Faculty of Health and Medical Sciences

Initiation of statin therapy for primary prevention: Overprescribing in postmenopausal women with 'hypercholesterolemia'?

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Agenda

- Background
- Aims
- Data and Methods
- Results
- Conclusion and perspectivation

Background

1994

Statins, the first cholesterol-lowering medicine to reduce the high mortality after myocardial infarction (MI)

To day

One of the most prescribed medicine
Recommended in guidelines for

- ❑ A range of ischemic cardiovascular diseases (CVD)
- ❑ Diabetes
- ❑ People without CVD or diabetes, but at high CVD risk
  - The high risk strategy for primary CVD prevention
  - Risk scoring charts (e.g. SCORE): Lipid & blood pressure
  - Lowering limits for 'high' - US vs Europe

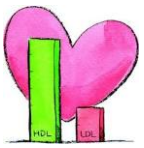
Statins for primary prevention, evidence based?

1) **Trials on statins for primary prevention**
   Participants with CVD (largely) excluded – *not* diabetes
   Unclear beneficial effect esp. in women; Stratifying by gender?
   Under reporting of 'subjective' side effect i.e. muscle problems
2) **Treatment goal (expert):** Total cholesterol < 5mmol/l-
3) **Menopause:** Increase in cholesterol levels
4) **Cholesterol as risk factor:** Sex differences

Overprescribing of statin for primary prevention – especially for women?

Aims

1) Explore incident statin-prescribing for primary prevention according to gender and age during 2005-2009
2) Estimate the fraction of statin initiation prescribed for primary prevention.



Data and methods

Study population:

All Danish inhabitants aged 20+ (N=4,424,818, full follow-up since 1996) were followed in the individual-level registries during 1996-2009.

Register data

- Demographic data: Linkage encrypted code; sex; birth, death, emigration date
- Patient registry: Discharge diagnoses, hospital procedures
- Prescription registry: Dispensing date, ATC code, volume
  No information on prescribing indication

➢ **Register based indication hierarchy**

Register based indication hierarchy

Actual CVD status for each cohort member

- Information from Patient and Prescription Registry
  Applied as disease and diagnosis markers

Diagnosis markers as proxy for statin prescribing indication

- Most serious CVD diagnosis or diabetes
- Left with two groups
  1) primary hypertension, 2) 'no diagnosis' (hypercholesterolemia)
  Target group for the high risk strategy / 'Asymptomatic persons'

Wallach-Kildemoes H, Hendriksen C, Andersen M (2012) Drug utilization according to reason for prescribing: A pharmacoepidemiological register-based method. Pharmacoepidemiology and Drug Safety

Two outcome measures

1. Incidence of statin therapy according to indication:
   Number incident users *per* person year at risk (PYR)

2. Incidence MI *(fatal or non-fatal)* in 'asymptomatic' individuals:
   Number MI events *per* PYR

Analysis

1. Graphical comparison across gender and age
   a. Asymptomatic individuals without prior statin use
      - Incidence of statin therapy compared to
      - Incidence of fatal myocardial
   b. Fraction of incident statin users (2005-2009) prescribed statins for primary prevention

2. Poisson regression analysis

   Incidence rate ratios (IRR) 95% confidence intervals (CI)

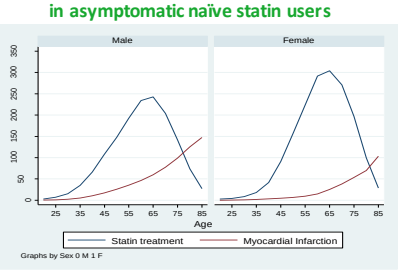
   Outcome: First statin prescription in naïve statin users

   Explanatory variables: Gender and age

   - Analyses stratified into ages below and above 65

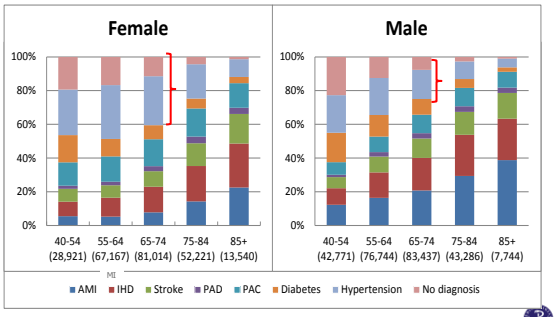
Results

Incidence of statin use compared MI incidence in asymptomatic naïve statin users



Wallach-Kildemoes H, Diderichsen F, Krasnik A, Lange T, Andersen M (2012). Is the high-risk strategy to prevent cardiovascular disease equitable? A pharmacoepidemiological cohort study. BMC Public Health. 12(1): 610.

Fraction of incident statin-users by indication



Poisson regression analyses

	Hypertension		No diagnosis			Hypertension		No diagnosis	
	IRR	95% CI	IRR	95% CI		IRR	95% CI	IRR	95% CI
Male	1.00	-	1.00	-	**Male**	1.00	-	1.00	-
Female	0.73	(0.72-0.74)	1.03	(1.01-1.05)	**Female**	1.11	(1.09-1.14)	1.36	(1.32-1.40)
40-44	1.00	-	1.00	-	**65-69**	1.00	-	1.00	-
45-49	1.64	(1.58-1.71)	1.83	(1.77-1.90)	**70-74**	0.89	(0.87-0.91)	0.86	(0.83-0.89)
50-54	2.32	(2.24-2.40)	2.92	(2.82-3.01)	**75-79**	0.66	(0.64-0.68)	0.66	(0.63-0.69)
55-59	2.81	(2.72-2.91)	3.86	(3.74-3.99)	**80-84**	0.39	(0.38-0.41)	0.40	(0.37-0.43)
60-64	3.35	(3.24-3.46)	5.24	(5.07-5.40)	**85+**	0.14	(0.13-0.15)	0.13	(0.11-0.15)

Conclusion and perspectivation

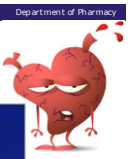
Initiation of statin for primary prevention

- Higher incidence in postmenopausal women than same aged men despite unclear beneficial effect esp. in women
- Consequence of increasing cholesterol levels in postmenopausal women & recommendations on cholesterol goals?

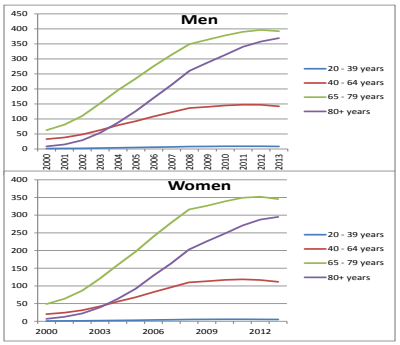
Perspectivation

- Overprescribing of statins in postmenopausal healthy women
  - More harm than good, e.g. muscle problems
  - Waste of health care resources
- Preventing overdiagnosis/treatment of 'hypercholesterolemia':
  Not merely a question of arguing on the evidence?

Questions



Prevalence of statin use in Denmark between 2000-2013



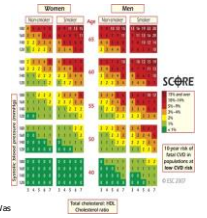
Prevention of CVD in General Practice

Risk scoring charts

10 years risk of fatal CVD (cholesterol & blood pressure levels)

- Preventive drug if fatal CVD risk is high, 10%?
- Lowering the limit for 'high' in guidelines - US vs Europe

➢ Increasing statin prescribing for primary prevention



Diagnoses in the hierarchy	Indication Hierarchy	Register-marker description[1]		
	No markers of	Hospital diagnosis	Hospital procedures	Dispensed prescriptions
1. Myocardial Infarction (MI)		MI (acute or previous)		
2. Ischemic Heart Disease (IHD)	1	Angina pectoris	Coronary by-pass, PCI	Consecutive nitrate dispensing, ASA
3. Stroke	1-2	Ischemic stroke		
4. Peripheral Arterial Disease (PAD)	1-3	Peripheral arterial disease: lower limbs	Lower limb revascularization	
5. Potential Atherosclerotic Conditions (PAC)	1-4	E.g. arrhythmia, heart failure, aorta aneurism, nephropathies	Peripheral; central; intestinal Revascularization	e.g. loop-diuretics, antiarrhythmic
6. Diabetes	1-5	Diabetes, type I or type II		Antidiabetics: Insulin or per-oral
7. Primary hypertension	1-6	Primary hypertension, i.e., no organ damage		Antihypertensive
8. No diagnosis / hypercholesterolemia	1-7	No register markers of arteriosclerotic cardiovascular disease or diabetes		

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