



Cost-benefit analysis of a national influenza vaccination program in preventing hospitalisation costs in Australian adults aged 50–64 years old



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ARTICLE INFO

Article history:

Received 10 March 2019

Received in revised form 1 July 2019

Accepted 16 August 2019

Available online 28 August 2019

Keywords:

Influenza

Vaccination

Economic evaluation

Cost-benefit analysis

ABSTRACT

Introduction: Influenza causes a significant burden among Australian adults aged 50–64, however, vaccine coverage rates remain suboptimal. The National Immunisation Program (NIP) currently funds influenza vaccinations in this age group only for those at high risk of influenza complications.

Aims: The main aim of this study was to determine whether a strategy of expanding the government-funded vaccination program to all adults 50–64 in preventing influenza-related hospitalisations will be cost beneficial to the government.

Methods: A cost-benefit analysis from a governmental perspective was performed using parameters informed by publicly available databases and published literature. Costs included cost of vaccinations and general practitioner consultation while benefits included the savings from averted respiratory and acute myocardial infarction (AMI) hospitalisations.

Results: In the base-case scenario, the proposed policy would prevent 314 influenza/pneumonia, 388 other respiratory and 1482 AMI hospitalisations in a year. The government would save \$8.03 million with an incremental benefit-cost ratio of 1.40. Most savings were due to averted AMI hospitalisations. In alternative scenarios cost savings ranged from saving of \$31.4 million to additional cost to the government of \$15.4 million, with sensitive variation in vaccine administration practices (through general practitioner or pharmacists) and vaccine effectiveness estimates.

Discussion: Extension of the NIP to include adults 50–64 years of age is likely to be cost beneficial to the government, although this finding is sensitive to vaccine administration cost, which varies if provided through general practitioners or pharmacists; and to variation in vaccine effectiveness. An increased role of pharmacists in immunisation programs would likely result in cost savings in an expanded adult immunisation program.

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1. Introduction

Influenza causes significant morbidity and mortality as well as an economic burden on the healthcare system and society [1,2]. Vaccination remains the most effective method of prevention and is recommended for all persons ≥ 6 months of age and strongly recommended for high-risk groups, which includes all adults ≥ 65 years of age, persons with certain medical conditions

Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; AR-DRG, Australian Refined Diagnosis Related Groups; ED, emergency department; GP, general practitioner; ICD, International Classification of Disease; ILI, influenza-like-illness; MACE, major adverse cardiovascular event; NEP, National Efficient Price; NHMD, National Hospital Morbidity Database; NIP, National Immunisation Program; RTI, respiratory tract infection; RCT, randomised-controlled trial.

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(e.g. cardiac disease, chronic respiratory disease and immunocompromising disease), pregnant women and children <5 years of age [3]. Since 1999, vaccines for those ≥ 65 have been provided free in Australia through the National Immunisation Program (NIP) as an effort to increase uptake. In 2010, this was extended to include adults <65 with certain medical conditions [4]. However, vaccination rates outside these high-risk groups remain poor. Coverage rates are below 50% among adults aged 50–64 years old despite influenza annually contributing to approximately 2800 excess respiratory hospitalisations and costing the Australian healthcare system about A\$15 million in hospitalisation and general practitioner (GP) costs in this age group [2,5,6].

These estimates are also conservative as only the respiratory burden of influenza was considered. Increasing evidence suggest a contribution of influenza to coronary heart disease, by specific and non-specific mechanisms affecting the inflammatory and coagulation pathway [7–11]. Observational case-control studies have found that acute myocardial infarction (AMI) cases are related to laboratory-confirmed influenza infection, influenza-like-illness (ILI) and respiratory tract infection (RTI) [10]. Unsurprisingly, vaccination has been associated with a lower risk of AMI and composite cardiovascular endpoints in observational studies as well as randomised-controlled trials (RCTs), namely the FLUCAD and FLUVACS studies involving 301 participants with either MI or percutaneous coronary intervention (PCI) and 658 participants with coronary artery disease respectively [10,12,13]. Economically, vaccination of patients with acute coronary syndrome (ACS) is cost

effective in reducing hospitalisation costs of major adverse cardiovascular endpoints [14].

Coronary heart disease is the greatest contributor of disease burden among the 45–64-year age group in Australia, and there may be a significant benefit in improving influenza vaccination rates [15]. This could be achieved by providing free influenza vaccinations to those ≥ 50 years old. Age-based immunisation programs can result in greater increases of vaccination coverage compared to risk-based programs [16,17].

In Australia, universal vaccination among those aged 50–64 has been the subject of previous cost effectiveness analyses and have shown promising results [18,19]. Studies in the United States, United Kingdom and Europe have found favourable results in studying vaccination of adults, reporting either net savings or cost-effective outcomes [20–23]. These evaluations considered the societal perspective and did not include the protective effect of influenza vaccination against AMI. This study aimed to determine the costs and benefits to the government in hospitalisation costs in funding a universal influenza immunisation program for all Australians aged 50–64.

2. Methods

A cost-benefit model was developed to determine the difference in costs of an influenza vaccination program for all adults 50–64 years old compared to current eligibility of adults 50–64 with certain underlying medical conditions. The primary outcome

Table 1
Parameters and values used for sensitivity analysis.

Parameter	Base-case value	Sensitivity analysis values (low value, high value)	Source
Population	4,379,216		Australian Bureau of Statistics [24]
Vaccine coverage of general population aged 50–64			
Existing policy	46%	(30,55)	Newspoll Omnibus Survey on Adult Flu Vaccinations [5]
Proposed policy	73%		
Vaccine coverage among high risk group aged 50–64	51%		Cheng, 2017 [25]
Vaccine administration at GP			
Existing policy	73%	(0,100)	Newspoll Omnibus Survey on Adult Flu Vaccinations [5]
Proposed policy	50%*		
Vaccine administration at pharmacy			
Existing policy	–	(0,100)	
Proposed policy	50%*		
Vaccine administration at work			
Existing policy	21%		Newspoll Omnibus Survey on Adult Flu Vaccinations [5]
Proposed policy	21%		
Vaccine efficacy/effectiveness			
Against influenza/pneumonia and respiratory hospitalisations	59%	(51, 67)	Osterholm, 2012 [27]
Against AMI hospitalisations	29%	(9, 44)	Barnes, 2015 [10]
Hospitalisation rates			
Influenza/pneumonia	32.8 per 100,000		Moa, 2018 [28] National Hospital Morbidity Database [29]
Other respiratory	40.5 per 100,000		[28,29]
AMI	374.5 per 100,000		[29]
Costs			
Vaccine dose	\$ 11.88		Mogasale, 2011 [19]
GP administration	\$ 18.53		Medicare Benefits Schedule [31]
Hospitalisation costs			
Influenza/pneumonia	\$ 6277		Independent Hospital Pricing Authority [32]
Other respiratory	\$ 5234		[32]
AMI	\$ 16,124		Heart Foundation [34]

AMI – Acute myocardial infarction.

* Excluding the population vaccinated at work.

variable is the incremental benefit–cost ratio comprising of costs of additional vaccinations as well as general practitioner consultations and benefits (cost savings) due to averted influenza-associated respiratory and AMI hospitalisations. A governmental perspective was taken, and the timeframe of analysis was 2017–18.

2.1. Parameters

Parameter assumptions (Table 1) were informed by information from public databases, published literature and one set of unpublished data.

2.2. Population

The population of adults aged 50–64 was estimated from the Australian demographic statistics [24]. The population at high risk of developing influenza-related complications was estimated using Newall's et al. assumption of 30% [18].

2.3. Vaccine parameters

Vaccine coverage among the 50–64 year age group was estimated at 46% from a Department of Health-commissioned survey [5]. Coverage among persons at high risk of influenza-related complications and therefore eligible for free vaccination under existing policy was estimated using the Influenza Complications Alert Network (FluCAN) [25]. In the new policy it was assumed that vaccine uptake among those 50–64 years of age would increase to that of the coverage among those ≥ 65 years of age, i.e. 73% [5,25].

Vaccine administration practices, whether vaccines are administered by a GP or otherwise, influence the cost to the government as GP consultations are covered by the government under the Medicare Benefits Schedule. The proportion of vaccinated persons aged 50–64 vaccinated by a GP in 2014 was estimated to be 73% [5]. The proportion of persons receiving their vaccination at work, and thus not incurring a cost to the government, was estimated to be 21% and assumed not to change with the new policy. In 2015–17, vaccinations started to be administered by pharmacists [26]. For the base-case scenario of the new policy, we assumed that of the remainder of persons not receiving vaccinations at work, 50% would be vaccinated by a GP and 50% by pharmacists.

Vaccine efficacy against influenza-attributable influenza/pneumonia and other respiratory hospitalisations was estimated to be 59% from a meta-analysis of RCTs that determined efficacy of trivalent inactivated vaccine against laboratory-confirmed influenza in adults 18–64 years of age [27]. Effectiveness against AMI was estimated at 29% from a meta-analysis of case-control studies [10].

2.4. Disease estimates

Rates of influenza-attributable influenza/pneumonia [International Classification of Disease (ICD)-10-AM codes J09-18] and other respiratory hospitalisations were obtained from a modelling study of average seasonal influenza-attributable respiratory hospitalisations in Australia from 2001 to 2013 [28]. This study used age groups 0–14, 15–64, 65–84 and ≥ 85 years. To estimate counts of hospitalisations for the 50–64 age group, the National Hospital Morbidity Database (NHMD) principal diagnosis data cubes were used to estimate the proportion of ICD-coded influenza/pneumonia (ICD-10-AM J09-18) hospitalisations among the 50–64 year old age group within the 15–64 year old age group [29]. Hospitalisations were excluded for the year 2008–2009 and 2009–2010 due to the 2009 pandemic. The proportion was then multiplied by the hospitalisation counts from the modelling study to obtain hospitalisation

counts among 50–64-year-olds. AMI hospitalisation counts were obtained from the NHMD (ICD-10-AM codes I21 and I22) [29].

Rates of hospitalisations was then calculated using the formula:

$$\frac{\text{Estimated Hospitalisation counts}}{\text{Estimated Australian resident population for age group 50 – 64 June 2017} \times 100,000}$$

2.5. Averted hospitalisations

Calculation of averted hospitalisations was done using a model obtained from Reed et al. [30]. The model predicts the net difference in hospitalisations between the existing and new policy. Firstly, the expected rate of hospitalisations in a scenario of no influenza vaccination is calculated using the following formula:

$$\text{Expected rate without vaccination} = \frac{\text{observed rate in existing policy}}{1 - VC_{ep} \times VE}$$

where VC_{ep} – vaccine coverage of existing policy, VE – vaccine effectiveness.

The expected rate of hospitalisations under the new policy is then calculated using the following formula:

$$\text{Expected rate with new vaccination policy} = \text{expected rate without vaccination} \times (1 - VC_{np} \times VE)$$

where VC_{np} – vaccine coverage under the new policy.

The number of hospitalisations were calculated by multiplying the rate by the estimated population. The difference in hospitalisations between the existing and new policy represents the averted hospitalisations.

2.6. Cost estimates

2.6.1. Vaccine costs

The price of vaccines purchased by the government is not publicly available. This cost was estimated at \$11.88 from Mogasale and Barendregt, whom estimated cost from the period when influenza vaccinations were purchased under the Pharmaceutical Benefits Scheme [19]. The number of persons aged 50–64 assumed to be vaccinated under the existing NIP was estimated as the vaccine coverage among those at high risk of influenza-complications. The cost of GP-administered vaccination was assumed to be 50% of a Level B consultation, as was assumed by Mogasale and Barendregt [19,31]. It was assumed that the government does not bear any costs for vaccines administered by pharmacies besides that of the vaccine.

2.6.2. Health costs

2.6.2.1. Influenza/pneumonia and other respiratory hospitalisations. The average cost of influenza/pneumonia and other respiratory hospitalisations was estimated from the National Efficient Price (NEP) Determination 2017–18 [32]. The report provides price weight tables for admitted acute patients according to Australian Refined Diagnosis Related Groups (AR-DRGs). The AR-DRGs used are as follows:

Influenza/Pneumonia:

E62A Respiratory Infections/Inflammations, Major Complexity
E62B Respiratory Infections/Inflammations, Minor Complexity

Other respiratory:

All E – codes excluding E62A and E62B

The average price weight of an inlier of these AR-DRGs was determined, weighted by number of separations of the corresponding DRGs from the NHMD [33]. The average price weight was then multiplied by the NEP of \$4910 per National Weighted Activity Unit to determine the average cost per hospitalisation.

2.6.2.2. Acute myocardial infarction hospitalisations. The cost of AMI hospitalisations was obtained from an economic report of the costs of acute coronary syndrome to the Australian Government [34]. Using custom requested data from AIHW, the authors forecasted the number of ST elevation MI (STEMI) and non-ST elevation MI (NSTEMI) separations and respective costs for the year 2017–18 for the 45–64 age group. These costs were weighted by the number of separations also forecasted by the authors prior to calculation of the average cost of an AMI hospitalisation.

2.6.2.3. Benefit-cost ratio. Benefit-cost ratio was calculated as the total incremental benefits (costs of averted hospitalisations) divided by the total incremental costs (costs of vaccine and GP administration).

2.6.3. Sensitivity analysis

Vaccine effectiveness, vaccine administration and vaccine coverage were estimated to have significant effects on outcomes. Sensitivity analysis was performed on influenza vaccine effectiveness against respiratory and AMI hospitalisations using the maximum and minimum values of the 95% CI provided by the respective studies (Respiratory: 51% and 67%; AMI: 9% and 44%) (10, 27). Scenarios of varying proportions of GP or pharmacy vaccination was also analysed, i.e. 100% at GP or 100% at pharmacies. Variable existing vaccine coverage rates of 30% and 55% were also analysed.

3. Results

Extension of the current NIP to include adults 50–64 would increase the number of government-funded vaccinations from 529,316 to 2,525,494 in the base-case scenario.

3.1. Health outcomes

Increasing vaccine coverage through the proposed policy would result in averted respiratory and AMI hospitalisations (Table 2). In the base-case scenario, the new policy would prevent 314 influenza/pneumonia, 388 other respiratory (22% difference) and 1482 AMI hospitalisations (9% difference).

3.2. Cost outcomes

The cost or savings incurred by the government were calculated as the difference in costs of the proposed and existing policy, with cost indicated by a positive number and savings in brackets (Table 3). Implementation of the proposed policy will result in the government saving \$8.03 million. Additional costs incurred by the new policy include only the cost of purchasing more vac-

Table 3
Base-case cost outcomes.

Type of cost	Existing policy (\$)	Proposed policy (\$)	Incremental Cost (Saving) (\$)
Costs			
Vaccine	6,288,272	30,002,867	23,714,595
GP administration	27,249,120	23,398,701	(3,850,419)
Total costs	33,537,392	53,401,568	19,864,176
Benefits			
Influenza/pneumonia	9,017,666	7,046,057	(1,971,609)
Other respiratory	9,289,579	7,258,520	(2,031,060)
AMI	264,461,255	240,566,360	(23,894,895)
Total benefits	282,768,501	254,870,937	(27,897,564)
Total net cost (savings)			(8,033,388)
Incremental Benefit-cost ratio			1.40

AMI – Acute myocardial infarction.

cines. Averted GP visits due to assumed increase of pharmacist vaccination will result in savings of \$3.85 million.

Most of the savings in hospitalisation costs is due to the reduction of AMI hospitalisations, saving the government \$23.9 million compared to respiratory hospitalisations saving \$4.0 million when combined.

The calculated incremental benefit-cost ratio is 1.40, meaning that for every additional \$1 the government spends on the new policy it will receive a return of \$1.40.

3.3. Alternative scenarios

Varying vaccine administration between the GP and pharmacies had a significant effect on costs (Table 4). The scenario of 100% pharmacy vaccination resulted in net savings increasing to \$31.4 million. As the savings in GP administration costs was greater than

Table 4
Alternative scenario cost outcomes.

	Net cost (saving) (\$)	Benefit-cost ratio
Base-case	(8,033,388)	1.40
Vaccine administration		
100% Pharmacy	(31,432,088)	indeterminate*
100% GP	15,365,313	0.64
Existing vaccine coverage		
High estimate (55%)	(4,769,983)	1.33
Low estimate (30%)	(12,422,137)	1.42
Vaccine efficacy/effectiveness		
Respiratory		
High estimate (67%)	(8,817,913)	1.44
Low estimate (51%)	(7,324,301)	1.37
AMI		
High estimate (44%)	(23,529,161)	2.18
Low estimate (9%)	9,157,555	0.54

AMI – Acute myocardial infarction.

* As there was zero incremental cost of vaccination in the scenario of 100% pharmacy administration, the benefit-cost ratio was indeterminate.

Table 2
Base-case hospitalisation outcomes.

	Hospitalisations (n)			
	Existing policy	Proposed policy	Averted*	Percentage difference
Influenza/Pneumonia	1437	1122	314	22%
Other Respiratory	1775	1387	388	22%
AMI	16,402	14,920	1482	9%

AMI – Acute myocardial infarction.

* Calculated before rounding.

the incremental cost of vaccine doses, there was no incremental cost of the new policy, and thus the incremental benefit-cost ratio is indeterminate. Conversely, if the vaccines were provided exclusively at the GP with the associated consultation cost, the new policy is not cost saving (0.64 incremental benefit-cost ratio) and would cost the government a net amount of \$15.37 million.

Assuming the low estimate of existing vaccine coverage of 30%, the savings of the program increased to \$12.4 million (1.42 incremental benefit-cost ratio). Assuming a high estimate of 55% coverage reduced the savings to \$4.77 million (1.33 incremental benefit-cost ratio) although still results in a cost-saving program.

Varying vaccine efficacy against respiratory hospitalisations had less of an effect on cost outcomes compared to effectiveness against AMI hospitalisations. Assuming the high estimate of efficacy resulted in an additional \$0.78 million in savings (\$8.82 total net savings) compared to base-case while the low efficacy estimate resulted in a \$0.71 million reduction in net savings compared to base-case (\$7.32 million total net savings). Both scenarios still resulted in savings with incremental benefit-cost ratios of 1.44 and 1.37 for the high and low estimate respectively. Assuming the high estimate of vaccine effectiveness against AMI hospitalisations increased the net savings of the policy to \$23.5 million. Use of the low estimate resulted in the policy no longer being cost saving (0.54 incremental benefit-cost ratio) and would cost the government an additional \$9.2 million.

4. Discussion

The base-case scenario of the proposed universal vaccination program of Australian adults 50–64 is cost beneficial for the government. The main cost of the new policy was the cost of purchasing additional vaccines. Most savings were from averted AMI hospitalisations due to the greater number of averted AMI hospitalisations compared to respiratory. The estimated cost of an AMI hospitalisation is also more than twice that of respiratory hospitalisations.

Previous economic evaluations of a universal vaccination program of adults aged 50–64 in Australia were cost-effectiveness analyses, used different perspectives, did not consider AMI hospitalisations averted and used decision analytic models. Direct comparison of overall conclusions is thus difficult, but results may be compared to individual outcomes [18,19]. Newall et al. calculated an overall net cost of \$23.7 million to the government for the new policy compared to the savings of \$8.03 million we found. Our inclusion of averted AMI hospitalisations is most likely the biggest factor in this difference. Another cost-benefit analysis also estimated that vaccinating healthy working adults would result in savings of US\$13.66 per person vaccinated [20]. The savings are difficult to compare to ours as this study included adults 18–64 years of age, used the societal perspective and compared the vaccination strategy to no vaccination as opposed to our comparison of vaccination in high risk persons.

This study may be one of the first economic evaluations to incorporate the protective effect of influenza vaccination against AMI in the Australian setting. In the base-case scenario 1482 AMI hospitalisations could be averted in the 50–64 age group, resulting in \$23.9 million in savings. Two other economic evaluations of influenza vaccination against cardiovascular disease in Korea and Thailand also reported cost-effective outcomes [14,35]. Suh et al. estimated that vaccination would prevent 16,514 major adverse cardiovascular event (MACE)-related hospitalisations among patients with ACS and save US\$86.2 million. This suggests that there is a significant potential amount of savings if vaccine coverage can be increased among those at risk of ACS.

Influenza vaccination is believed to reduce the risk of AMI by preventing acute infections and related inflammatory-mediated

plaque disruption, thrombus formation and occlusion [8]. Therefore, the cardioprotective effects of influenza vaccination may extend from AMI to ACS. AMI was chosen as the endpoint in this study as it was a definitive outcome for which diagnosis codes could be assigned. There was also the availability of a vaccine effectiveness measure against AMI obtained from Barnes et al. that could be used in the model. Other possible endpoints that could be analysed include ACS and MACE, which would likely increase the cost savings observed. However, randomised-control vaccine effectiveness studies using these endpoints vary in their definitions of MACE and have relatively small sample sizes [12,13,36]. Nonetheless, they show efficacy against MACE. This highlights the need for continued research in this area in the form of large-scale prospective RCTs to obtain more accurate effectiveness measures.

Pharmacist vaccination has only been introduced in Australia in the last few years, and the 50–64 age group may be ideally suited for vaccination in pharmacies. Studies have argued the case for an increased role of non-traditional vaccination settings in improving cost-savings as well as improving accessibility [37,38]. Distribution of vaccine administration between GPs and pharmacists significantly influenced cost outcomes. Savings increased with increased pharmacist vaccinations while assuming 100% GP vaccination resulted in the program no longer being cost saving. This is due to the assumption that there would be no added cost to the government other than the vaccine itself if vaccinations were administered by pharmacists as opposed to the added cost of GP consultations. However, these assumptions are simplistic and have some caveats. If more vaccinations are being provided by pharmacists, the workload on pharmacists will increase and may result in additional costs such as in hiring additional staff. In addition, the time previously used by GPs for vaccination may be used for more patient consultations. This study thus likely overestimated the benefit of pharmacist vaccination. Exclusive vaccination by GPs was not cost saving and may also result in additional costs not studied here. As with pharmacists, more vaccination by GPs will increase their workload and more patients may require costly emergency department (ED) services instead of visiting a busy GP.

Not all possible costs and benefits were able to be included in this study. This study focussed on costs and savings to the government from the vaccine effect in preventing the initial respiratory and AMI hospitalisation as this contributes most of the costs of influenza-related disease. Other direct costs associated with influenza-related disease include GP visits for ILI, ED visits and costs of death [2,18]. However, these costs are considered small relative to hospitalisation costs. For influenza-related respiratory disease, the cost of GP ILI visits and ED costs combined constitute <10% of the cost of a hospitalisation [18]. Additional costs of vaccination programs such as equipment, information campaigns, cold chain maintenance and pharmacist costs were also not considered, which would increase the true costs of the new policy and underestimate its benefit [39]. Other indirect costs such as lost productivity, medication purchased by the patient and travel costs were also unable to be included [18]. It is estimated that acute coronary syndrome alone would cost households \$4.83 billion in 2017–18 [40]. The savings presented are thus likely an underestimate of the true benefits of a universal vaccination program of adults 50–64 years of age.

Another limitation of this study is the uncertainty of vaccine impact against respiratory disease. This was estimated from a meta-analysis of 8 RCTs investigating efficacy against lab-confirmed influenza [27]. None of these trials were performed in Australia and there may be some uncertainty in validity due to the variability in influenza subtype strains across different locations and seasons [39]. However, sensitivity analysis of varying efficacy estimates resulted in changes in net savings of less than

\$1 million. This study also estimated the efficacy of trivalent influenza vaccines. Recently, quadrivalent vaccines have been introduced in Australia. A Phase III RCT of a quadrivalent vaccine found superior immunogenicity for the added B strain and may thus have improved efficacy against influenza-related hospitalisations [41]. Herd immunity, which could improve the health outcomes of vaccination further, was not accounted for in this study due to the complexity of the required modelling.

Another limitation is the lack of a large scale RCT to measure the efficacy of influenza vaccine against AMI. Vaccine effectiveness against AMI hospitalisations was instead estimated from a meta-analysis of case-control studies [10]. In the absence of large RCTs of vaccine against AMI, these are a reasonable source of data for the estimate of vaccine effectiveness, noting relatively narrow confidence intervals in the summary estimate used for our model [10]. Besides the inherent risk of bias in observational studies, the age of participants of the studies included in this meta-analysis tended to be older than the target population of our vaccination policy of 50–64 years. The risk of AMI associated with influenza infection may be more apparent in the elderly [42], thus benefit of vaccination may be lower in the 50–64 year age group. However, of the case-control studies that examined association between AMI and vaccination by age group, MacIntyre [43] calculated vaccine effectiveness against AMI to be higher in the 40–64-year age group compared to those ≥ 65 . There is also the possibility that the lower rates of AMI occurring in vaccines is due to the “healthy user” effect. Those whom get vaccinated may practice more health-promoting behaviour compared to unvaccinated counterparts, resulting in a lower AMI incidence [44]. The vaccine effectiveness value in our calculations may thus be an overestimate, reducing the estimated benefit. However, given the lack of adequately powered RCTs, case-control studies likely provide the best estimate of vaccine effectiveness against AMI. The IAMI trial, currently underway, may provide more robust data to inform economic studies [45].

Accuracy of the results are largely dependent on the parameters. Where possible the assumptions were made to reflect the period of 2017–18 in Australia. However, this was not always possible due to limitations in data and literature. One instance was in estimating rates of influenza-related respiratory hospitalisations. This estimate was made based on a modelling study using hospitalisation counts from 2001 to 2013 as this was the most recent modelling study estimating influenza-related disease in Australia, thus possibly reducing the accuracy of this estimate in reflecting rates of disease in the analysed period of 2017–18. However, use of data from this relatively long 12-year span likely provide a reasonable average of influenza-related disease correcting the yearly variability of influenza.

Vaccine rates of adults aged 50–64 in the new policy were estimated to increase to the current rate of adults ≥ 65 , whom currently receive government-funded vaccinations. This assumption has been commonly used [19,23]. However, examination of vaccine coverage in Ontario, Canada before and after implementation of a Universal Influenza Immunization Program (UIIP) in 2000 did not result in coverage of adults 50–64 equalling that of adults ≥ 65 prior to the program [46]. Differences with this program and ours is the extension of providing free vaccinations for the entire population as opposed to just adults 50–64 years old, which may have resulted in a “dilution” of coverage rate increment. However, this may suggest that the actual increase in coverage rates of our proposed policy may be lower than estimated and reduce the savings observed.

This study may also overestimate the incremental benefit of the policy compared to the current policy as some adults that are at high-risk of AMI such as those with diabetes and ischaemic heart

disease are already being targeted in the current vaccination programme. However, vaccine uptake among this group is low, with only about 50% coverage among all those ≤ 65 at high risk of influenza complications due to any comorbidity [25]. The risk of AMI hospitalisations among the remaining low-risk population may be lower, resulting in a reduced number of averted hospitalisations. However, the current Australian vaccination programme does not target individuals with other risk factors of AMI such as smoking, hypertension and hypercholesterolaemia, in which subgroups may experience considerable averted AMI hospitalisations. Therefore, we have chosen to use an average AMI hospitalisation risk of the general population in our calculations to reflect the real-world risk of AMI. Under the new policy, we also expect that vaccine coverage rates among both high-risk and low-risk groups will increase at comparable rates, resulting in considerable incremental averted hospitalisations among current high-risk groups between the new and existing policy [46].

These results suggest that extending the NIP to Australian adults 50–64 years old may be cost saving to the government. This study recognises the substantial uncertainty of parameter assumptions such as vaccine administration practices and vaccine effectiveness, particularly against AMI, with vaccine effectiveness being influential in the analysis. A more refined and in-depth economic evaluation such as a cost-effectiveness analysis with appropriate thresholds may be useful. Future research such as an adequately powered RCT to inform vaccine efficacy is also required to better inform parameters in future economic evaluations. Nevertheless, influenza vaccination should be actively recommended for adults in this age group to prevent respiratory and cardiovascular disease. An increased role of pharmacists and other non-traditional settings or changes to current vaccine administration practices should also be considered in improving cost benefit of an expanded program.

Acknowledgements

The authors would like to thank Ms. Aye Moa and Dr. Gary Gan for their expert opinion, intellectual input and support during the development of this manuscript.

All authors attest they meet the ICMJE criteria for authorship.

Funding

This work was supported by a grant from the National Health and Medical Research Council (NHMRC) Centre for Research Excellence in Integrated Systems for Epidemic Response (ISER) (grant number 1107393). Raina MacIntyre is supported by a NHMRC Principal Research Fellowship (grant number 1137582).

Author contributions

CRM and AAC conceived the research topic, aims and design of the project. SMR acquired data required for the calculations and performed the calculations. SMR, CRM, AAC, AS and TCT analysed and interpreted the results. SMR drafted the manuscript. CRM, AAC, AS and TCT revised the manuscript for intellectual content.

Declaration of Competing Interests

Raina MacIntyre has received funding for investigator-driven research on influenza and influenza vaccines from Sanofi and Seqirus.

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