non-smoker, exercises daily. Vote for what you would typically recommend:

a: Do not prescribe a statin
b. Prescribe a moderate intensity statin (simvastatin 20 to 40 mg)
c. Prescribe a high intensity statin (rosuvastatin 10 mg)

Domande?