Would vaccination against nicotine be a cost-effective way to prevent smoking uptake in adolescents?

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ABSTRACT

Aims We used epidemiological modelling to assess whether nicotine vaccines would be a cost-effective way of preventing smoking uptake in adolescents.

Design, Setting, Participants and Measurements We built an epidemiological model using Australian data on age-specific smoking prevalence; smoking cessation and relapse rates; lifetime sex-specific disability-adjusted life years lived for cohorts of 100 000 smokers and non-smokers; government data on the costs of delivering a vaccination programme by general practitioners; and a range of plausible and optimistic estimates of vaccine cost, efficacy and immune response rates based on clinical trial results. We first estimated the smoking uptake rates for Australians aged 12–19 years. We then used these estimates to predict the expected smoking prevalence in a birth cohort aged 12 in 2003 by age 20 under (i) current policy and (ii) different vaccination scenarios that varied in cost, initial vaccination uptake, yearly re-vaccination rates, efficacy and a favourable vaccine immune response rate.

Findings Under the most optimistic assumptions, the cost to avert a smoker at age 20 was $44,431 (95% confidence interval (CI) $40,023–49,250). This increased to $296,019 (95% CI $252,307–$355,930) under more plausible scenarios. The vaccine programme was not cost-effective under any scenario.

Conclusions A preventive nicotine vaccination programme is unlikely to be cost-effective. The total cost of a universal vaccination programme would be high and its impact on population smoking prevalence negligible. For these reasons, such a programme is unlikely to be publicly funded in Australia or any other developed country.
INTRODUCTION

Nicotine vaccines are being developed as an aid to smoking cessation. They induce the immune system to produce antibodies that bind to nicotine and prevent it from crossing the blood–brain barrier to produce its rewarding effects by acting on receptors in the brain [1–3]. If successful, nicotine vaccination could reduce the risk of relapse to smoking within the first few months after quitting by attenuating the rewarding effects of nicotine [3] and making it less likely that a momentary lapse will lead to daily smoking [3,4].

The term ‘vaccine’ has prompted proposals in both the scientific [3–6] and popular media [7] that vaccines could also be used to prevent smoking uptake in adolescents. A spokesman for one vaccine developer (Dr Henrik Rasmussen, Senior VP Clinical, Medical and Regulatory Affairs, Research and Development Facility, Nabi Biopharmaceuticals) has endorsed the preventive use of the vaccine [7].

In this paper we assess the plausibility of these proposals by asking: how much would preventive vaccination against nicotine cost? Would this expenditure be cost-effective by the standards used to evaluate other health-care interventions, including other preventive vaccines? These are critical questions, because preventive nicotine vaccination is only likely to have a population-level impact on smoking prevalence if it is implemented widely, and this would probably require funding by government. We use Australia to represent the situation in other developed countries with a similar smoking prevalence, health-care systems and expenditure on smoking prevention and cessation.

METHODS

There are three nicotine vaccines undergoing human trials [8]. Each uses a unique antigenic molecular approach (see Siu & Tyndale [9] for details). All have undergone Phase 1 and Phase 2 trials, but so far results have been reported for only two of these; for details see Hall & Gartner [10] and Table S1 (details of online Supporting information for this paper are given at the end).

We used the clinical trial data to model the public health impact of preventive vaccination of young people against nicotine in the Australian population. The modelling was conducted in two stages. In the first stage we estimated the age- and year-specific smoking uptake rates among Australians aged 12–19 years, the target age group for preventive vaccination. In the second stage, we used these smoking uptake estimates to predict what the smoking prevalence would be in an Australian birth cohort born in 1991 (aged 12 in 2003) by age 20 in 2011. This was performed under two conditions: (i) the current policy mix and (ii) different nicotine vaccination scenarios. The model was constructed in Microsoft Excel (Microsoft, Redmond, WA, USA). For simplicity, we use the term ‘rate’ for what is more correctly a proportional change in the prevalence of smokers and non-smokers in the cohort. The effect of smoking on mortality was ignored in the model because there would be no difference in mortality between smokers and non-smokers in the 12–19-year age group attributable to smoking.

Estimating smoking uptake rates

Stage 1 of the model used the following data:
1 data from the Australian Bureau of Statistics on the population size in 1-year age bands [11];

2 national survey data on the prevalence of smoking from the Australian Secondary School Survey on Alcohol and Drugs (ages 12–17, years 1993–2005) [12–14], the Cancer Council Victoria surveys (age 20, years 1993–1995) [15,16] and the National Drug Strategy Household Surveys (age 20, years 2001–2004) [17,18]; and

3 smoking cessation and relapse rates in an Australian longitudinal study [19].

We assumed that smoking uptake would be completed by age 20 because the survey data, when interpreted from a cohort perspective, indicate that smoking prevalence peaks in the 20–24-year age group. The prevalence of current smoking in 20–24-year-olds was used to determine the prevalence of current smoking in 20-year-olds. The prevalence of current smoking at all ages for years without survey data (and for ages 18 and 19 for all years) was estimated by interpolating between survey data points using a cubic spline [20] (see Table S2).

The model estimated the 32 unknown smoking uptake rates for each age (12–19) and four time-periods (1993–95, 1996–98, 1999–2001 and 2002–05). The weighted least-squares estimation method selected the uptake values that best fitted the observed prevalence of smoking using the Down-hill Simplex optimization algorithm implemented in Ersatz [21,22]. We took account of differences in sample sizes between surveys by using the inverse of the variance of the observations to weight the observed smoking prevalence estimates.

**Vaccination programme**

We used demographic data from the Australian Bureau of Statistics to determine the number of 12-year-old boys (142 437) and girls (135 051) in the population in 2003 [11]. The 2003 cohorts of 12-year-old boys and girls were divided into smokers and non-smokers using the prevalence of smoking from survey data. Non-smokers were divided into vaccinated and unvaccinated according to the assumed vaccination rate in each scenario. Those who were vaccinated were divided into low and high responders, depending on the assumed immune response rate in each scenario.

After 2003, the smoking prevalence in each of these subpopulations was modelled according to a Markov process (Fig. 1). The number of smokers and non-smokers in the cohort in the years 2004–11 was estimated from: (i) the number in each subpopulation in the preceding year; (ii) the smoking uptake rates among unvaccinated non-smokers, vaccinated high responders and vaccinated low responders; (iii) the rate of annual discontinuation of vaccination in the high and low responder groups; and (iv) the cessation rate among current smokers and the relapse rate among ex-smokers. We used the age-specific smoking uptake rates estimated in stage 1 of the model for the period 2002–05 as the smoking uptake rates in unvaccinated non-smokers. The uptake rates in vaccinated high and low responders were estimated by multiplying this proportion by the relative risk of smoking uptake in these groups. The cessation and relapse rates were those used in stage 1 of the model [19]. Limits were placed on the calculation of the number of smokers and non-smokers at each age and year to avoid negative values or values that exceeded the total cohort size.
Figure 1. Overview of model used to compute smoking prevalence at age 20 for cohort of 12-year-olds in 2003; RR: relative risk

Once a person became an unvaccinated non-smoker (e.g. by not entering the vaccination programme in the baseline year, by dropping out of the yearly vaccination programme or by quitting smoking), they were not eligible to re-enter the vaccination programme. Any person who became a smoker was assumed to leave the vaccination programme. All transitions were assumed to occur at the end of the year. Those leaving the vaccination programme in a given year were assumed to complete that year's vaccination schedule before doing so.

For each vaccination scenario we estimated the number of smokers at age 20, the total cost of the programme from 2003 to 2011 and the life-time disability-adjusted life years (DALYs) expected for the cohort (see below). We compared these to the number of DALYs expected under current policy, which does not include a nicotine vaccination programme.

Vaccination scenarios

We examined 24 possible scenarios for three vaccine costs by varying assumptions about vaccination rate in 2003, yearly dropout and vaccine efficacy. We assumed optimistically that the proportion of the population with a high immune response (antibody titre) to the vaccine was 80%. This is 2.4 times higher than the response observed in a Phase 2 trial of the NIC002 nicotine vaccine (i.e. 33.3%). The values examined for each of these parameters in the chosen scenarios were: relative risks of 0.33 and 0.20 for high responders and 1.00 for low responders; vaccination rates at age 12 of 100, 75, 50 and 25%; and yearly discontinuation rates of 0, 25 and 50% in high responders and 100% in low responders.

Vaccination costs

We estimated the yearly average cost of the vaccination programme for each recipient under three vaccine costs ($100, $150 and $200 per vaccination). In estimating the costs to government of delivering the programme via general practitioners we used the Australian government's Medical Benefits Schedule fees and bulk billing rates [23]. An estimated private
patient cost was based on the Australian Medical Association’s recommended fee schedule for a longer initial consultation and five shorter follow-up consultations. The cost of immunogenicity testing (IGG) in the baseline year ($15.47) was based on the Medical Benefits Schedule cost and the average patient copayment for pathology testing [23]; see Tables S6–S8 for more details.

We assumed a dosage schedule of six vaccinations per year based on a dose optimization study for NicVAX that reported an acceptable immune response in more than 80% of vaccinated smokers with this number of vaccinations over a 6-month period [24]. We did not include either cost savings attained by avoiding future treatment of tobacco-related disease in the model, or the additional costs of treating diseases in non-smokers with a longer life expectancy.

*Disability-adjusted life years*

We used a multi-state life table (implemented in Excel) to calculate life-time disability adjusted life years (DALYs) for cohorts of 100 000 smokers and non-smokers (Table 1) aged 20 (with equal numbers of males and females). The life table modelled 14 smoking-related diseases using a simple disease model with incidence, a single prevalent stage and disease-specific mortality [25,26]. Total and disease-specific mortality were obtained from the Australian Bureau of Statistics [27]. Disease incidence, prevalence and disability weight and disability from all other causes were obtained from the Australian Burden of Disease 2003 study [28]. Unlike DALYs used in burden of disease calculations (which express the DALYs lost by summing years of life lost and years lived with disability), the calculation here is of (disability-adjusted) years lived: total years lived by the cohort of 100 000, adjusted for disability. DALYs lost by 100 000 20-year-old smokers can be calculated by subtracting the DALYs of the cohort of smokers from the DALYs of the non-smokers cohort. Smoking prevalence was linked to smoking-related disease incidence using risk ratios from various sources (see Table S3) in potential impact fraction (PIF) equations [29]. A conservative 3% discount was applied. We used a threshold of $50 000 per DALY for the intervention to be cost-effective.

Table 1. The disability-adjusted life years (DALYs) for 100 000 non-smokers and 100 000 smokers aged 20 (3% discount applied).

<table>
<thead>
<tr>
<th>Sex</th>
<th>Median</th>
<th>Mean</th>
<th>95% CI</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2 539 671</td>
<td>2 539 957</td>
<td>(2 533 168–2 548 208)</td>
<td>3935</td>
</tr>
<tr>
<td>Female</td>
<td>2 626 887</td>
<td>2 627 181</td>
<td>(2 622 657–2 633 809)</td>
<td>2726</td>
</tr>
<tr>
<td>Smokers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2 470 684</td>
<td>2 470 249</td>
<td>(2 454 220–2 483 765)</td>
<td>7570</td>
</tr>
<tr>
<td>Female</td>
<td>2 586 279</td>
<td>2 585 929</td>
<td>(2 574 997–2 594 047)</td>
<td>4797</td>
</tr>
</tbody>
</table>

CI: confidence interval; SD: standard deviation
The cohorts of 20-year-old smokers were subjected to cessation rates (Table S4) from our earlier projection study [30]. Uncertainty in the life-time DALYs was assessed by Monte Carlo simulation (2000 iterations) using Ersatz [22], an add-in software application for bootstrapping in Excel that takes random draws from the assumed distributions of risk ratios and cessation rates.

**Modelling uncertainty in smoking prevalence**

Table 2 summarizes the assumptions made for each of the variables used to estimate the uncertainty interval for the smoking prevalence in the cohort at age 20. We assumed the prevalence of smoking, and rates of cessation and relapse observed in the survey data [12–14,17–19,31] had beta distributions. We performed a Monte Carlo simulation (2000 iterations) using Ersatz.

**Table 2. Model assumptions.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Type of distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of smoking</td>
<td>Beta</td>
</tr>
<tr>
<td>Cessation rates</td>
<td>Beta, rescaled to −1..1</td>
</tr>
<tr>
<td>Smoking relapse rate</td>
<td>Beta, rescaled to −1..1</td>
</tr>
<tr>
<td>Relative risks of smoking uptake in vaccine high and low responders (versus unvaccinated)</td>
<td>Log-normal</td>
</tr>
<tr>
<td>Life-time DALYs for smoker and non-smoker aged 20</td>
<td>Log-normal</td>
</tr>
</tbody>
</table>

1. DALY: disability-adjusted life year.

**Threshold analysis**

We performed a threshold analysis to determine under what conditions a preventive nicotine vaccination programme might be cost-effective.

**RESULTS**

The estimated proportions of Australian adolescents taking up smoking each year according to age are shown in Table 3. The smoking uptake rates ranged from 2% (12-year-olds in 2002–05) to 13% (13-year-olds in 1996–98); see Table S5 for smoking uptake rates in the vaccinated population.
Table 3. Year and age-specific smoking uptake rates for 12–19-year-olds—median and 95% confidence interval.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>0.082 (0.070–0.094)</td>
<td>0.071 (0.061–0.082)</td>
<td>0.018 (0.008–0.028)</td>
<td>0.020 (0.012–0.028)</td>
</tr>
<tr>
<td>13</td>
<td>0.116 (0.100–0.131)</td>
<td>0.127 (0.111–0.144)</td>
<td>0.086 (0.073–0.098)</td>
<td>0.044 (0.033–0.056)</td>
</tr>
<tr>
<td>14</td>
<td>0.111 (0.091–0.129)</td>
<td>0.057 (0.038–0.077)</td>
<td>0.071 (0.055–0.087)</td>
<td>0.040 (0.025–0.054)</td>
</tr>
<tr>
<td>15</td>
<td>0.097 (0.072–0.120)</td>
<td>0.108 (0.085–0.130)</td>
<td>0.064 (0.040–0.088)</td>
<td>0.069 (0.051–0.086)</td>
</tr>
<tr>
<td>16</td>
<td>0.096 (0.068–0.126)</td>
<td>0.124 (0.094–0.154)</td>
<td>0.058 (0.028–0.085)</td>
<td>0.036 (0.011–0.057)</td>
</tr>
<tr>
<td>17</td>
<td>0.105 (0.059–0.144)</td>
<td>0.078 (0.049–0.109)</td>
<td>0.082 (0.044–0.116)</td>
<td>0.058 (0.024–0.086)</td>
</tr>
<tr>
<td>18</td>
<td>0.102 (0.054–0.150)</td>
<td>0.083 (0.049–0.112)</td>
<td>0.067 (0.024–0.096)</td>
<td>0.067 (0.038–0.090)</td>
</tr>
<tr>
<td>19</td>
<td>0.085 (0.038–0.130)</td>
<td>0.090 (−0.026–0.178)</td>
<td>0.056 (0.009–0.082)</td>
<td>0.088 (0.041–0.135)</td>
</tr>
</tbody>
</table>

Table 4 and 5 show the estimated cost of the vaccination programme per 20-year-old smoker averted and the cost per DALY for each of the three vaccine cost estimates. The cost per smoker averted ranged from approximately $44 000 to nearly $300 000, depending on the assumed cost of the vaccine and the yearly discontinuation rate in high responders.

Table 4. Cost per 20-year-old smoker averted by the vaccination programme.

<table>
<thead>
<tr>
<th>Yearly discontinuation</th>
<th>RR</th>
<th>Low vaccine cost (95% CI)</th>
<th>Medium vaccine cost (95% CI)</th>
<th>High vaccine cost (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>0.2</td>
<td>$44 431 (40 023–49 250)</td>
<td>$59 534 (53 628–65 992)</td>
<td>$74 638 (67 233–82 733)</td>
</tr>
<tr>
<td></td>
<td>0.33</td>
<td>$53 312 (48 366–59 430)</td>
<td>$71 433 (64 806–79 631)</td>
<td>$89 553 (81 246–99 831)</td>
</tr>
<tr>
<td>25%</td>
<td>0.2</td>
<td>$74 459 (67 785–81 013)</td>
<td>$99 689 (90 754–108 464)</td>
<td>$124 920 (113 723–135 914)</td>
</tr>
<tr>
<td></td>
<td>0.33</td>
<td>$89 800 (82 505–98 250)</td>
<td>$120 226 (110 460–131 540)</td>
<td>$150 652 (138 415–164 829)</td>
</tr>
<tr>
<td>50%</td>
<td>0.2</td>
<td>$147 128 (123 890–177 897)</td>
<td>$196 775 (165 696–237 928)</td>
<td>$246 422 (207 502–297 958)</td>
</tr>
<tr>
<td></td>
<td>0.33</td>
<td>$176 743 (150 643–212 514)</td>
<td>$236 381 (201 475–284 222)</td>
<td>$296 019 (252 307–355 930)</td>
</tr>
</tbody>
</table>

Table 5. Cost per DALY averted by the vaccination programme (3% discount applied).
The vaccination programme is not cost-effective under any of the scenarios examined when a 3% discount is used. The cost per DALY ranged from $79 750 (95% confidence interval (CI) $65 786–$100 138) to $532 373 (95% CI $419 317–$687 289). All these are above $50 000, a value above which very few drugs would be recommended for subsidy by the Australian Pharmaceutical Benefits Advisory Committee (PBAC) (which advises government on which drugs to subsidize publicly). PBAC uses an even stricter discount of 5%, making the vaccination programme even less cost-effective than we have estimated.

The threshold analysis found that there was no level of vaccine efficacy at which the preventive vaccination programme would be cost-effective for a dose schedule of six vaccinations and a cost of >$70 per vaccination, even assuming 0% dropout and 90% immune response (see Tables S9 and S10).

The total cost of the vaccination programme for the birth cohort ranged from $104.6 million to $2801 million over the 8 years (ages 12–19), depending on scenario. This was equivalent to a range of $377 to $10 096 per capita for the birth cohort. The maximum decrease in smoking prevalence that would be achieved in the cohort at age 20 was 14% (95% CI 12–15%) under the most optimistic scenario [100% vaccination coverage in first year, no yearly dropout, relative risk (RR) 0.2 and high responder rate of 80%]. This outcome would cost between $1668 million and $2801 million, depending on the cost of the vaccine.

DISCUSSION

Population impact

The population impact of a vaccination programme will depend on the proportion of the population that takes up the vaccination, its effectiveness and the yearly adherence to the vaccination schedule. The schedule considered in this modelling exercise consisted of six
injections per year based on the NicVax dose optimization study results [24]. Because this schedule requires a substantial commitment from parents and their teenagers, we think it is highly likely that the uptake would be considerably less than 100% and that the yearly dropout rate would be substantial. The initial uptake, for example, of a publicly subsidized and heavily promoted vaccine against human papilloma virus in Australia was only 75%. The completion rate of its schedule of three injections in a year varied between 55% and 77% [32], giving a full compliance rate of 41–58% in one year. The completion rate for six injections in a year would be less than this; the completion rate for six injections per year over 8 years would be even lower still.

If only a quarter of vaccinated teens dropped out of the programme each year, then even a highly effective vaccine (RR 0.2 and high responder rate of 90%) with a 100% initial participation rate would reduce smoking prevalence by just 4% after 8 years of the programme. This is because the cohort only represents a small proportion of the total Australian population. As we have shown previously, decreasing smoking uptake only reduces smoking prevalence in the long term. In the short to medium term, increasing cessation among existing smokers has a much greater impact on population smoking prevalence [30].

Universal versus targeted vaccination programme

A universal nicotine vaccination programme requires a high rate of vaccination and compliance with a demanding vaccination schedule by a large proportion of the Australian teenage population, most of whom are unlikely to become smokers in the absence of vaccination. Targeting the vaccine to those at highest risk of becoming smokers would reduce the costs of the programme, but the challenge would be in identifying those at higher risk of smoking. We have shown by modelling that neither a panel of genetic tests for susceptibility to smoking nor family history of smoking would be an acceptable screening test for this purpose [33]. Including a greater number of environmental risk factors such as socio-economic status in a screening test may improve its utility but would still produce substantial false positive and negative results. We would also need to consider the possible effects of stigmatizing some young people as ‘at risk’.

Likelihood of government funding

Experience with the Gardasil vaccine against human papillomavirus suggests that a preventive nicotine vaccine is very unlikely to be publicly funded in Australia. Gardasil is administered at age 11 or 12 to prevent cervical cancer, a disease with peak incidence after age 30 [34], decades after vaccination. The initial application for public funding was rejected by the PBAC because of its uncertain cost-effectiveness [35].

Gardasil was subsequently included in Australia’s National Immunisation Program for 12-year-old girls at an expected cost of $436 million over the period 2007–10 (just for the vaccine and not including the costs of administering it). This included a 2-year catch-up programme for girls and women aged 13–26. The cost of the vaccine for girls in the first year of high school was estimated at under $50 million a year [36]. Discounting the health gains by 3–5% made a substantial difference to the cost-effectiveness of HPV vaccination [37], which was found likely to be cost-effective in girls but not in boys [38]. Our modelling shows that preventive nicotine vaccination is not cost-effective under the discount rates used by the PBAC in deciding to recommend public funding of Gardasil.
Furthermore, having a nicotine vaccine approved for preventive use will require meeting much
tougher efficacy and safety requirements than required for cessation. Large-scale clinical trials
to determine preventive efficacy will be very expensive, and biopharmaceutical companies are
unlikely to conduct such preventive trials given the difficulty they have encountered
demonstrating efficacy for cessation.

**Opportunity costs of a preventive nicotine vaccination programme**

In considering the proposed vaccination strategy, any government would also need to consider
the overall cost of the programme and the alternative uses to which such funds could be put.
Government funding for population-wide tobacco prevention programmes in Australia is a
great deal less than plausible estimates of the costs of a nicotine vaccination programme. In
2006, for example, the Australian government committed $25 million over 4 years to an anti-
smoking campaign to reduce youth smoking. In 2009, the Australian Federal, State and
Territory governments entered into a Partnership Agreement on Preventive Health which is
expected to fund anti-smoking social marketing campaigns worth $60 million between 2010
and 2013 [39]. In the United Kingdom, expenditure on mass media anti-smoking campaigns
was £14.79 m in 2009/2010 [40]. These funding commitments suggest that most governments
would be unlikely to fund the total cost of a vaccination programme, even if it was cost-
effective.

The vaccination programme would also cost more than the Australian Government has spent
on subsidizing bupropion and varenicline for smoking cessation. In 2001, its first year,
bupropion cost the government $83 million, but this dropped in subsequent years to $12
million, for a total cost of $145 million over 5 years [41]. This was seen as causing a major cost
blow-out. Varenicline, which was approved for subsidy in 2007, cost the government $40.37
million in its first year of subsidy (2008). This increased to $60 million in 2009 [42] before
dropping to $53 million in 2010. In the United Kingdom, the government spent £83.9 million
on the National Health Service Stop Smoking Services and a further £61.8 million on smoking
cessation medication in 2009/2010 [40]. If governments are not prepared to spend larger
amounts than these on smoking cessation, they are unlikely to fund preventive nicotine
vaccination.

**Limitations**

Our study did not consider the use of a nicotine vaccine for smoking cessation. A vaccine could
well prove to be cost-effective for this purpose if immune responses to vaccination can be
improved [10]. We had no data on the relative risks of smoking uptake in vaccinated
adolescents, but made extremely favourable assumptions about the vaccine's efficacy.

We assumed that the number of doses required each subsequent year was the same as the
initial year and that vaccine efficacy remained constant each subsequent year. It is unknown if
immune response could be maintained with fewer booster vaccinations each year, or whether
the immune response to booster vaccinations decreases over time.

We assumed that the vaccination programme continued from ages 12 until 19 with the same
dropout rate each year. In practice, commitment to the vaccination programme is likely to
decrease over time, particularly if six booster injections are required each year. Also, as the
participants reach school-leaving age, continuation in the programme may decline because
parents have less influence over their children's behaviour.
Our analysis did not consider the cost savings from avoiding treatment of tobacco-related diseases, productivity gains from increasing healthy life-expectancy or the increased costs of aged care among the larger number of non-smokers who live longer than smokers [43]. It is controversial whether all or some of these costs and cost offsets should be included in cost-effectiveness analysis [44,45].

CONCLUSION

A universal preventive nicotine vaccination programme is very unlikely to be a cost-effective public health intervention in Australia and most other developed countries. The total cost of a publicly funded universal vaccination programme would be much larger than that of any currently publicly funded preventive or tobacco cessation programmes in Australia and other developed countries. Its likely impact on population smoking prevalence would be negligible.

Declarations of interest

C.G., A.W. and W.H. have no competing interests to declare. J.B. is founder and owner of Epigear International, which sells the Ersatz software used in the analysis.

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