Cardiovascular risk management: Current controversies

Medwise

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Clinical Controversy

‘Middle English *controversie,* from Anglo-French, from Latin *controversia,* from *controversus*

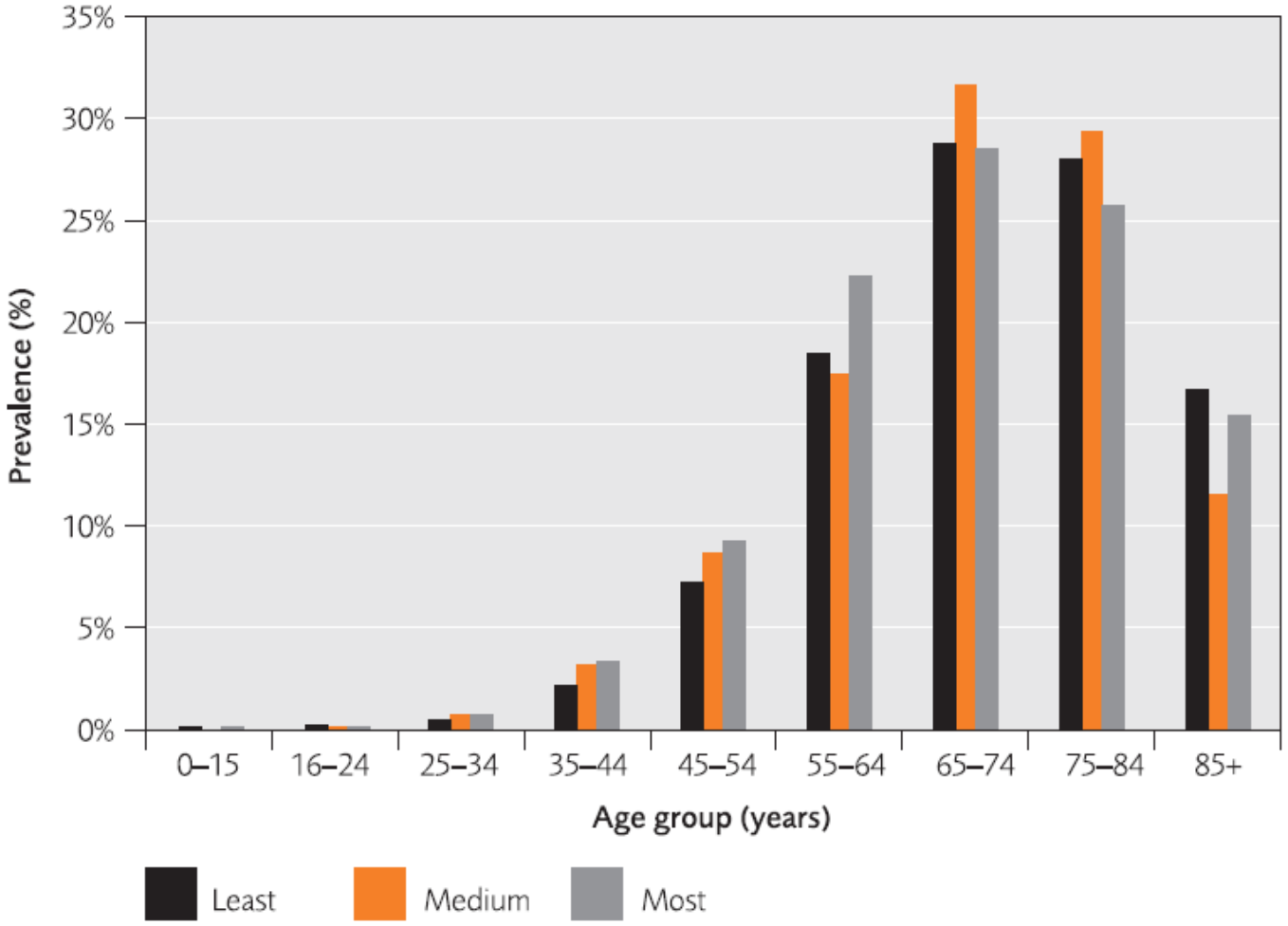
strong disagreement about something among a large group of people’

Despite claims of consensus, scientific findings are rarely absolute because it's the nature of science to evolve.

- Cardiovascular disease is the second leading cause of mortality in New Zealand
  - Mortality falling
  - Growing burden of morbidity

- 20% CVD due to smoking (WHO 2002)
- 20% CVD in developed countries due to physical inactivity (WHO 2002)
- Also obesity, psychosocial wellbeing, social deprivation, & poor nutrition
- CHD risk is related to cholesterol levels and blood pressure correlates with risk of death from CHD

Figure 2. Prevalence of statin use by age and socioeconomic deprivation (percentage of population)



J PRIM HEALTH CARE 2014;6(1):17-22

- Cardiovascular risk management
  - patient selection for treatment
- Statins (& doses)
  - in primary and secondary prevention
- Aspirin
  - in primary prevention

NZ Primary Care Handbook

- Updated 2013
- New CVDRA equations available in 2014 to assess *Combined* risk
- Intensity of interventions = proportional to risk

- Intervention based on combined risk (not primarily on individual risk factor levels) – no change
- Recommended age to offer assessment – no change

2013 Update: NZ Primary Care Handbook - *Recommended interventions*

- People with CVD risk 10-20%
  - discuss statins
  - discuss BP lowering
  - aspirin not recommended
  - No target LDL or BP

- People with CVD risk > 20% (or established CV disease)
  - Statins & BP meds STRONGLY recommended

  - Aspirin
    - Can be considered for people with CVD risk > 20% (BUT no established CV disease)
    - STRONGLY recommended for people with established CV disease

Table 5: The recommended interventions, goals and follow-up based on cardiovascular risk assessment

Cardiovascular risk	Lifestyle	Drug therapy	Follow-up
Established CVD	Intensive lifestyle advice (diet, physical activity, smoking cessation) simultaneously with drug treatment	Strong evidence of benefit from BP-lowering, statins and antiplatelet therapy in this group	Risk factor monitoring initially at 3 months, then as clinically indicated
CVD risk calculated >20%	Intensive lifestyle advice (diet, physical activity, smoking cessation) simultaneously with drug treatment	Strong evidence of benefit from BP-lowering, statins and antiplatelet therapy in this group	Annual review or as clinically indicated
10% to 20%	Specific individualised lifestyle advice (diet, physical activity, smoking cessation)	Good evidence demonstrating benefit from BP-lowering and/ or statin therapy in this group. The absolute benefits will be smaller at lower levels of combined risk, with increasing benefit of treating both BP and lipids for those with higher five-year combined risk Shared decision-making approach to consider benefits and harms of drug treatment of modifiable risk factors	As clinically indicated, with a more intensive focus for higher combined risk patients If patient not on drug treatment, offer CVD risk assessment at reassessment – at one year for 15% to 20% risk and every two years for 10% to 15% risk
<10%	Lifestyle advice (diet, physical activity, smoking cessation)	Evidence of benefit from BP-lowering and statin therapy in this group is unclear; use a shared decision-making approach to consider benefits and harms of treatment of modifiable risk factors	Offer further CVD risk assessment in 5 to 10 years

New Zealand Primary Care Handbook 2012 , Updated December 2013

CVRA – Patient Selection

- NZ treatment threshold ↓ - previously 15%
- US and proposed NICE guidance also ↓ threshold

- Worldwide trend to extend the use of statins to people at LOW risk of cardiovascular disease
- Statins effectively reduce relative CV risk by ~ 20-30%
  - If 10 yr risk of MI is 1% → reduction to 0.8%
  - If 10 yr risk is 12% → reduction to 9%

- Overtreatment risk?
- Increases importance of shared decision-making
- Why has this trend occurred?

Statins in primary prevention (low risk) - Yes

- The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Cholesterol Treatment Trialists' (CTT) Collaborators. Lancet 2012; 380(9841):581-590.
  - *In individuals with 5-year risk of major vascular events lower than 10%, each 1 mmol/L reduction in LDL cholesterol produced an absolute reduction in major vascular events of about 11 per 1000 over 5 years*

- Taylor F et al. Statins for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2014, Issue 1
  - *Reductions in all-cause mortality, major vascular events and revascularisations were found with no excess of adverse events among people without evidence of CVD treated with statins.*

Statins in primary prevention (low risk)- No

- Statins and All-Cause Mortality in High-Risk Primary Prevention: A Meta-analysis of 11 Randomized Controlled Trials Involving 65 229 Participants
  Arch Intern Med. 2010;170(12):1024-1031
- Do statins have a role in primary prevention? An update.
  THERAPEUTICS LETTER 2010:77
- Statins for the primary prevention of cardiovascular disease.
  Cochrane Database Syst ev. 2011
  - *Any decision to use statins for primary prevention should be made cautiously and in the light of an assessment of the patient's overall cardiovascular risk profile. Widespread use of statins in people at low risk of cardiovascular events--is not supported by the existing evidence.*

Year	Number of RCTs [ref]	Total mortality RR[95%CI]	Total CHD RR[95%CI]	Conclusions	Declared conflict of interest
2006[2]	7 [8-14]	0.92 [0.84-1.01]	0.71 [0.60-0.83]	Mortality not decreased	4/4 authors no conflicts
2007[3]	8 [8-14, 17]	0.95 [0.89-1.01]	0.77 [0.71-0.83]	Mortality not decreased	1 author none 1 author consultant in litigation against Pfizer
2008[4]	20 [8-12, 14-18, 20-29]	0.93 [0.87-0.99]	0.77 [0.63-0.95]	Mortality significantly decreased	6/6 authors no declaration
2009[5]	10 [8-14, 17-19]	0.88 [0.81-0.96]	0.70 [0.61-0.81]	Mortality significantly decreased	6/12 authors financial conflict
2010[6]	11 [8-12, 14-19]	0.91* [0.83-1.01]	NR	Mortality not decreased	5/7 authors financial conflict

Do statins have a role in primary prevention? An update.
THERAPEUTICS LETTER ISSUE 77 / MAR - APR 2010

Statins in primary prevention: NNT Summary

- NNT = 60 for non fatal heart attack

For those who took a statin for 5 years;

- 98% saw no benefit
- 0% were helped by being saved from death
- 1.6% were helped by preventing a heart attack
- 0.4% were helped by preventing a stroke

- And 10% experienced muscle pain

- Insufficient RCT evidence to support using LDL goals or targets
  - No trials have directly compared effects of low intensity with high intensity statin therapy for primary prevention.
    - Statin INTENSITY relates to LDL lowering ability
  - The absolute benefit of treatment will be proportional to the underlying absolute risk. Determining when the benefits of treatment outweigh its burdens, requires determination of the patient's underlying risk rather than aiming to target a specific goal LDL-C.
- Hence, no additional lipid-lowering medication recommended if targets not reached.

- HIGH INTENSITY
  - Daily dose lowers LDL-C by approx ≥ 50%
  - e.g. *Atorvastatin 40-80mg* or *Rosuvastatin 20mg*

- MODERATE INTENSITY
  - Daily dose lowers LDL-C by approx 30% - 50%
  - e.g. *Atorvastatin 10mg, Rosuvastatin 10mg, simvastatin 20-40mg, Pravastatin 40mg, Fluvastatin 40mg bd*

- LOW INTENSITY
  - Daily dose lowers LDL-C by < 30%
  - e.g. *Simvastatin 10mg, Pravastatin 10-20mg*

2013 ACC/AHA Blood Cholesterol Guideline

Starting Doses

New Zealand Primary Care Handbook 2012 , Updated December 2013

- People with known CVD (or combined risk >20%)
  - 20-40mg atorvastatin
- People with acute coronary syndrome (ACS)
  - 80mg atorvastatin
- People without known CVD (combined risk 10% - 20%)
  - 20mg atorvastatin

- cardiovascular disease events and total mortality ↓ irrespective of the initial cholesterol concentration

Statins -HIGH dose better than LOW dose?

- No difference in death, cardiovascular death, or fatal MI
- High dose reduced non-fatal MI and CHD death;
  - 9.4% vs 10.5%,

High dose statins	Low-moderate statins
↓ mortality ↓ combined endpoint of non-fatal MI and CHD death	↓ mortality
With an NNT of 91 And a NNH of 47	With an NNT of 56

European Heart Journal (2011) 32, 1409–1415

2013 ACC/AHA Blood Cholesterol Guideline

- *Treatment Benefits for 4 groups*

1. People with cardiovascular disease (ACS, MI, angina, stroke, TIA, PAD)
2. People with LDL-C levels ≥ 5mmol/L
3. People 40-75 years old with diabetes and LDL-C levels 1.8 – 4.8mmol/L
4. People 40-75 years old with LDL-C levels 1.8 – 4.8mmol/L and a 10 year risk of 7.5% or higher.

NICE Lipid Modification
to be updated Jul14

- DRAFT Priorities*
  - Primary prevention - statin therapy is recommended for adults who have a ~~20%~~ ***10%*** or greater 10-year risk of developing CVD. Treatment for the primary prevention of CVD should be initiated with ~~simvastatin 40 mg~~ ***atorvastatin 20mg***.
  - Secondary prevention – statin therapy indicated. People with acute coronary syndrome should be treated with ***atorvastatin 80mg***. Consider increasing dose if ~~TC > 4mmol/L or LDL-C > 2mmol/L~~ ***a greater than 40% reduction in non-HDL cholesterol is not achieved***

Is Aspirin useful in primary prevention?

- Seshasai et al. Effect of Aspirin on Vascular and Nonvascular outcomes. Meta-analysis of RCTs. *Arch Intern Med 2012;172(3):209-216.*
  - *Despite important reductions in nonfatal MI, aspirin prophylaxis in people without prior CVD does not lead to reductions in cardiovascular death. Clinically important bleeding events offset the benefits of aspirin.*
- Antithrombotic Trialists' (ATT) Collaboration. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet 2009;373(9678):1849-60*
  - *In primary prevention without previous disease, aspirin is of uncertain net value as the reduction in occlusive events needs to be weighed against any increase in major bleeds.*

Event	Odds ratio (95% CI)
Cardiovascular events	0.90 (0.85-0.96)
Nonfatal MI	0.80 (0.67-0.96)
Cardiovascular death	0.99 (0.85-1.15)
Cancer mortality	0.93 (0.84-1.03)
Nontrivial bleed	1.31 (1.14-1.50)

Arch Intern Med 2012; 172(3):209-16.

Aspirin in primary prevention: NNT Summary

- NNT = 1667 for heart attack or stroke

For those who took aspirin daily for 1 year;

- 99.94% saw no benefit
- 0% were helped by avoiding death
- 0.05% were helped by preventing a non-fatal heart attack
- 0.01% were helped by preventing a non-fatal stroke

- And 0.03% were harmed by developing a major bleeding event

References

- *Cochrane Database Systematic Reviews 2011*
- *Cochrane Database of Systematic Reviews 2013.*
- *Journal of Primary Healthcare 2014;6(1):17-22*
- *Lancet 2012;380(9841):581-590.*
- *Therapeutics Letter 2010:77*
- *Arch Intern Med. 2010;170(12):1024-1031*
- *www.thennt.com*
- *Arch Intern Med 2012; 172(3):209-16.*
- *Lancet 2009;373:1849.*
- *European Heart Journal 2013;34:3412–3418*
- *BMJ 2009;339:b4531*
- *Health Technol Assess 2013;17(43)*
- *New Zealand Primary Care Handbook 2012; Updated Dec 2013*
- *2013 ACC/AHA Blood Cholesterol Guideline*
- *NICE Guidance.*

REFER if your patient:

- Needs help with optimal control of a chronic condition
  - such as diabetes, hypertension, CHF, pain, arthritis
- Is taking multiple medications
  - to simplify, ensure appropriate dosing times, manage or prevent drug related problems
- Recent hospitalisation
  - & potential medicine changes
- Is taking medication with a high risk of adverse effects, narrow therapeutic index and/or monitoring requirements.
- Is non-adherent or unable to manage their medicines
- Could benefit from medication counselling
  - new medications
- Needs help tapering or changing a medication

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