

**Almeno un terzo
di tutti gli eventi cardiaci e cerebro-vascolari
possono essere evitati
con l'uso di statine ad alto dosaggio
nei pazienti a rischio cardio-vascolare
indipendentemente dai valori di colesterolo
basale**

Studio HPS

HPS

È il più grande studio mai effettuato sulla riduzione del colesterolo: 20 536 pz per 5 anni

Ha dimostrato chiaramente il beneficio del trattamento in pazienti con rischio vascolare per precedente malattia e normali o bassi valori di colesterolo:

riduzione di almeno un terzo degli attacchi cardiaci e degli stroke

Tali risultati modificheranno la pratica clinica e le attuali linee guida internazionali

HPS

Questo studio ha reso obsoleto il controllo preliminare del colesterolo ed il concetto di soglia LDL oltre cui iniziare il trattamento con statine.

Il trattamento dovrebbe essere iniziato, indipendentemente dai valori basali di colesterolo, in tutti i pazienti a rischio vascolare.

**Prof. Richard Peto
Oxford University
HPS statistician**

Principali studi clinici

Prevenzione primaria:

- | | | | |
|---------------|------|--------------|---------|
| • Woscop | 1995 | pravastatina | 6565 pz |
| • AF/Tex-CAPS | 1998 | lovastatina | 6605 pz |

Prevenzione secondaria:

- | | | | |
|---------|------|--------------|---------|
| • 4S | 1994 | simvastatina | 4444 pz |
| • Lipid | 1998 | pravastatina | 9014 pz |
| • Care | 1996 | pravastatina | 4159 pz |

I benefici della riduzione del colesterolo possono essere estesi ad altre categorie di pazienti ?

**colesterolo medio-basso
anziani
donne
diabetici
arteriopatia non coronarica**

Prevenzione primaria e secondaria:

hps

Clinical trial commentary: HPS



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Long-term treatment

The event curves began together and gradually diverged over the course of the study

"This is a treatment that should not be given for the short term, but should be given, probably, for life."



Califf

Vitamins

"There was absolutely no effect of vitamins, proving once again that vitamins only enrich the urine and the people who make them "

Califf



Belief in vitamins persists

Patients take these vitamins and think they are helping their cardiovascular health

"So many trials have put the nails in the coffin for vitamins for cardiovascular benefit; I don't know why it persists."



Topol

Challenging previous wisdom

Fascinating results for the low LDL group

- **overturns CARE and others that implied a plateau of benefit for LDL-lowering**
- **AFCAPS/TexCAPS showed benefit when patients had high CRP and low LDL**

Have we reached the point of not even measuring LDL and instead just giving a statin?



Topol

Reserving judgment

We do need to see more detailed data

"As you know, there is nothing that would be more exciting to someone like me than being able to say, 'Don't worry about measuring LDL cholesterol, the whole concept was wrong to begin with.'"



Califf

LDL as a surrogate

LDL has held up well for many years as a surrogate, now it might be shot down

"I think the combination of cerivastatin and HPS really gives the one-two punch to the concept that one can just develop a drug based on lowering LDL cholesterol and then really believe that you know what its total effects on human health are going to be."



Califf

Choice of statin

Which statin should be used at which dose?

- **HPS group implied lovastatin comes off-patent and could be used cheaply**
- **Crestor (rosuvastatin) and the other "superstatins" offer even more LDL-lowering**

Statin strategy

Do we stay with our current strategy?

- **we currently start with simvastatin or pravastatin because we have the data and we should maybe use a higher dose of simvastatin**
- **if LDL doesn't drop enough, we recommend atorvastatin – this is brought into question by HPS**



Califf

Practice in light of HPS

- **we should use simvastatin 40 mg as reference standard**
- **the unproven statins shouldn't be the first choice until they have comparable data**

Califf

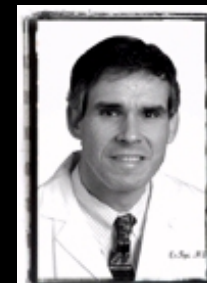
How do statins work?

Unanswered questions remain about statins

pleiotropic effects come into play

"we don't know how the darn statins work."

Topol



Lovastatin by LDL/CRP level in AFCAPS/TexCAPS

Treatment	event rate: lovastatin (%)	event rate placebo (%)	RR (95% CI)	p value
All cases of LDL > median (n=2866)	2.9	5.3	0.53 (0.37-0.77)	0.001
LDL < median CRP > median (n=1428)	2.9	5.1	0.58 (0.34-0.98)	0.04
LDL < median CRP < median (n=1448)	2.5	2.2	1.08 (0.56-02.08)	0.74

*Event rates over 5-year follow-up

** LDL cutoff = 149.1 mg/dL

*** CRP cutoff = 0.16 mg/dL;

Using CRP in the clinic

How often should you measure CRP?

- needs prospective study
- for now we measure as part of routine blood sample in a clinic visit
- if patient is on a statin, CRP is measured when they come back for their liver function test
- costs <\$8 to run the assay



Topol

Practice in light of HPS

I don't believe potent LDL lowering means you have a better drug, but opinions differ

- **work with agents with the longest track record (simvastatin, pravastatin)**
- **save atorvastatin for unmanageable LDL**
- **in LDL <100, give a statin if the patient has elevated CRP**



Topol

Cheap and independent trial

Much was made of HPS as a cheap and independent trial

- **avoided industry interference**
- **\$30 million for a 20 000 patient trial**
- **extended follow-up**

Is this a model for future trials?



Topol

Outcome trial

**We need comparative, competitive study
with clinical outcomes**

- **surrogates won't tell us enough**
- **beyond the age of placebo in many
areas of CV medicine**
- **we should not spend millions on queries
about data that are irrelevant to the
main outcomes**

Califf

Independence

Independence does **not mean industry has nothing to contribute; clinical trial is a shared responsibility**

"I would argue strongly that the interpretation of the data should be in the hands of people who don't work for the company that would stand to benefit from the treatment."



Califf

Topol: 2 thumbs up



"It will be interesting to see in the months and years ahead if LDL measurements are abandoned, and what the clinical community decides to do regarding HPS's findings."

Topol

Califf: 2 thumbs up



"If we can just talk people who are currently taking vitamin E to stop and donate half of the money that they were spending to worthy causes, we would not only improve the health of the population but also contribute to lots of other worthwhile endeavors."

Califf

**Lo studio HPS è stato inserito
dall'AHA nell'elenco dei primi dieci
risultati scientifici ottenuti in campo
cardiologico nel 2001**

Conclusioni

Alla luce di questi dati, nel nostro reparto, le statine risultano attualmente sottoutilizzate e sottodosate

Possiamo scegliere di aspettare la pubblicazione dello studio e la modifica delle linee guida internazionali oppure

Conclusioni

**Prendere atto di questi dati
nell'interesse dei nostri pazienti ed
utilizzare le evidenze disponibili**

**Inizio del trattamento con statine
ad alto dosaggio:
durante il ricovero nel nostro reparto**

**Indipendentemente dai valori di colesterolemia
a tutti i pazienti con:**

- **cardiopatía ischemica**
- **arteriopatia ostruttiva non coronarica**
- **diabete**
- **ipertensione**