



New Models of Primary Prevention: How well do they translate into action?

Emeritus Professor Stewart Truswell AO
Chairman, Nutrition Research Foundation, University of Sydney

The Contribution of Pharmaceutical Products

20th September 2006



A debate fired up by Wald & Law's ingenious suggestion of a POLY PILL, with 6 ingredients:

- a statin
- a thiazide (1/2 standard dose)
- a β -blocker (1/2 dose)
- an ACE inhibitor (1/2 dose)
- Aspirin, 75 mg
- Folic acid, 800 μ g

BMJ, 2003; 326 : 1419-23



Incidentally Professor Nick Wald planned and directed the British MRC international trial that gave definitive proof that FOLIC ACID prevents neural tube defects.

Lancet 1991; 338 : 131-7.

Here is a pharmaceutical product, first synthesised at Lederle in 1948, today being used for primary prevention of NTD, either taken as a tablet by women planning a pregnancy or put into some of the staple foods.



94 letters about the Poly pill followed on the BMJ's Website.

- Many old people are already on multiple medications, taking most of its components
- May not work, needs extensive clinical trials
- Aspirin could cause bleeds; might prevent colon cancer
- Folic acid for CVD and dementia (by 2006) looks unlikely
- Doesn't include fish oil, drugs for osteoporosis, prostate, etc
- Less CVD, so more cancer and dementia
- Individual physician prescriptions vs. public health approach.

The approach has been endorsed, however, by Professor Lawrence Green,
EJCN, 2005; 59 Suppl 1 : S4-S9

And by Gaziano, Opie & Weinstein,

Lancet, August 19, 2006 pp 679-686.



INFECTIOUS DISEASES

Many have been made rare by vaccines, which use pharmaceutical products.

- (Smallpox)
- Diphtheria
- Pertussis
- Tetanus
- Poliomyelitis
- Measles
- Mumps
- Rubella
- Varicella/zoster
- H. influenzae B
- Fluvax
- Pneumococcus
- Meningococcus
- Hepatitis A, B
- BCG (TB)
- Typhoid
- Cholera
- Yellow fever
- Q fever

The search is on for vaccines against HIV, malaria.



DENTAL CARIES

Water fluoridation 1st site USA 1945.

In Sydney water from 1968 and added to toothpastes.

There are still vociferous critics of this “mass medication” but F achieves more than nutritional prevention.

Now the battle of the bottles.



HYPERTENSION

Nutritional prevention is

NaCl below 6 g (100 m mol Na)

Avoid overweight/obesity

Limit alcohol intake.

But 85% of our salt intake is put in before we buy the food.

Modern anti-hypertensive medications are effective, side effects usually adjustable

Thiazides: '–ide'

B-adrenergic blockers: '—ol'

Calcium channel blockers: '—dipine'

ACE inhibitors: '—pril'

Angiotensin II receptor antagonists: '—artan'.



RAISED SERUM CHOLESTEROL

Until about 15 years ago the best primary prevention was nutritional.

Clofibrate (Atromid) probably increased mortality

Cholestyramine resin was bulky and unpleasant to take.

Statins : a remarkable breakthrough.

Widely used in Australia. 2004-5 cost to PBS \$885,000,000 for over 15 million prescriptions.

But Brown & Goldstein point out CHD rates still higher in people taking statins than in people with lifetime low serum cholesterols.

Science, 2006; 311 : 1721-1723.

And as statins prescriptions have shot up in UK, AMI admissions have hardly changed

BMJ, 2004; 329 : 645.

Increased LDL-cholesterol not the only risk factor for CHD.

Diet, smoking and physical activity are all still important.



OBESITY

- Primary prevention is for 'overweight' (BMI 25 – 30).
 - George Bray 'History of drug treatment of obesity is strewn with catastrophes'
Thyroid, dinitrophenol, amphetamines, diuretics,
 - Today orlistat ('Xenical') and sibutramine ('Reductil') approved for obesity in Australia. Each cost \$115/month. No PBS. Side effects. Weight loss quite small.
 - Very difficult to develop a drug that antagonizes neurotransmitters involved in appetite without affecting other nervous system functions – and other circuits likely to compensate.
 - What if national funds spent on statins used for multiplication of Finish Prevention Study and US Diabetes Prevention Program?
 - Diet and exercise more effective preventing diabetes than metformin.
Tuomilehto, et al. NEJM, 2001; 344 : 1343-1350.
DPPRG, NEJM, 2002; 346 : 393-403.
 - Smoking reduction success gives hope. (It also contributed to our overweight).
-



OSTEOPOROSIS

- Enough calcium, enough sun (or vit D meds)
- Enough exercise (Obesity, however, is protective)
- Pharmaceuticals have a role: vit D, and alendronate.

CANCER

- Papillomavirus vaccine, 'Gardasil' (\$120 x 3).

ARTHRITIS

- ? chondroitin sulphate.

DEPRESSION

- Early recognition, perhaps by genetic methods.
 - Problem of mis-use of anti-depressants
-



Contribution of Pharmaceutical Products to PRIMARY Prevention

	Per Cent
FOETAL MALFORMATION	20
INFECTIONS	70
TEETH	60
HYPERTENSION	65
CHOLESTEROL	40
CARDIOVASCULAR DISEASE*	55
OBESITY	5
DIABETES	10?
OSTEOPOROSIS	15
CANCER	2
DEPRESSION	?
ARTHRITIS	?

- *Two preceding lines plus fish oil, aspirin, anti-arrhythmics.
-