9:45 – 10:30 pm

ACC-AHA Cardiovascular Prevention Guidelines

SPEAKER
Karol E. Watson, MD, PhD, FACC

Presenter Disclosure Information

The following relationships exist related to this presentation:

- Karol Watson, MD, PhD, FACC: Consultant for Daiichi Sankyo; Merck & Co., Inc.; and Quest Diagnostics.

Off-Label/Investigational Discussion

- In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Cardiovascular Prevention Guidelines

2015

Karol E. Watson, MD, PhD, FACC
Professor of Medicine/Cardiology
David Geffen School of Medicine at UCLA
Co-director, UCLA Program in Preventive Cardiology

CASE

- A 61 year-old man with hypertension presents as a new patient. He hasn't seen a doctor regularly, but is now worried because his "best friend just dropped dead of a heart attack." He feels well and has begun drinking wine because he heard it's "good for your heart," but he wonders what else he should be doing to protect his heart.

Current medications:
Lisinopril 10 mg daily
Aspirin 81 mg daily

Pertinent physical exam findings:
BP-149/82, BMI-34.9

Pertinent lab findings:
LDL-115, HbA1c-6.1

History of NHLBI CVD Adult Clinical Prevention Guidelines

In 2013 the NHLBI decided to get out of the guidelines writing business, so turned all guidelines over to the professional organizations:
ACC / AHA and Obesity Society

HYPERTENSION

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

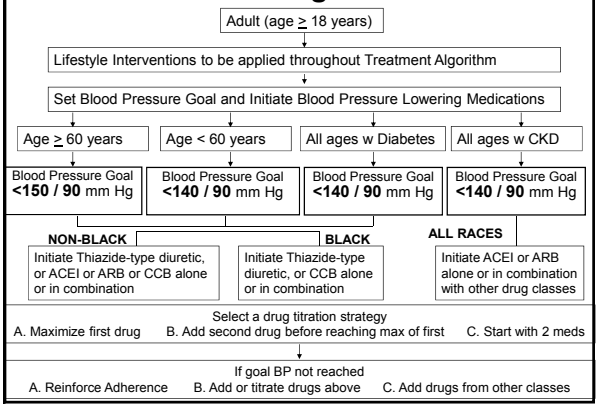
JAMA. Published online December 18, 2013. doi:10.1001/jama.2013.284427

Important to Note…

• RCTs
• conducted 1966 to present
• Minimum 1-year follow-up period
• Sample size > 100

- JNC 7 was "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure"
- JNC 8 is the "2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults"
- In JNC 8 they give 9 Evidence based Recommendations
- "… these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient."

JNC 8 Algorithm



JNC 8 in a nutshell

- Ease up on hypertension treatment in older adults (Adults 60 and older) BP goal in older adults < 150/80)
- In all others blood pressure goal < 140/90
  - Including those with diabetes and CKD
- Initial antihypertensive therapy can be a thiazide-type diuretic, CCB, ACE-I, or ARB
  - In black patients initial therapy should be with a CCB or thiazide-type diuretic
- In adults with CKD, make sure an ACE-I or an ARB is part of the antihypertensive regimen
- Don't dilly dally! If goal not reached within a month, make a change!

JAMA. Published online December 18, 2013. doi:10.1001/jama.2013.284427

CASE

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How the Guidelines Compare…

	2014 HTN (JNC 8)	2014 ASH/ISH	2013 CHEP	2013 ESH/ESC	2013 ADA
General BP goal	140/90	140/90	140/90	140/90	140/80
BP goal (elderly)	150/90 (60 yrs)	150/90 (80 yrs)	150/90 (80 yrs)	150/90 (80 yrs)	---
BP Tx - Blacks	CCB or thiazide	CCB or thiazide	---	---	---
BP goal CKD	140/90	140/90 130/90*		140/90 130/90*	140/90
BP goal DM	140/90				140/80
Initial drug choice for most	Thiazide ACE / ARB CCB	ACE / ARB If < 60 CCB or thiazide if >60	Thiazide ACE / ARB BB	Thiazide ACE / ARB CCB, BB	ACE / ARB

* With proteinuria

Not even all JNC 8 Authors Agreed with easing up at age 60

14 January 2014

Evidence Supporting a Systolic Blood Pressure Goal of Less Than 150 mm Hg in Patients Aged 60 Years or Older: The Minority View

Jackson T. Wright Jr., MD, PhD; Lawrence J. Fine, MD, DrPH; Daniel T. Lackland, PhD; Gbenga Ogedegbe, MD, MPH, MS; and Cheryl R. Dennison Himmelfarb, PhD, RN, ANP

"Landmark NIH study shows intensive blood pressure management may save lives"

- "More intensive management of high blood pressure… significantly reduces rates of cardiovascular disease, and lowers risk of death in a group of adults 50 years and older"
- This is according to initial results of the NIH sponsored Systolic Blood Pressure Intervention Trial (SPRINT).
- "The intervention in this trial…a target systolic pressure of 120 mm Hg, reduced rates of cardiovascular events…by almost a third and the risk of death by almost a quarter, as compared to the target systolic pressure of 140 mm Hg".

NHLBI press release September 10, 2015

CHOLESTEROL

CASE

- A 61 year-old man with hypertension presents as a new patient. He hasn't seen a doctor regularly, but is now worried because his "best friend just dropped dead from a heart attack." He feels well and has begun drinking wine because he heard it is "good for your heart," but he wonders what else he should be doing to protect his heart.

Current medications:
Lisinopril 10 mg daily
Aspirin 81 mg daily

Total cholesterol – 186 mg/dL
HDL – 41mg/dL
Triglycerides – 200 mg/dL

Pertinent physical exam findings:
BP-149/82, BMI-34.9

Pertinent lab findings:
LDL-115, HbA1c-6.1

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

Neil J. Stone, MD, MACP, FAHA, FACC, *Chair*
Jennifer Robinson, D, MPH, FAHA, *Vice Chair*
Alice H. Lichtenstein, DSc, FAHA, *Vice Chair*

Anne C. Goldberg, MD, FACP, FAHA	Donald M. Lloyd-Jones, MD, ScM, FACC, FAHA
Conrad B. Blum, MD, FAHA	J. Sanford Schwartz, MD
Robert H. Eckel, MD, FAHA	Patrick McBride, MD, MPH, FAHA
Daniel Levy, MD*	Sidney C. Smith, Jr, MD, FACC, FAHA
David Gordon, MD*	Karol Watson, MD, PhD, FACC, FAHA
C. Noel Bairey Merz, MD, FAHA, FACC	Susan T. Shero, MS, RN*
	Peter W.F. Wilson, MD, FAHA

General Principles of the Guidelines

- **All adults should adhere to a healthy lifestyle**.
- **Statin therapy is recommended for adults in groups demonstrated to benefit** .

1. Adults with clinical ASCVD
2. Adults with LDL-C ≥190 mg/dl
3. Adults with diabetes
4. Adults with an estimated 10 year ASCVD risk of ≥ 7.5%

Statin Effects on Major Vascular Events

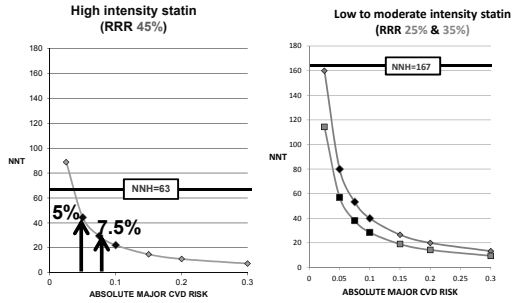
All fixed dose trials
NONE were titration trials

Endpoint	Events (%) Treatment	Control	Rate Ratio (CI)
Non-fatal MI	2001 (4·4)	2769 (6·2)	0·74 (0·70 – 0·79)
CHD death	1548 (3·4)	1960 (4·4)	0·81 (0·75 – 0·87)
Any major coronary event	**3337 (7·4)**	**4420 (9·8)**	**0·77 (0·74 – 0·80)**
CABG	713 (3·3)	1006 (4·7)	0·75 (0·69 – 0·82)
PTCA	510 (2·4)	658 (3·1)	0·79 (0·69 – 0·90)
Unspecified	1397 (3·1)	1770 (3·9)	0·76 (0·69 – 0·84)
Any coronary revascularisation	**2620 (5·8)**	**3434 (7·6)**	**0·76 (0·73 – 0·80)**
Haemorrhagic stroke	105 (0·2)	99 (0·2)	1·05 (0·78 – 1·41)
Presumed ischaemic stroke	1235 (2·8)	1518 (3·4)	0·81 (0·74 – 0·89)
Any stroke	**1340 (3·0)**	**1617 (3·7)**	**0·83 (0·78 – 0·88)**
Any major vascular event	**6354 (14·1)**	**7994 (17·8)**	**0·79 (0·77 – 0·81)**

0·5 1·0 1·5
Favors statin

CTT. Lancet 2008 371: 117-125

Statins for primary prevention of CVD NNT to prevent one major CVD event compared to NNH over 5 years



ASCVD Risk Estimator

- Gender
- Age
- Race
- Total Cholesterol
- HDL Cholesterol
- Systolic BP
- Treatment for BP?
- Diabetes
- Smoking

http://www.apple.com/itunes/affiliates/download/?id=808875968

Or just google:
"ASCVD risk calculator"

Age provides an integrated estimate of lifetime exposure to risk factors

New guidelines may put 13 million more on statins
TIME By Alice Park, TIME.com updated 6:12 PM EDT, Wed March 19, 2014

Risk Calculator for Cholesterol Appears Flawed
By GINA KOLATA
Published: November 17, 2013 | 794 Comments

EDITORIAL
Cholesterol Guidelines Under Attack
By THE EDITORIAL BOARD
Published: November 18, 2013

Headlines from NPR, *The New York Times*, and *Time*

"Evidence"

The New York Times

Risk Calculator for Cholesterol Appears Flawed

By GINA KOLATA
Published: November 17, 2013 | 794 Comments

Last week, the nation's leading heart organizations released a sweeping new set of guidelines for lowering cholesterol, along with an online calculator meant to help doctors assess risks and treatment options. But, in a major embarrassment to the health groups, the calculator appears to greatly overestimate risk, so much so that it could mistakenly suggest that millions more people are candidates for statin drugs.

Enlarge This Image

Mark Graham for The New York Times

Dr. Nancy Cook and Dr. Paul M. Ridker of Harvard Medical School found that a new online calculator used to assess heart treatment options overestimated the risks that many people face.

The apparent problem prompted one leading cardiologist, a past president of the American College of Cardiology, to call on Sunday for a halt to the implementation of the new guidelines.

"It's stunning," said the cardiologist, Dr. Steven Nissen, chief of cardiovascular medicine at the Cleveland Clinic. "We need a pause to further evaluate this approach before it is implemented on a widespread basis."

The controversy set off turmoil at the annual meeting of the American Heart Association, which started this weekend in

General Principles of the Guidelines

NO MORE LDL GOALS

- **All adults should adhere to a healthy lifestyle**.
- **Statin therapy is recommended for adults in groups demonstrated to benefit.**
- **Current evidence is inadequate to support treatment to specific LDL-C and/or non-HDL-C goals.**
- **Initiate the appropriate intensity of statin therapy**

Stone NJ et al. Circulation. 2014;129:S1-45.

Intensity of Statin Therapy

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 **Rosuvasatin 20** *(40)* **mg**	**Atorvastatin 10 (***20***) mg** **Rosuvastatin** *(5)* **10 mg** **Simvastatin 20-40 mg‡** **Pravstatin 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*

Common Misconceptions About the Cholesterol Guidelines

- **All patients with a 10-year CVD risk of ≥ 7.5% must be treated with a statin**
  - Guidelines emphasize patient-provider discussion
- **There is no longer a role for rechecking lipids**
  - Lipids should be re-checked at 3-12 weeks to verify therapeutic response and monitor adherence; Re-checks should occur q 3-12 months
- **There is no role for non-statin therapy**
  - There remains a role for add-on therapy at provider's discretion in higher risk patients
- **The new risk estimator abandons Framingham**
  - The new risk estimator includes Framingham along with 3 other cohorts that add power and diversity

Adapted from Blaha and Wong. FEBRUARY 05, 2014 Cardiosource

OBESITY

CASE

- A 61 year-old man with hypertension presents as a new patient. He hasn't seen a doctor regularly, but is now worried because his "best friend just dropped dead from a heart attack." He feels well and has begun drinking wine because he heard it is "good for your heart," but he wonders what else he should be doing to protect his heart.

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Pertinent physical exam findings:
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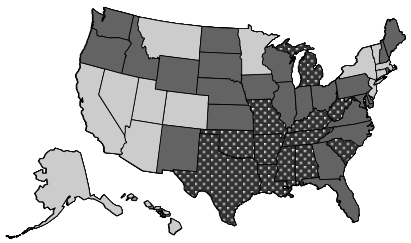
Pertinent lab findings:
LDL-115, HbA1c-6.1

US Obesity trends

2010

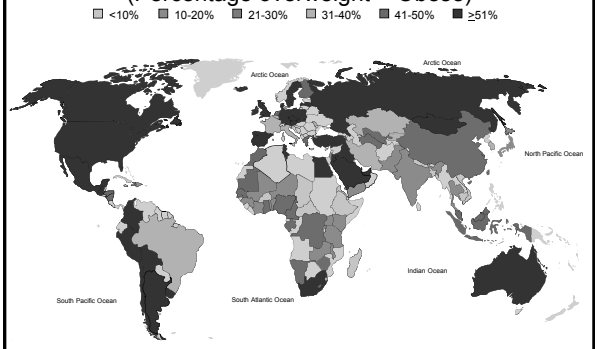
(*BMI ≥30, or ~ 30 lbs overweight for 5'4" woman)



No Data | <10% | 10%–14% | 15%–19% | 20%–24% | >20% | >25%

Worldwide Obesity trends

(Percentage overweight + Obese)



2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Nutrition, American Society for Parenteral and Enteral Nutrition, American Society for Preventive Cardiology, American Society of Hypertension, Association of Black Cardiologists, National Lipid Association, Preventive Cardiovascular Nurses Association, The Endocrine Society, and WomenHeart: The National Coalition for Women with Heart Disease

Jensen MD, et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22(S2):S1-S410.

For Weight Loss

- Assess
  - Weight, BMI, Waist circumference
- Advise
  - Sustained weight loss of even 3%–5% is likely to result in clinically meaningful benefit
- Assist
  a. Prescribe 1,200–1,500 kcal/d for women; 1,500–1,800 kcal/d for men
  b. Prescribe one of the evidence-based diets (such as low-carbohydrate, high-fiber, or low-fat)
  c. a *comprehensive lifestyle program* including physical activity

Jensen MD, et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22(S2):S1-S410.

For Weight Maintenance

- Assess
  - monitor body weight regularly (at least weekly)
  - Regular contact (at least monthly)
- Advise
  - Regular physical activity (i.e., 200–300 min/wk),
  - consume a reduced-calorie diet (needed to maintain lower body weight).
- Assist
  - Trained interventionist

Jensen MD, et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22(S2):S1-S410.

Obesity guidelines Diet Recommendation

Prescribe a diet to achieve **reduced calorie intake** for obese or overweight individuals who would benefit from weight loss, as part of a comprehensive lifestyle intervention. Any one of the following methods can be used to reduce food and calorie intake:

a. Prescribe **1,200–1,500 kcal/d for women and 1,500–1,800 kcal/d for men** (kilocalorie levels are usually adjusted for the individual's body weight);
b. Prescribe a 500-kcal/d or 750-kcal/d energy deficit; or
c. Prescribe one of the evidence-based diets that restricts certain food types (**such as high-carbohydrate foods, low-fiber foods, or high-fat foods**) in order to create an energy deficit by reduced food intake.

Jensen MD, et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22(S2):S1-S410.

Obesity guidelines- Pharmacotherapy Recommendation

- Conspicuous by its absence from the guidelines, is pharmacotherapy.
- When the obesity guidelines were developed, the only medications that were FDA approved for weight loss were sibutramine and orlistat, with sibutramine having since been taken off the market.
- The writing group included pharmacotherapies for obesity based on expert opinion
- Pharmacotherapy is recommended for patients who are unable to achieve and sustain weight loss with comprehensive lifestyle alone. If they are not effective in for a given patient's weight loss, they should not be continued.

Obesity guidelines- Surgery Recommendation

Advise adults with a BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 with obesity-related comorbid conditions who are motivated to lose weight and who have not responded to behavioral treatment with or without pharmacotherapy with sufficient weight loss to achieve targeted health outcome goals that bariatric surgery may be an appropriate option ...

Jensen MD, et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22(S2):S1-S410.

Weight regulation in Humans

- The human body is hardwired to know how many fat cells are on board and to keep body weight stable
- At ~ 5% to 10% weight loss the human body responds by:
  - Lowering metabolic rate (more than 5%-10%)
  - Lowering the hormones that signal satiety after eating
  - Increase thoughts and hormones to make humans seek out and eat more food
  - All as part of a defense of body weight to survive
    - This does not change with time (always trying to get back to that highest weight)

Sumithran P et al. *N Engl J Med*. 2011;365:1597-1604

CASE

Recommendations

1. Daily walking for exercise
2. Calorie reduced diet of his choice
3. Referral to our weight loss center
4. Screening for diabetes
5. Increase Lisinopril to 20 mg daily
6. Continue Aspirin 81 mg daily
7. Begin Atorvastatin 40 mg daily

The Safety of Statins

- Liver
- Muscle
- Cognitive Effects
- Cancer
- Diabetes

FDA: Liver Injury Called Rare

February 2012

- In early clinical trials LFT elevations were seen, so health care providers were advised to regularly follow LFTs. However, the FDA found that statin liver damage is rare, and LFTs are not effective at predicting or preventing this rare side effect.
- "So FDA is now recommending that LFTs be performed before statin treatment begins and then as needed if there are symptoms of liver damage."

www.fda.gov/ ForConsumers/ConsumerUpdates

The Safety of Statins

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- Muscle
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- Cancer
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Statin Muscle Adverse Effects

Muscle AE	Incidence above placebo (per 100,000)
Myalgias	1,500 to 10,000
Myopathy (Sx + CK)	5
Rhabdomyolysis	1.6

Adapted from Law M, Rudnicka AR. *Am J Cardiol.* 2006;97:52C-60C

Statin related Muscle Adverse Effects

- In randomized trials, myalgia is reported in < 5% of patients in both the statin and placebo arms.
- Clinical experience suggests closer to 10%.
- Myopathy and rhabdomyolysis are associated with statin therapy, as a class effect
- This risk increases with increased statin dose and with drug-drug interactions
- Prior to initiating statins, patients need to know to promptly report any unexplained muscle pain and/or weakness

.McKenney JM et al. Am J Cardiol. 2006;97:89C-94C.

Factors That Increase the Risk of Statin-Induced Myopathy

Patient Characteristics	Statin Properties
Increasing age	High systemic exposure
Female sex	Increased dose
Renal insufficiency	High bioavailability
Hepatic dysfunction	Limited protein binding
Hypothyroidism	Potential for drug-drug interactions metabolized by CYP pathways (particularly CYP450 3A4)
Diet or Meds	
Polypharmacy	

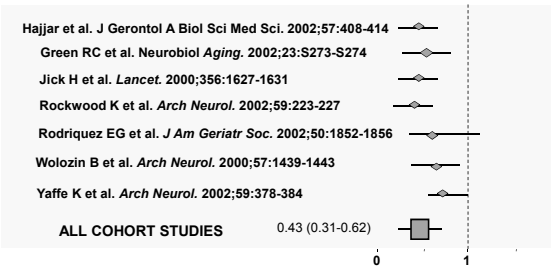
Adapted from Rosenson RS. *Am J Med.* 2004;116:408-416

The Safety of Statins

- Liver
- Muscle
- Cognitive Effects
- Cancer
- Diabetes

Statins and Cognitive Function: NO impairment seen in observational studies

Results of 7 observational studies



Etminan et al. *Pharmacotherapy.* 2003;23:726-730

HPS – Results of Testing for Neuropsychiatric Disorders

20,536 adults (aged 40-80 years) with atherosclerotic disease or diabetes were randomized to 40 mg simvastatin daily or matching placebo for 5 years. No effect on cognition

Measure	Simvastatin	Placebo
Cognitively Impaired*	23.7%	24.2%
Dementia	0.3%	0.3%
Psychiatric Disorder	0.7%	0.7%
Suicide	0.1%	0.1%

Heart Protection Study Collaborative Group. *Lancet.* 2002;360:7-22

PROSPER – Results of Testing for Cognitive Function

5804 elderly (> 70 yo) patients were randomized to 40 mg of pravastatin daily or matching placebo for 5 years. No effect on cognition

Measure	Pravastatin - Placebo
Number of correct letter digits recalled	-0.01 (-0.24-0.23) p=0.95
Number of words Remembered	+0.02 (-0.12-0.16) p=0.80
Time needed to complete Stroop test	+0.8 s (-0.4-2.0) p=0.19
MMSE score	+0.06 (-0.04-0.16) p=0.26

Shepherd J et al. *Lancet.* 2002;360:1623-1630

FDA Investigating Reports of Memory Loss

February 2012

- Rare post-marketing reports of cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use.
- These reported symptoms are generally not serious and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptom resolution (median of 3 weeks).

www.fda.gov/ ForConsumers/ConsumerUpdates

The Safety of Statins

- Liver
- Muscle
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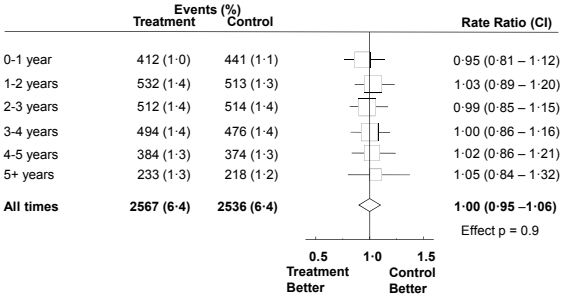
Effects on CANCER incidence per mmol/L LDL cholesterol by year



Cholesterol Treatment Trialists. Lancet 2005 366: 1267-1134

The Safety of Statins

- Liver
- Muscle
- Cognitive Effects
- Cancer
- Diabetes

Association between statins and development of diabetes

Statin	Odds ratio (95% CI)
Overall (n=91 140)	1.09 (1.02–1.17)
Atorvastatin only (n=7773)	1.14 (0.89–1.46)
Simvastatin only (n=18 815)	1.11 (0.97–1.26)
Rosuvastatin only (n=24 714)	1.18 (1.04–1.33)
Pravastatin (n=33 627)	1.03 (0.90–1.19)
Lovastatin (n=6211)	0.98 (0.70–1.38)

Sattar N et al. *Lancet* 2010;375:735-42.

FDA reports on the Risk of Diabetes with statins

February 2012

- A small increased risk of elevated blood sugar levels and the development of Type 2 diabetes have been reported with the use of statins.
- *"Clearly we think that the heart benefit of statins outweighs this small increased risk"* But blood-sugar levels may need to be assessed after instituting statin therapy.

www.fda.gov/ ForConsumers/ConsumerUpdates

Statins

- Statins are the most efficacious LDL-C lowering drugs and have the greatest CV risk reduction
- Liver damage due to statins is extremely rare
- Statins can produce muscle pain and weakness, but the risk of true rhabdomyolysis is very small
- Clinical trials have not found evidence of cancer or cognitive impairment with statins
- Statins can increase blood glucose levels minimally leading to increased reports of diabetes
- In patients at high CVD risk, the benefits of statins far outweigh the risks