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Review

Mandatory infant & childhood immunization: Rationales, issues and knowledge gaps

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ABSTRACT

Globally, infant and childhood vaccine uptake rates are not high enough to control vaccine preventable diseases, with outbreaks occurring even in high-income countries. This has led a number of high-, middle-and low income countries to enact, strengthen or contemplate mandatory infant and/or childhood immunization to try to address the gap. Mandatory immunization that reduces or eliminates individual choice is often controversial. There is no standard approach to mandatory immunization. What vaccines are included, age groups covered, program flexibility and rigidity e.g. opportunities for opting out, penalties or incentives, degree of enforcement, and whether a compensation program for causally associated serious adverse events following immunization exists vary widely. We present an overview of mandatory immunization with examples in high-, middle-, and low-income countries to illustrate variations, summarize limited outcome data related to mandatory immunization, and suggest key elements to consider when contemplating mandatory infant and/or child immunization. Before moving forward with mandatory immunization, governments need to assure financial sustainability, uninterrupted supply and equitable access to all the population. Other interventions may be more effective and less intrusive than mandatory. If mandatory is implemented, this needs to be tailored to fit the context and the country's culture.

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1. Introduction

There is a growing global recognition that infant and childhood vaccine uptake rates are not where they need to be for adequate control of vaccine preventable diseases [1]. The large measles outbreaks in high- and middle-income countries in the past decade have highlighted the dangers of the many coverage gaps. These outbreaks have led several countries to enact, strengthen, or contemplate mandatory childhood immunization legislation [2–5].

There are three main triggers that historically have prompted calls for a shift to mandatory immunization. One has been a failure of less coercive methods to motivate people to vaccinate, such as public health education campaigns, nudge strategies such as requesting documentation of immunization on school entry, and other interventions aimed at overcoming vaccine hesitancy. When interventions such as these do not lead to increased uptake rates, there can be increased pressure from public health and/or policy makers to move from persuasion and nudges to strategies that explicitly limit choice [6].

The second is an outbreak of one or more vaccine-preventable diseases, which results in harm and increased public concern about low vaccination coverage. The 2015 measles outbreak in the United States of America (USA) in California is an example, with ripples felt across the United States [7,8] and beyond (Canada [9]). This outbreak was associated with improved parental confidence in vaccines and good support for mandates among parents who were aware of the outbreak (USA [10]). In Italy, the move to change measles-mumps-rubella vaccine from voluntary to mandatory in 2017 was due in part to the large measles outbreak [3].

In the third instance, to achieve the global vaccine preventable disease elimination goal for wild polio, the mean uptake rates must be high enough to prevent transmission, pockets of unimmunized must be minimized and disease surveillance high in order to detect break through cases so further local rounds of immunization can be undertaken. Mandatory immunization has proven to be a compelling component in the polio global elimination plan. As this goal grows closer, the pressure on the remaining countries with cases has increased [11].

In these first two situations, the adoption of legislation or decrees to mandate childhood immunization can be appealing as this appears to be a straight-forward solution to addressing the important public health problem of low vaccine uptake with the failure to prevent outbreaks of vaccine-preventable disease. Even some countries with high uptake rates and no vaccine preventable disease outbreaks have considered this policy because of the high profile mandatory immunization has gained globally. However, as history has shown, mandatory immunization is neither a simple nor fail safe intervention [12]. Furthermore, the planning and implementation of a mandatory programme can be challenging, from both practical and operational perspectives.

In this article, we offer an overview of some policy considerations relevant to mandatory infant and/or child immunization in high-, middle-, and low-income countries with examples to illustrate differences. First, we briefly define mandatory immunization programs, elucidating the range of rigidity of these mandates from soft i.e. flexible to hard i.e. rigid. Second, we consider the primary ethical issues inherent in mandatory immunization. Third, we explore key legal components for consideration in a mandatory immunization framework and note the importance of tailoring these to fit a country's culture and the context. Fourth, we offer some evidence of the effectiveness of hard mandates as well as evidence of unintended consequences. Fifth, we identify key knowledge gaps regarding mandatory childhood immunization. Lastly, we conclude by suggesting that careful thought should be exercised before mandating childhood immunization, as other interventions may be more effective and less intrusive. Governments need to assure financial sustainability, uninterrupted supply and equitable access (and more importantly, equitable extension of the benefits of vaccination and services) to all their child population before considering mandating immunization. If mandatory immunization is implemented, this needs to be tailored to fit the country's culture and the context.

2. Definitions of mandatory immunization and variations in frameworks

Broadly defined, mandatory infant and childhood immunization programs are immunization requirements implemented at the individual level to control a vaccine preventable disease(s) at the population level [13]. There is, however; no World Health Organization (WHO) definition of mandatory immunization. In 2010, a meeting in Europe (2010 Venice Study) exploring mandatory immunization proposed the definition that a 'mandatory' vaccine is one that every child in the country/state must receive by law without the possibility for the parent to accept or refuse it, independent of whether a legal or economical implication or sanction exists for the refusal [14]. Regardless, immunization programs described as mandatory vary widely, even in high income countries, ranging from:

- Laws requiring immunization although anyone can opt out without penalty; no enforcement (soft i.e. flexible mandates e.g. France before changes in 2018 [4];
- Laws requiring immunization but can easily opt out with personal or philosophical objection without penalty (medium soft mandate e.g. Ontario, Canada before changes in 2016 [15];
- Laws requiring parental education about immunization (rather than immunization itself); may opt out with personal or philosophical objection but requires specific forms and notarization but no penalty for noncompliance (medium hard mandate i.e. "informed consent" mandates e.g. Ontario, Canada [16];
- Laws requiring immunization but can opt out with personal or philosophical objection that requires specific forms and added effort. There is a penalty for noncompliance and strict enforcement (higher medium hard mandate) e.g. Australia before changes in 2016 [17];
- Laws requiring immunization with serious financial penalties or social restrictions; only allow medical exemptions; strict enforcement (hard mandates e.g. State of California USA post 2016 [2,7], Australia after 2016 [17].

To illustrate the diversity of approaches to mandatory immunization we have summarized in Table 1 three frameworks; one from a high-income country, one from a middle-income country, and one from a low-income country, each of which have similar and differing mandatory elements.

3. Ethical justification of mandatory immunization

Mandatory immunization, particularly more rigid forms, has long been controversial predominately because of ethical concerns

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Table 1
Three examples of hard mandatory immunization programs in a high-middle-and low income country.

Country	Overview of the mandatory immunization program
Australia (High-income country) Hard Mandatory	The government funded National Immunisation Program (NIP) implemented a Seven Point Plan in 1997 (http://www.ncirs.edu.au/assets/provider_resources/history/Immunisation-policy-and-practice-September-2017.pdf) to address low national coverage rates for children. Vaccine funding is determined by cost-effectiveness assessment within the Pharmaceutical Benefits Scheme and contingent on cabinet approval. The Australian Technical Advisory Group on Immunisation provides technical advice to government and other entities. The NIP is supported by the Australian Immunisation Register. Vaccination was linked to eligibility of family assistance payments in 1998 and required documentation of complete child vaccination on the Register. Medical, conscientious and religious exemptions could be acquired via a declaration signed by the parent and provider. By 2012, the vaccination requirement was linked to a Family Tax Benefit Part A (Supplement) and assessed for compliance when the child turned 1, 2 and 5 years of age. It was also linked to childcare benefit and childcare rebate payments. Together these payments could be worth up to $A15, 000. In 2016, the "No Jab No Pay" legislation amendment removed conscientious and religious exemptions and records were assessed for compliance every year from ages 1 through 19 years. In addition, some states have extended existing requirements for documentation of vaccination at child care enrolment into requirements for full vaccination. Under No Jab No Play policies, exemptions for "conscientious objection" have been either removed (New South Wales) or were not introduced with new legislation (Victoria and Queensland). Other states and territories are considering such legislation.
Slovenia (Middle-income country) Hard Mandate	The National Institute of Public Health (NIPH) prepares a proposal annually for the Vaccination and Protection Products Programme, which it submits for adoption to the Ministry of Health. This proposal defines the vaccination and protection products and programmes for different population groups. The Minister of Health then passes the Rules on the Vaccination and Protection Products Programme for the current year in the Official Gazette of the Republic of Slovenia (https://read.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-europe-2016_9789264265592-en#page1). Slovenia's program represents one of the most aggressive and comprehensive vaccination programs, which is mandatory for nine designated diseases: infants must be vaccinated for tuberculosis, tetanus, polio, pertussis, and Haemophilus influenza type B within the first three months of life; infants must be vaccinated for measles, mumps and rubella within 18 months; and children must be vaccinated for hepatitis B prior to starting school (https://vaccine-schedule.ecdc.europa.eu/Scheduler/ByCountry?SelectedCountryId=188&IncludeChildAgeGroup=true&IncludeChildAgeGroup=false&IncludeAdultAgeGroup=true&IncludeAdultAgeGroup=false). A medical exemption request can be submitted to a committee, but there are no exemptions for reasons of religion or conscience. Failure to comply can result in a fine of €84; mean income per household €22, 256. The program also contains a no-fault compensation scheme for those injured from vaccines. Slovenia is developing a centralized Immunization Information System that will, it is believed, encourage complete and timely vaccination and facilitate reporting of AEFIs (https://ecdc.europa.eu/sites/portal/files/documents/immunisation-systems.pdf).
Kenya (Low-income country) Moderate soft Mandate	In 2010, Kenya adopted a new Constitution and Bill of Rights, which included rights to health and social care, including for children (Article 53). That, together with the Children Act 2001, as amended, informs immunization policy in Kenya, which is articulated in the National Policy Guidelines on Immunization 2013(https://www.medbox.org/kenya/kenya-national-policy-guidelines-on-immunization-2013/preview?). The Public Health Act establishes the bodies which are tasked with promoting public health, preventing, limiting, or suppressing infectious, communicable, or preventable disease, promoting or undertaking research, advising local authorities, and preparing public health reports. It states that it is the duty of health authorities to take all lawful, necessary, and reasonably practicable measures for preventing the occurrence of, or dealing with, any outbreak or prevalence of any infectious, communicable, or preventable disease. Under ss 35 and 36, the Minister of Health may make rules for the vaccination of those threatened by a 'formidable epidemic, endemic, or infectious disease', which is deemed to apply to smallpox, plague, Asiatic cholera, yellow fever, sleeping sickness or human trypanosomiasis and any other disease which the Minister may, by order, declare to be so. Pursuant to this legislation, in 2007, the Ministry of Health founded the Division of Vaccines & Immunization, which promotes immunization and coordinates immunization services. The Kenya National Immunization Technical Advisory Group (KENITAG) serves as a scientific and technical advisory body on matters relating to vaccines and immunization. There is no penalty for non-compliance but immunization is checked on school entry. Currently the program covers BCG, Polio [three oral types 1 & 3 and one IPV), DPT, HBV, Hib, PCV, Rotavirus, MR vaccines and in a few regions yellow fever vaccines.

about coercion [18]. At its core, mandatory immunization requires a principled calculus, a careful weighing of the indications, evidence and arguments, regarding the responsibilities of public authorities to act in support of the public good, and the potentially countervailing (but also potentially complimentary) rights and responsibilities of individuals. We offer a brief exploration here, emphasizing these two aspects but also noting broader values and virtues that are implicated.

Governments have moral and legal responsibilities to safeguard their populations, both collectively and individually, facilitating as much freedom as can be justified in a democratic, rights-oriented society. One way to achieve this broad goal of safe-guarding the health of the population is through immunization programs. Immunizations confer benefit to both the individuals and the public (through community immunity). However, those who choose not to be immunized are at risk of being both victim of a vaccine preventable disease and the vector for spread of the disease to others in the community [19]. Given that some in the community must rely on community protection because they have underlying medical conditions that preclude immunization or make it ineffective, those who opt out put others at risk. Furthermore, the risk is not uniform in a community as the non – immunized tend to cluster, further increasing the risk locally for those who cannot be immunized [20]. Hence, for vaccine preventable diseases where the consequences of individuals not accepting a vaccine can be viewed as a considerable risk for others in the community, mandating immunization may be an appropriate and acceptable intervention. Increased risks of harm to others by those who don't immunize (clean hands principle: those seeking justice must themselves act justly and fairly) is one of the ethical justifications for mandatory immunization policies [21].

Refusal to accept immunization based on conscientious grounds (i.e. religious, moral or philosophical/personal reasons), is seen by some ethicists as comparable to conscientious objection to mandatory military service. When refusing mandated immunization, they suggest that the objectors "*should make an appropriate contribution to society in lieu of being vaccinated*" [22]. There is a lack of clarity and agreement on this but it might be a financial penalty or access restriction to specified societal services/benefits noted in some mandatory childhood immunization policies.

Even if a mandatory immunization policy is justifiable from the ethical standpoint of decreasing risk of harm to others or making an appropriate contribution to society in lieu of immunization, there still may be other ethical reasons not to embark on this route. One is the principle of the "least restrictive alternative". Globally, justification of restrictions on individual rights as articulated in the International Covenant on Civil and Political Rights (ICCPR), must be proportional, i.e. the least restrictive alternative must be

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adopted [23]. While specifically applied in public health emergencies, wider application beyond the narrow emergency context is justified [24]. With respect to mandatory immunization, policies that do not eliminate the ability to opt out but make opting-out more difficult to obtain may be such a "least restrictive alternative" (e.g. Ontario Canada "informed consent" mandatory program [16].

These ethical arguments concerning mandatory immunization all assume that it is being applied to address low uptake rates due to vaccine refusers. Low uptake may be due to other reasons such as barriers to access; especially in middle-and low-income settings [25,26]. Even in high-income countries, some barriers to access to immunization can be present and are not remedied by a mandatory immunization decree with penalties (Australia [17]). This brings up the ethical principle of justice i.e. equity of benefit and risk. This is not a simple equation as mandatory immunization may or may not address equity issues and/or support social integration of minorities who may have been stigmatized in the past for being seen as major vectors for vaccine preventable diseases (Greece [27]). If a mandatory approach leads to increased funding for mandated vaccines and more resources for the immunization program then higher vaccine uptake may increase community immunity and may support more equitable access to vaccines, including, access by minorities [28]. Hard mandates for influenza immunization of healthcare workers in hospitals, while controversial, has been shown to result in very high uptake rates sustained over a number of years (USA [29]) leading to more protection for the most vulnerable patients.

Given that vaccines, like any drug, are neither 100% effective nor 100% safe, another ethical consideration relevant when assessing the justification of a mandatory program for a country or state is compensation for causally associated serious, albeit rare, adverse events following immunization (AEFI) e.g. anaphylaxis [30], immunization program errors [31]. How the mandatory program deals with AEFIs that are causally determined to be due either to the mandatory vaccine itself or to a flaw in the immunization program delivering the vaccine also raises ethical justice issues. Ultimately, there is a strong argument that mandatory immunization programs can be ethically justified when AEFI compensation programs for serious AEFIs also exist. However, it is not currently clear what percentage of countries (or states) with mandatory childhood immunization programs also have compensation programs nor how easy these are to access. A 2011 review documented 19 countries with AEFI compensation programs, though the relationship to mandatory immunization was not discussed [32], and none of the observed compensation programs were in low-income countries.

4. Legal frameworks for mandatory childhood immunization

Importantly, there is no uniform method for establishing mandatory immunization programs, nor is there a common scope for such programs, nor any single model for what these programs will cover (see Table 2 for a checklist of components to consider in a mandatory immunization framework). The exceptions are mandatory immunization programs related to International Health Regulations, such as for polio and yellow fever (http://www.who.int/topics/international_health_regulations/en/). These health regulations may include mandatory immunization for specific vaccines in certain contexts. The regulations are supported by an international legal instrument that is binding on the 196 countries across the globe, including all the Member States of WHO.

With respect to method of implementation or foundation, mandatory programs may be legally grounded in legislation (statutes or laws enacted by state legislative bodies) (California, USA [33]), regulations (statutory instruments usually enacted by government technical experts, under authority granted to them by legislation) (Ontario, Canada [34]), a combination of legislation and regulation, or more informal governance structures and practices (e.g. ministerial decrees or departmental policies and practices). Mandate legislation and regulations are not necessarily static but may be changed as context or political will changes. As noted above a serious measles outbreak led to a hardened mandate in California [2] and a move from a moderately soft to a moderately hard mandate in Ontario [16]. In Italy, the 2017 hard mandate may or may not be softened given anti-vaccine protests and the election of a more populist government in 2018 (https://www.theguardian.com/world/2018/jul/11/rise-of-italian-populist-parties-buoys-anti-vaccine-movement). Context, culture and politics matter.

With respect to scope, the mandate may apply to the entire country (Italy [3], France [4]), or to specific constituent states, territories or provinces (California, USA [2]), (Ontario, Canada [16]), or it may apply more narrowly to an identified population [35]. In Saudi Arabia, the program stipulates that Hajj or Umrah pilgrims to the Kingdom, including children, must show proof of having had meningococcal vaccination at least 10 days and no more than three years before arrival for polysaccharide vaccine, and no more than eight years before arrival for conjugate vaccine.

With respect to the specific components in a mandatory framework (Table 2), these may differ widely, even with respect to the vaccines specified. Some programs cover most but not all of the WHO-recommended vaccines (Italy [3]), another may identify a limited range of vaccines (e.g. France a specific list [4], and another only one vaccine (Belgium polio vaccine (http://venice.cineca.org/documents/belgium_ip.pdf) [36]. Some may specify an age group or milestone such as on school entry (Italy on enrolment in kindergarten [3], California USA, on school entry [33]). With respect to flexibilities, some contain exemptions for medical contraindications only, while others include or previously included exemptions for religious and philosophical reasons (California, USA [2] and Australia [17] prior to 2016). The program may focus on financial incentives to encourage compliance [17], while others impose penalties that maybe be financial or social (i.e., children can be precluded from daycare (Ontario, Canada [34], Australia [17]) or school entry (California, USA [33], Kazakhstan (http://egov.kz/cms/en/articles/2Fprivivki)). Individuals may be precluded from access to theme parks (California [33) or they may be fined (Slovenia [36]) or even imprisoned (Uganda [37]). As noted above, some countries with mandatory programs may have vaccine compensation for serious AEFIs (e.g. USA) but others do not (e.g. Ontario Canada) (32). Strictness of application and levels of enforcement can vary, as can the body responsible for enforcement of the mandatory requirements (California, USA [2]). Other programs may not enforce the mandate, or may change enforcement with change in context (Serbia [5]).

5. Outcomes of mandatory programs

Importantly, there are surprisingly few systematic reviews, and very little comparative evidence on the outcomes (i.e., effectiveness) of mandatory infant and childhood immunization programs. Single country reports are more common, though these are also sparse and appear to come predominately from high-income countries, especially states in the USA. Typically, assessment of impact is via aggregate data without comparator groups, making it difficult to disentangle policy changes from other potential influencers.

A 2016 systematic review of outcomes of mandates by Lee and Robinson defined mandate "as a legal requirement that a child have any routine immunization prior to entering childcare or school even if medical or nonmedical exemptions were allowed" [38]. They excluded low resource countries; found only 11 before

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Table 2
Checklist of major components to contemplate when mandatory childhood immunization is being considered.

Component	Example options
Basis and method of implementing mandatory immunization. *What is the justification for mandate? Why now? What means will be used to enact mandate?*	Legislation Regulation Ministerial decree Departmental policies or practices Or a Combination of the above
Scope of application: *Where will the mandate be applied?*	County-wide State, Province, Territory Specific Program: e.g. visitors to country
Focus: *What will be the structure of the mandate? If flexible, exemptions will be permitted?*	Type of Mandate Soft i.e. flexible, Medium Soft Medium Hard Hard i.e. rigid Exemptions Medical contraindication Opt out Religious Personal/ philosophical
Vaccines: *What vaccines to be covered by mandate and why?*	All infant/childhood vaccines Specific vaccines only Only infant vaccines Only infant/young child vaccines Specified list of infant and/or child Vaccines Single vaccine
Penalties and Incentives*: What penalties and incentives will accompany mandate, if any?*	Financial Fines Incentive payment Restricting access to universal goods and services Daycare attendance Public Private School attendance Primary/Secondary Public Private Required education session(s) or lectures for parent/caregiver (i.e. mandatory informed choice) Freedom restrictions Incarceration parent/caregiver No entry theme parks Other
Enforcement. *Will there be enforcement of mandates? If yes, what is locus of enforcement: Who, how, when and where will enforce mandate?*	Public health Schools Police/courts
*If No-Will compliance be monitored? (*e.g. *record immunization status on school entry)*	Other
Assessment and Evaluation*: How will the impact of the planned mandate be assessed and evaluated? What outcomes will be measured (just vaccination coverage and rates of VPD, or also unexpected outcomes and costs)? Who will do this and to whom will this be reported?*	
Compensation for Serious Adverse Event Following Immunization: *Is there a program? If yes- what is basis of the compensation program?*	Legislative – no fault Regulations- no fault Industry based- no fault Default - no compensation program – law suits
If no, how will compensation decisions made? How will serious causally linked AEFI be dealt with? What will be compensated? (e.g. medical costs, disability pensions benefits for noneconomic loss and death)	Criteria based Case-by-case
Accountability: *To whom is the mandatory immunization program accountable? When and how often will the program be reviewed, evaluated and updated based upon the evaluation findings? If major revisions are needed, who has the authority to do this?*	

and after studies, and 10 comparing immunization rates in similar populations with and without mandates. Eighteen of these studies were in the USA, two in Canada and one in France. Their conclusion was that mandates lead to short and long-term increases in uptake in groups to whom the mandate applied. They also found that the impact varied by vaccine and by age group targeted.

There have not been studies of mandates in high-income countries in jurisdictions with relatively high baseline rates or with mandates for child care centers. A more recent single high-income country (USA) report examined the impact of the effects of the Advisory Committee on Immunization Practices (ACIP) recommendation for Hepatitis A vaccine compared to mandating this vaccine in young children [39]. Vaccine recommendation increased uptake by about 20% while mandates increased uptake by a further 8%. It is unclear whether these findings are generalizable beyond this vaccine or this country.

Several high-income countries provide evidence of differential outcomes for mandatory and non-mandatory vaccines within a country [36]. For example, in Belgium and Italy some vaccines were mandatory and others were not for historical reasons. Non-mandatory vaccines may have been perceived by the public as being less important and less necessary. In Italy, this differential

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program led to high coverage of the mandatory vaccines e.g. diphtheria, tetanus, poliomyelitis, hepatitis B, all >93% but lower than needed coverage of other recommended but not mandated vaccines e.g. measles 87% [3]. Measles outbreaks led Italy to move to broader mandatory immunization [3].

There is a lack of data on how mandatory childhood immunization has evolved in previously communist countries. The 15 ethnic Republics that composed the former United Soviet Socialists Republic (USSR) and its communist neighbours all had very strong centralized public health systems with mandatory vaccination that enabled enforcement without question and was associated with high uptake rates. By 2018, however; much had changed with respect to childhood immunization in many of these countries. The Ukraine now has the lowest childhood uptake rate in the WHO European Region [1] and Serbia [5] and Poland are experiencing protests against mandatory immunization (http://www.euronews.com/2018/06/02/thousands-of-people-in-warsaw-protested-against-compulsory-vaccinations). Context, history and politics appear to have altered support for and acceptance of mandatory childhood immunization in several of these countries.

Beyond the potential effect on uptake rates, there may be other non-uptake related advantages with mandatory immunization. Even if no penalty for non-compliance with immunization, verification of immunization on school entry is of great value to public health. During a vaccine preventable disease outbreak, public health officials can rapidly decide who needs to be excluded from school until immunized or immunization documented. In some settings these data may also be known without a mandatory policy if the jurisdiction has an immunization registry but many country's/states do not have such registries.

6. Unintended consequences

A key consideration relating to mandatory immunization adoption is the recognition of the potential for unintended consequences. A number have been documented in country or state reports and in experimental studies.

In Australia, in 2015, the No Jab No Pay amendment bill (2015) removed non-medical exemptions from existing vaccination requirements that had been linked to receipt of family assistance payments since 1998 [17]. For those in the lowest tax bracket this was estimated to amount to $15,000 AUS per year. Three states also passed "No Jab No Play" legislation tightening requirements for day care or pre-school (nursery) attendance, which included full exclusion for children of non-vaccinators without the possibility of conscientious objection exemptions, a provision that had relied on the federal system of registering objection.

During this period, a range of other federal and state initiatives sought to improve coverage, including reminder systems, special initiatives for Aboriginal and Torres Strait Islander families, campaigns, and intensive efforts to address register recording errors. By March 2018, these changes were associated with an increase in vaccine uptake among 5 year olds from 92.59% to 94.34%. Of those previously registering conscientious objection, 19% were reported to have been vaccinated within 9 months of the policy, meaning that 81% had yet to comply [17]. During the year following the policy's announcement, medical exemptions more than doubled nationally from 635 to 1401, then reduced to 975 by 2016 when the eligibility for medical exemption was narrowed. Thus a small overall increase in coverage (under 2%) resulted from a range of initiatives and potential correcting of the registry recording entry for children already fully vaccinated. Recent evidence for an impact on the main target group – vaccine refusers – is not available and the government has not released a formal evaluation.

Qualitative research on the program's impact has reported reactance and family hardship among resolute vaccine objectors [40]. Negative effects were reported for families experiencing disadvantage and migrant families with children; both of whom often face access barriers to obtaining full immunization easily [41,42]. Many vulnerable families experienced added stress due to direct significant financial loss of the child rebate and limitation of education experiences for their children due to exclusion from child-care. Two of the payments linked to vaccination are income-tested, meaning they disproportionately penalize lower income families. Furthermore, exclusion from child day care meant some could not work compounding the negative financial impact. Despite vulnerable families often being pro-vaccine, many had problems accessing vaccination while others were not able to easily correct the immunization register error that indicated non-immunization. This disparate impact raises ethical concerns around justice and equity that are even harder to justify given the modest gain in overall vaccine uptake rates. Furthermore, having immunization compete with access to pre-school, particularly for vulnerable disadvantaged children, may be especially problematic given the ever growing evidence of the great importance of early child development programs for disadvantaged children for optimizing school success [43]. One might also question the linking of immunization to school attendance applied in other countries [13] given the importance of education as a social determinant of health. It could be argued that children are "punished" by being removed from their right to an education due to a parental decision about immunization.

In California, USA (2), as in Australia, the removal of non-medical exemptions (i.e. personal belief exemptions) has led to an increase in medical exemptions in some counties. Counties with the highest previous rates of personal exemptions before the more restrictive law, now appear to have the highest increasing rates of medical exemptions. This suggests a 'gaming' of the system, which is concerning, and a failure to impact the target group, which is disappointing.

In Serbia, the government responded to the fall in MMR immunization and 2014/2015 outbreak of measles with substantial tightening of mandatory immunization and harsher penalties [5]. As they had not addressed the problem with the families and the general public, the response to the tightened law was heightened anti-vaccine sentiments and enhanced attention to negative vaccination messages in the media. This was an unexpected but predictable outcome due to failure in communication. Now, the vaccine uptake problem is compounded by low confidence in the program, which may have been further undermined by the new harsher penalties.

A recent German study undertaken has shown that partial compulsory immunization can affect the vaccine uptake intention for other recommended vaccines [44]. Mandatory immunization increased the reactance (anger/resistance) of individuals with negative vaccination attitudes and decreased their intention to accept other recommended vaccines. Choice was important. Although many experts consider that these policies can increase polarization on vaccination issues in the public [4], there are no data to know if this would be similar in other countries, but the Serbia example noted above suggests that mandating vaccines may exacerbate negative vaccine sentiments and backfire for some who were hesitant prior to the tightened law.

7. Evidence and research gaps

As should be clear from the above, the evidence for or against mandatory immunization for infants and children is meager. Not only is there no universal framework for mandatory immunization, but there is no compendium of examples of the different

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framework components, their value, costs and impact on uptake rates that countries that are contemplating mandating childhood immunization might examine. What combination of factors is most effective in what contexts? Does having an AEFI compensation program make a difference in public acceptability of mandated programs? Do links to other (critical) services create back-lash? What method of enforcement is the most cost effective in what settings? How have different countries fared over time with mandates? Have uptake rates and outcomes of mandatory childhood immunization in countries previously part of the USSR or its close neighbour's changed overtime and what factors have influenced the changes? The unintended consequences of mandatory immunization in Australia needs further analysis, and similar justice and equity problems need to be searched for in other high income settings to determine if similar consequences are being suffered elsewhere. The rise in medical exemptions in California and in Australia is also disturbing, and it is not clear if this is happening elsewhere and/or if other "work-arounds" are being developed to avoid penalties for non-compliance.

What other unintended consequences might also arise. Does mandatory immunization lead to a perception that mandated vaccines are more important than non-mandated ones (as occurred in Italy)? Is immunization seen as more valuable only for a specific mandated age group and not for other age groups where not mandated? Will governments employing mandates now consider the issue of low vaccine uptake as "solved" and conclude that there is now no need to invest in other evidence based non-coercive approaches to improve uptake? Will questions arise from the public about whose agenda is being served by mandatory programs? Is the private sector supporting mandatory programs in countries where they provide a significant percentage of immunizations? [http://www.who.int/immunization/sage/meetings/2017/april/2_Review_private_sector_engagement_Mitrovich_et_al.pdf?ua = 1] What happens when a vaccine is compulsory but there are supply issues, such as stock-outs and/or inequity in distribution? Will such instances erode public confidence in the government and the immunization program given that by making immunization mandatory the government has emphasized the importance of vaccines but then has not followed through by ensuring access? Will mandatory immunization maintain or increase equity gaps by making immunization mandatory only for the registered population? What about migrants, transients and refugees; a growing issue as globally 1.5 million people move from rural to urban settings every week [1]. How do these mobile populations fit in mandatory immunization programs? The paucity of data from middle-income countries is particularly glaring given that many of these countries have expressed interested in mandatory immunization or stiffening of penalties in their current program.

The cost of implementing mandatory immunization versus recommended vaccination – both in vaccine and in program delivery cost – has not been well studied in a variety of countries in any income setting. Is mandatory immunization the best use of immunization program resources, or are other tools known to increase immunization uptake more helpful, and if so in what settings? If public health is called upon to enforce the mandatory program, what other public health initiatives have to be curtailed to do this? What are the opportunity costs? Given the limited increase in uptake rates in Australia noted above, are these costs justified or is there a better use for the immunization program resources? Does mandatory immunization result in more or less resources coming to the immunization program overall, and if so what factors influence this government budget decision-making? More work is needed in the area of knowledge, attitudes and behaviours of the community when mandatory immunization is introduced, and what cultural and contextual factors affect this. Similar work needs to be done to examine the knowledge, attitudes and behaviours of those who must implement and/or are required to enforce mandatory immunization in childhood.

8. Conclusions

Mandatory immunization for childhood vaccines is no guarantor that the complex problem of lower-than-desired vaccine uptake rates that enable vaccine preventable diseases to flourish will be overcome in a country or state. Indeed, while comprehensive and systematically generated data does not exist, there is evidence that there is no strong difference in vaccination rates between countries that only recommend certain vaccinations and countries that mandate them [12]. While mandatory immunization can be an ethically defensible solution to low vaccination uptake, the propriety of specific programs is dependent on evidence of (1) their effectiveness, (2) an absence of negative impact on other important public health programs, especially those aimed at vulnerable populations, and (3) sufficient compensation schemes for serious AEFIs assessed to be causally related to immunization. Furthermore, governments need to assure financial sustainability, uninterrupted supply, equitable access (and more importantly, equitable extension of the benefits of vaccination and services) to all the population before considering mandating immunization. If mandatory immunization is the preferred route, careful thought, planning, and follow up are critical. Pertinent questions include:

- Is there a problem with uptake rates? Or is it another problem that is being addressed?
- Is this the right solution at this time in this context?
- What components need to be in the mandatory framework (Table 2)?
- Do these components fit the culture, the context, and the specific problem that the mandatory program is trying to solve at this time?
- Do other proven strategies need to be part of this change to the immunization program?
- Will the shift to a mandatory program be accompanied by an increase in resources to the immunization program, and where will those resources come from (i.e., will other public health actions be compromised)?
- What might be the public response to such a change, especially if choice is restricted, and can this be effectively managed?
- Is there potential for harm to vulnerable populations? i.e. unintended consequences

Ultimately, decision-makers would be greatly aided in addressing these questions if quality research were funded in order to generate the evidence needed to make such program/ policy decisions. Studies of the impact of mandatory immunization (on programs, practices, and outcomes) in high-, middle- and low-income countries in different contexts are urgently needed given that so many countries have enacted or are contemplating mandatory childhood immunization programs.

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