Exhibit 6 to the Statement of Dr Jan Fizzell





ACE-PREVENTION PAMPHLETS SERIES

OVERALL RESULTS PAMPHLET 1 COST-EFFECTIVENESS OF PREVENTION IN THE GENERAL POPULATION

MAIN MESSAGES

- Many interventions for prevention have very strong cost-effectiveness credentials (43 that are either
 dominant or cost less than \$10,000 per DALY prevented). Such interventions should only be ignored if
 decision-makers have very serious reservations about the evidence base or are facing insurmountable
 problems in relation to stakeholder acceptability or feasibility of implementation.
- Another group of preventive interventions (31) are good value for money compared to the decision threshold of less than \$50,000 per DALY prevented.
- There are also interventions for prevention that have poor cost-effectiveness credentials (38); have
 an insufficient evidence base (4); are associated with more harm than benefit ('dominated': 2); or are
 dominated by more cost-effective alternatives (2). It is vital to recognise that prevention is not always value
 for money and is not always 'better than cure'.
- A large impact on population health (i.e. >100,000 DALYs prevented per intervention) can be achieved
 by a limited number of cost-effective interventions: taxation of tobacco, alcohol and unhealthy foods;
 regulating the salt content of processed food; improving the efficiency of blood pressure- and cholesterollowering drugs; gastric banding for severe obesity; and an intensive SunSmart campaign.
- There are more cost-effective interventions with a moderate impact on population health (between 10,000 and 100,000 DALYs prevented per intervention). The main missed opportunities at the national level among these are screening programs for pre-diabetes, chronic kidney disease and low bone mineral density in elderly women. Smoking cessation aids, pedometers and mass media for physical activity are other approaches with moderate population health impact.
- Of the cost-effective interventions with a smaller population health impact (<10,000 DALYs per intervention), the growing list of potential preventive measures for mental disorders deserves special mention.

BACKGROUND

In ACE-Prevention we set out to perform cost-effectiveness analyses of 150 interventions. We strived to be comprehensive in our evaluation of prevention of non-communicable disease and its main risk factors. Eventually, we selected and analysed 123 preventive interventions. We also completed analyses for 27 treatment interventions.

In this pamphlet we present the cost-effectiveness results for each of the individual preventive interventions in what is often called a league table format. A big advantage of ACE-Prevention is that all interventions were analysed using common methods allowing valid comparisons. The league table is a first sifting of interventions into those that are and are not good value for money. We also indicate the relative size of the annual intervention costs and the amount of health gain projected over the lifetime of the 2003 Australian population receiving the interventions. If other important policy considerations might facilitate or hinder the implementation, these are raised.

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This approach is not fully informative for two reasons. First, some interventions appear cost-effective when analysed in isolation but have more efficient alternatives. Second, the one-by-one analyses do not take into account that many interventions are not implemented in isolation. When combinations of interventions are analysed, care must be taken not to double-count shared costs and benefits. The latter tends to be the more important consideration: other interventions in the chosen package reduce disease rates and any additional intervention cannot claim the same reduction. The pamphlets on specific topic areas (such as blood pressure and cholesterol-lowering, alcohol, physical inactivity, body mass and kidney disease) present the most cost-effective optimal mix to address a health problem. Another pamphlet shows the combined impact of the most cost-effective prevention intervention options across all topic areas.

LEAGUE TABLE CATEGORIES

For clarity of presentation, we have 'triaged' our cost-effectiveness results into five categories and then within each category reported on broader issues that impact on policy decisions. In ACE–Prevention we assume a decision threshold of '\$50,000 per DALY prevented' to determine whether an intervention is 'cost-effective' or not. The categories are:

- · Dominant: interventions that both improve health and achieve net cost savings;
- Very Cost-Effective: interventions that improve health at a cost of less than \$10,000 per DALY prevented;
- Cost-Effective: interventions that improve health at a cost of between \$10,000 and \$50,000 per DALY prevented;
- · Not Cost-Effective: interventions that improve health at a cost of more than \$50,000 per DALY prevented; and
- Dominated: interventions for which more cost-effective alternatives are available.

The results for 123 preventive interventions evaluated are classified by triage category. Full documentation (including treatment interventions and multiple variations of some interventions) are provided in Appendix 2 of the main report. The following is the key to reading the results tables:

Key to results					
Health impact	+	++	+++		
(lifetime)	Small 0–10,000 DALYs	Medium 10,000–100,000 DALYs	Large >100,000 DALYs		
Intervention cost	+	++	+++		
(annual)	Small <\$10 million	Medium \$10–100 million	Large >\$100 million		

DALY, disability-adjusted life year

4. RESULTS

4.1 RESULTS CLASSIFIED BY SIZE OF HEALTH IMPACT

A large impact on population health (i.e. >100,000 DALYs prevented per intervention) can be achieved by a limited number of cost-effective interventions (Table 1):

- taxation of tobacco, alcohol and unhealthy foods;
- a mandatory limit on salt in just three basic food items (bread, cereals and margarine);
- improving the efficiency of blood pressure- and cholesterol-lowering drugs using an absolute risk approach and choosing the most cost-effective generic drugs (or potentially introducing a low-cost polypill that combines three blood-pressure-lowering drugs and one cholesterol-lowering drug into one single pill);
- · gastric banding for severe obesity; and
- an intensive SunSmart campaign.

The evidence base is 'likely' for the taxation and regulation interventions, 'sufficient' for the treatment interventions and 'limited' for SunSmart (based on a comparison of skin cancer rates between states). Taxation and regulation changes have low implementation costs, but do involve 'political costs' that require political will to overcome. The proposed changes for blood pressure and cholesterol involve stakeholder acceptability issues for practitioners that would need to be carefully managed. Government subsidies for gastric banding would need to be accompanied by explicit guidelines, e.g. restricting access to people with severe obesity who have demonstrably failed to lose weight by diet and exercise.

Table 1: Lifetime health outcomes, intervention costs and cost offsets for the most cost-effective preventive interventions with the largest population health impact

	(Lifetime, discounted)			
Intervention	DALYs prevented	Intervention costs (A\$ billion)	Cost offsets (A\$ billion)	
Taxation				
Tobacco tax 30%	270,000	0.02	-0.7	
Alcohol tax 30%	100,000	0.02	-0.5	
Alcohol volumetric tax 10% above current excise on spirits	110,000	0.02	-0.7	
Unhealthy foods tax 10%	170,000	0.02	-3.5	
Regulation				
Mandatory salt limits on processed food	110,000	0.07	-1.5	
Preventive treatments				
Three blood-pressure-lowering drugs to				
replace current practice of preventive drug	20,000	–1.9 [†]	-0.3	
treatments*				
Polypill to replace current practice*	60,000	-7.0^{\dagger}	-0.8	
Laparoscopic gastric banding (body mass index >35)	140,000	3.7	-2.9	
Health promotion				
Intensive SunSmart	120,000	2.0	-0.3	

DALY, disability-adjusted life year

There are more cost-effective interventions with a moderate impact on population health (between 10,000 and 100,000 DALYs prevented per intervention). The main missed opportunities at the national level among these are screening programs for pre-diabetes, chronic kidney disease and low bone mineral density in elderly women. There is good evidence for the effectiveness of the drug and lifestyle treatments that are recommended for the high-risk individuals identified by such screening programs. Smoking cessation aids, pedometers and mass media for physical activity are other approaches with moderate population health impact. We note that a considerable health impact of physical activity can be achieved without reducing body weight.

Of the cost-effective interventions with a small population health impact (<10,000 DALYs per intervention), the growing list of potential preventive measures for mental disorders deserves special mention. Hepatitis B and HPV vaccination are cost-effective measures for preventing cirrhosis and cancers.



^{*}We estimate a lifetime health benefit of 230,000 DALYs prevented from current practice. The polypill or a combination of blood-pressure-lowering drugs targeting by absolute cardiovascular disease risk and 'realistic' assumptions on uptake and adherence would lead to large cost savings and some greater health gain additional to the 230,000 DALYs of current practice (hence we classify these as interventions with a large impact greater than 100,000 lifetime DALYs).

[†] The current practice of blood pressure- and cholesterol-lowering treatments is inefficient and hence the negative costs (i.e. cost savings) if replaced by more efficient treatment.

4.2 RESULTS CLASSIFIED BY COST-EFFECTIVENESS RATIO

Dominant (cost-saving) interventions

Twelve of the 23 dominant prevention interventions have a population-wide focus aiming to reduce exposure to harmful risk factors and behaviours by taxation (of alcohol, tobacco and unhealthy food) or regulation (alcohol advertising bans, raising minimum age of drinking, limiting salt in processed food and fluoridation of drinking water). Four others are health promotion interventions that advocate physical activity and fruit and vegetable consumption or address cardiovascular health in general. The remaining seven are screening interventions targeting treatment to those at high risk (Table 2). These seven interventions address cardiovascular disease, chronic kidney disease, suicide, psychosis and liver cirrhosis or liver cancer as long-term consequences of hepatitis B.

Table 2: Dominant (cost-saving) preventive interventions for non-communicable disease, ACE-Prevention

Topic area	Intervention	Lifetime health impact	Annual intervention cost	Strength of evidence
Alcohol	Volumetric tax	++	+	Likely
	Tax increase 30%	+++	+	Likely
	Advertising bans	+	+	Limited
	Raise minimum legal drinking age to 21	+	+	Limited
Tobacco	Tax increase 30% (with or without indexation)	+++	+	Likely
Physical activity	Pedometers	++	++	Sufficient
	Mass media	++	++	Inconclusive
Nutrition	Community fruit and vegetable intake promotion	+	**	May be effective
	Voluntary salt limits	+	+	Likely
	Mandatory salt limits	+++	+	Likely
Body mass	10% tax on unhealthy food	+++	+	May be effective
Blood pressure	Community heart health program	++	+	May be effective
and cholesterol	Polypill \$200 for >5% CVD risk	+++	+++	Likely
Osteoporosis	Screen women age 70+ and alendronate	++	++	Sufficient
Hepatitis B	Vaccine and immunoglobulin to infants born to carrier or high-risk mothers	+	+	Sufficient
	High-risk infant vaccination	+	+	Sufficient
	Selective vaccination of infants with mothers from highly endemic countries	+	+	Sufficient
Kidney disease	Proteinuria screen and ACE inhibitors for diabetics	++	+	Sufficient
Mental	Problem-solving post-suicide attempt	+	+	Sufficient
disorders	Treatment for individuals at ultra-high risk for psychosis	+	+	Likely
Oral health	Fluoridation drinking water, non-remote	+	+	Limited

 $\label{eq:acceleration} ACE, angiotens in-converting\ enzyme;\ CVD,\ cardiovas cular\ disease$

Very cost-effective interventions (\$0-10,000 per DALY)

Fifteen of the 20 very cost-effective preventive interventions (with a cost-effectiveness ratio less than \$10,000 per DALY) are interventions that involve screening people, either in primary care or in schools, for severe obesity, physical inactivity, hazardous or harmful alcohol use or increased risk of cardiovascular disease or symptoms of mental disorders. The screen is followed by pharmacological, psychological, health promotional or surgical intervention. Two more interventions in this category are of a regulatory nature (licensing controls of alcohol outlets and responsible media reporting of suicides). A further two interventions are in health education (for physical activity and fruit and vegetable intake), and a universal infant vaccination intervention is also in this category (Table 3).

Table 3 Very cost-effective preventive interventions (\$0-10,000 per DALY) for non-communicable disease, ACE-Prevention

Topic area	Intervention	Lifetime	Annual	Strength of
		health	intervention	evidence
		impact	cost	
Alcohol	Brief alcohol intervention GP with or without telemarketing and support Licensing controls	+	+	Sufficient Likely
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Tobacco	Cessation aid: varenicline	++	+++	Sufficient
	Cessation aid: bupropion	++	+++	Sufficient
	Cessation aid: nicotine replacement therapy	++	++	Sufficient
Physical activity	GP Green Prescription	+	+++	Limited
	Internet intervention	+	++	Sufficient
Nutrition	Information mail-out, multiple re-tailored to promote fruit and vegetable intake	*	+	Limited
Body mass	Gastric banding for severe obesity	+++	+++	Sufficient
Blood pressure	Low-dose diuretics >5% CVD risk	+++	+++	Sufficient
and cholesterol	Polypill \$200 to ages55+	+++	+++	Likely
	CCBs >10% CVD risk	++	++	Sufficient
	ACE inhibitors >15% CVD risk	++	++	Sufficient
Mental disorders drugs/suicide	Screen and bibliotherapy to prevent adult depression	+	++	Likely
g	Screen and psychologist to prevent childhood/adolescent depression	+	++	Sufficient
	Screen and bibliotherapy to prevent childhood/adolescent depression	+	+	Limited
	Responsible media reporting for the reduction of suicide	+	+	Likely
	Parenting intervention for the prevention of childhood anxiety disorders	+	+	Sufficient
Other	Universal infant HBV vaccination	+	++	Sufficient

ACE, angiotensin-converting enzyme; CCB, calcium channel blocker; CVD, cardiovascular disease; HBV, hepatitis B virus

Cost-effective interventions (\$10,000-50,000 per DALY)

Among the 28 cost-effective interventions with a cost-effectiveness ratio between \$10,000 and \$50,000 per DALY, one is of a regulatory nature (enforcement of laws on driving under the influence of alcohol) and four concern health education (addressing drink driving, fruit and vegetable intake, physical activity and skin cancer). The remaining 23 are targeted interventions following a screen to identify those with high levels of lifestyle-related diseases, cervical cancer or symptoms of mental disorders (Table 4). The level of evidence for the health promotional interventions was judged to be limited while all the targeted interventions in this category had sufficient or likely evidence to support effectiveness.



Table 4 Cost-effective preventive interventions (\$10,000-50,000 per DALY) for non-communicable disease, ACE-Prevention

Topic area	Intervention	Lifetime health impact	Annual intervention cost	Strength of evidence
Alcohol	Drink drive mass media Roadside breath testing	+ +	++	Limited Likely
Physical activity	TravelSmart	+	+++	May be effective
	GP referral	+	+++	Limited
Nutrition	Multiple tailored mailed fruit and vegetable promotion	+	+	Limited
Obesity	Diet and exercise for overweight	+	+++	Sufficient
	Low-fat diet for overweight	+	++	Sufficient
Blood pressure	Dietary counselling >5% CVD risk by dietitian	++	++	Sufficient
and cholesterol	Dietary counselling >5% CVD risk by GP	++	++	Sufficient
	Phytosterol supplementation >5% CVD risk	++	+++	Sufficient
	Statins >5% CVD risk	+++	+++	Sufficient
	Statins and ezitimibe >5% CVD risk Beta blockers >5% CVD risk	+++	+++	Sufficient Sufficient
	CCBs >5% CVD risk	+++	+++	Sufficient
	ACE inhibitors >5% CVD risk	+++	+++	Sufficient
Cancer	Pap screen (current practice)	+	++	Sufficient
	HPV DNA test screen 3-yearly from age 18	+	+	Likely
	HPV vaccination and Pap screen	+	++	Likely
	HPV vaccination and HPV DNA test screen 3- yearly from age 18	+	++	Likely
	SunSmart	+++	+++	Limited
Pre-diabetes	Screen and dietary advice	+	++	Sufficient
	Screen and exercise physiologist	++	++	Sufficient
	Screen and diet + exercise	++	++	Sufficient
	Screen and metformin Screen and acarbose	++	++	Sufficient Sufficient
Kidney disease	Screen and ACE-inhibitors for non-diabetics age >25	++	++	Sufficient
Mental disorders	Screen and group CBT to prevent adult depression	+	++	Likely
	Screen and CBT to prevent post-partum depression	+	+	Limited

 $ACE, angiotens in-converting\ enzyme; CBT, cognitive\ behaviour\ the rapy; CCB, calcium\ channel\ blocker; CVD, cardiovas cular\ disease; HPV, human\ papillomavirus\ descriptions and the converting enzyme; CBT, cognitive\ behaviour\ the rapy; CCB, calcium\ channel\ blocker; CVD, cardiovas cular\ disease; HPV, human\ papillomavirus\ descriptions and the converting\ enzyme; CBT, cognitive\ behaviour\ the rapy; CCB, calcium\ channel\ blocker; CVD, cardiovas cular\ disease; HPV, human\ papillomavirus\ descriptions and the converting\ enzyme; CBT, cognitive\ behaviour\ the rapy; CCB, calcium\ channel\ blocker; CVD, cardiovas cular\ disease; HPV, human\ papillomavirus\ enzyme; CBT, cognitive\ behaviour\ the converting\ enzyme; CBT, cognitive\ e$

Cost-ineffective interventions (>\$50,000 per DALY)

Cost-ineffective preventive interventions include the majority of fruit and vegetable interventions, dietary advice on salt and a multiple-component intervention addressing diet, weight and exercise (Table 5). Each of these has poor effectiveness and some have high cost. The commercial Weight Watchers program is not cost-effective as there is poor maintenance of weight loss. The high cost of orlistat and sibutramine makes them cost-ineffective.

Raloxifene has not been shown to prevent hip fractures and is too expensive a drug to be considered for prevention of osteoporosis. Aspirin has been considered for a long time to be an effective drug for preventing cardiovascular disease. As it is cheap, it would become one of the most efficient options for CVD prevention. However, recently two studies showed no beneficial effect of aspirin. As aspirin also carries a risk of bleeding in the stomach and brain, particularly in the elderly, not using it in primary prevention may be wiser.

A school-based drug intervention had poor effectiveness. The gun buy-back scheme introduced after the 1996 Port Arthur massacre in Tasmania was very expensive. The drop in suicide that followed cannot be unequivocally attributed to the scheme.

Table 5 Cost-ineffective preventive interventions (>\$50,000 per DALY) for non-communicable disease, ACE-Prevention

Topic area	Intervention	Comments
Diet	Fruit and vegetable interventions targeting individuals (except tailored mailings)	Poor effectiveness
	Fruit and vegetable interventions at workplace	Poor effectiveness
	Dietary advice on salt	Poor effectiveness and high cost
	Weight Watchers	Poor maintenance of weight loss
	Multi-component diet/physical activity/weight intervention	Poor effectiveness
	Orlistat, sibutramine	Too expensive
Osteoporosis	Raloxifene	No effect on hip fractures and too expensive
Cancer	Combined Pap and HPV DNA test screen 3- yearly from age 18	No benefit from start at age 18 instead of 25
	HPV vaccination and combined Pap and HPV DNA test screen 3-yearly from age 18	No benefit from start at age 18 instead of 25
	Anal cytology for MSM	Expensive screen for rare cancer
Pre-diabetes	Screen and orlistat Screen and rosiglitazone	Too expensive Too expensive
CVD	Aspirin	Risk of bleeding and ambiguous evidence for effect in primary prevention
Vision loss	Ranibizumab for age-related macular degeneration	Too expensive
Mental	School-based drug intervention	Poor effectiveness
health/drugs	Gun buy-back and legislation changes to reduce suicides	Only ecological evidence for reduction in suicide; high cost
Shingles	Varicella zoster vaccination at age 50	Low frequency of shingles; expensive

 ${\sf CVD, cardiovascular\, disease; HPV, human\, papillomavirus; MSM, men\, having\, sex\, with\, men}$

Dominated interventions ('do more harm than good' or 'better options available')

Three interventions fall in the category of dominated interventions (Table 6). The first is prostate-specific antigen (PSA) testing to screen for prostate cancer. A large proportion of false positive test results means a greater number of expensive and unpleasant follow-up diagnostic procedures and, in some cases, unnecessarily aggressive treatments for a disease that may never give symptoms during an individual's lifetime. These harmful effects are greater than the modest population health gain from detecting true cases of prostate cancer. While there is no official PSA screening program, there is an extensive level of de facto screening.

Table 6 Dominated interventions, ACE-Prevention

Topic area	Intervention	Comments
Cancer	Prostate cancer screen by PSA	More harm than benefit
Diabetes	Screen and rosiglitazone	Adverse effect on cardiovascular disease
Blood pressure and cholesterol	Beta blockers Dietary advice by a GP	Three more efficient drugs in class Less expensive option

PSA, prostate-specific antigen

The second dominated intervention is rosiglitazone for people identified with pre-diabetes. It is associated with an increased risk of cardiovascular disease. Third, beta blockers, while effective in preventing cardiovascular disease, compete with three more cost-effective blood-pressure-lowering drugs. Combining more than three such drugs is against clinical practice. Lastly, dietary advice by a GP is dominated by dietary advice provided by a dietician.



ACE-PREVENTION PAMPHLETS

ABOUT ACE-PREVENTION

To aid priority setting in prevention, the Assessing Cost-Effectiveness in Prevention Project (ACE-Prevention) applies standardised evaluation methods to assess the cost-effectiveness of 100 to 150 preventive interventions, taking a health sector perspective. This information is intended to help decision-makers move resources from less efficient current practices to more efficient preventive action resulting in greater health gain for the same outlay.

PAMPHLETS IN THIS SERIES

Methods:

- A. The ACE-Prevention project
- B. ACE approach to priority setting
- C. Key assumptions underlying the economic analysis
- D. Interpretation of ACE-Prevention cost-effectiveness results
- E. Indigenous Health Service Delivery

Overall results

- 1. League table
- 2. Combined effects

General population results

- 1. Adult depression
- 2. Alcohol
- 3. Blood pressure and cholesterol lowering
- 4. Cannabis
- 5. Cervical cancer screening, Sunsmart and PSA screening
- 6. Childhood mental disorders
- 7. Fruit and vegetables
- 8. HIV
- 9. Obesity
- 10. Osteoporosis
- 11. Physical activity
- 12. Pre diabetes screening
- 13. Psychosis
- 14. Renal replacement therapy, screening and early treatment of chronic kidney disease
- 15. Salt
- 16. Suicide prevention
- 17. Tobacco

Indigenous population results

- 1. Cardiovascular disease prevention
- 2. Diabetes prevention
- 3. Screening and early treatment of chronic kidney disease



