

**Hope 2
Update
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Hope 2 – the background

- A statistical correlation between homocysteine levels and frequency of cardiovascular disease and stroke.
- Hoped that reducing the Homocysteine levels with folate, vit B6 and B12 will reduce a composite primary end-point:
 - **the incidence of death from CV causes, MI and stroke**

Hope 2 - what happened? (1)

- Over 5000 patients with established vascular disease or diabetes randomised to vitamins (folate, B6, B12) or placebo
 - Over 70% living in countries with folate supplementation
- **Primary end point did not reach significance over 5 years follow – up**

Hope 2 - what happened? (2)

- **Small reduction in all strokes: 1.4% in absolute terms**
- **Increase in unstable angina**
- **Increased Heart failure in patients with low GFR**

**ALL OF DUBIOUS SIGNIFICANCE FOR
A VARIETY OF REASONS**

Dubious significance?

- Relatively small number of events
- Multiple comparisons in subset analysis
- Other studies do not agree
 - NORVIT
 - VISP
- Possible inaccuracy in classification eg unstable angina
- Lack of biological plausibility and internal consistency

Hope 2 - what's it all about?

- 1. Epiphenomenon - homocysteine goes up because of other risk factors**
- 2. Patients were not high enough risk and too many were on supplements to have a benefit or disease too advanced.**
- 3. Dose of folate may be too low to get any direct folate effect of improving endothelial function (*needs 5-20mg - 2.5mg/day used in Hope 2*)**

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Raised homocysteine

- Smoking
- BP raised
- Atheroma

- Inflammation and immune activation
- End-product of tissue repair

Hope 2 - what to do ?

- 1. Give up the quest?** – benefit likely to be small in a well nourished, supplemented population – but it is cheap and may be important in poorer communities
- 2. Go for different patient groups?**
 - higher risk
 - earlier disease and very long-term follow-up

Have to be brave with what is known now

Hope 2

At present there is no logic in recommending vitamin supplementation with Folate, B6, B12 in cardio or cerebrovascular disease

Hope 2

Appropriate that this session is in Barcelona

In Spanish

Esperar means to **Hope**

Hope 2

Appropriate this is Barcelona

In Spanish

Esperar means to **Hope**

but it also means to **Wait**