SUBMISSION TO THE JOINT OIREACHTAS COMMITTEE HEARING ON VACCINATION

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SUBMITTED ON BEHALF OR THE RCPI

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The benefit of vaccines is a Matter of Fact: Vaccines Work

- Vaccination has prevented more deaths than any other single medical intervention
- Vaccination prevents 6 million deaths globally every year
- Vaccines that are licensed for use in our National Program are safe
- Vaccines protect the health of our children, young people, and the community
- Vaccination programs bring economic benefits to a country

Vaccine Preventable Diseases in Ireland	
Measles	1948 – 63 deaths 1959 – 15,134 cases 1970's – Ave 7 deaths each year 1980-10,000 cases 1985 – 201 cases 2000 -1500 cases, 3 deaths (post Autism scare) 2016 – 43 cases
Diphtheria	1948 -521 cases, 30 deaths 2016 – 1 case, 0 deaths
Pertussis	1948 – 3343 cases notified, 204 deaths 2016 – 214 cases
Polio	1956 – 499 cases 2016 – 0 cases

The Myths

Myths are preventing people vaccinating their children

- Myth: The diseases are extinct or no longer a threat
- Myth: Vaccines cause autism
- Myth: Vaccines cause POTS (postural orthostatic tachycardia hypotension syndrome)
- Myth: Vaccines cause CRS (Chronic regional pain syndrome)
- Myth: Vaccines are not safe

- Dating back to the introduction of smallpox vaccine there have been strong anti-vaccine lobbies, whose misguided efforts have fueled recurrent cycles of misinformation dissemination, loss of vaccine confidence, drop in vaccine uptake and disease resurgence.
- No medicine is perfect, however most childhood vaccines produce immunity 90-100% of the time. Very rarely, vaccines can have problems and can be associated with a serious side effect in a susceptible person. Overall 1:1,000,000 vaccinees may suffer a serious adverse consequence, a risk ratio much, much, lower than that associated with the diseases that the vaccine prevents. Even, and importantly, after vaccine licensure there is continued surveillance for adverse events that could possibly be causally related to vaccines. This can detect a problem, should it occur, enabling prompt investigation.

Key Points:

- Vaccines have changed for the good the lives of infants, children and adults in Ireland.
- No medicine or therapy can be 100% safe for 100% of the population (nor was walking or driving to this meeting today), but any balancing of risks in relation to vaccines in our National Program shows that benefits far outweighs any risk.
- Misinformation dangerously undermines the public confidence in vaccines resulting in decreased uptake
- Decreased uptake will lead to disease resurgence, illness, death and economic loss
- Every effort must be made to strengthen the National Immunisation Program
- The vaccines in our National Immunisation Program are safe and effective

Vaccines work: The Benefits

Smallpox, was a much feared disease that caused widespread epidemics maiming and scarring its victims. In one epidemic of 5,889 Bostonians who had **smallpox,** 844 died. **Smallpox** caused more than three–quarters of all the deaths in **Boston** that year. Development of an effective vaccine ultimately led to its global eradication which was declared in 1980. Because of its successful eradication through vaccination, smallpox vaccination is no longer necessary.

Before polio vaccination in the 1950's, polio killed or paralysed 600,000 people every year. In Ireland, the last polio epidemic swept the country in 1954-1956. The wards of Cherry Orchard hospital filled with its victims; many of whom lived their days attached to 'iron lung' machines in order to breathe. Cappagh hospital was filled with children who survived the infection but were either paralysed or had withered limbs needing wheelchairs, callipers and braces.

Buoyed by the success of smallpox eradication and consequent to introduction of mass vaccination that had eliminated polio in the Americas, the global polio eradication initiative began in 1988. In 1988, an estimated 350,000 cases were paralysed for life annually. By 2006, polio transmission had been halted in all but four countries. One of the three types of polio virus (type 2) was eliminated. However, vaccination campaigns were interrupted due to political conflict, wars, and unfounded rumours of vaccine side effects leading to a resurgence in case numbers with spread to 12 additional countries with 650 confirmed cases reported in 2011. Resumption and strengthening of vaccination programs allowed confirmation of the successful eradication of type 2 polio, officially declared eliminated in 2015, an end to transmission of type 3 polio in 2012, and reduction of case numbers to 37 cases of type 1 polio in 2016. More than 16 million people are walking today who, were it not for polio vaccine, would have been paralysed. The eradication of polio is in sight but, and I quote the independent monitoring board of the polio eradication initiative, *"polio will not end everywhere untill everywhere ends it"!*

This is the power of vaccination. Diseases can be controlled and some even eradicated.

Measles Mumps and Rubella:

Disease Complications[1]					
Measles		Mumps		Rubella	
Ear Infection	(1 in 20)	Viral meningitis	(1 in 20)	Encephalitis	(1 in 6000)
Pneumonia/bronchitis	(1 in 25)	Encephalitis	(1 in 1000)	Birth defects – 90% chance if mother contracts Rubella early in pregnancy	
Convulsions	(1 in 200)	Testicular inflammation in adult males	(4 in 10)		
Diarrhoea	(1 in 6)	Permanent hearing loss	(1 in 20,000)		
Meningitis/encephalitis	(1 in 1000)				
Conditions affecting blood clotting	(1 in 6000)				
Late onset subacute sclerosing panencephalitis (1 in 8000 children who get measles under 2)					
1-2 deaths in 1000 reported cases					

Following an upsurge in measles cases in the early 1980's in Ireland, measles vaccine was introduced in 1985 and MMR (Measles, Mumps and Rubella) in 1988. Measles is a highly infectious condition. A vaccine uptake by 95% of susceptible individuals is requires to break the chain of transmission, protecting not only the direct recipients of the vaccine but also those vulnerable individuals in the community who, either because they are be too young or have weak immune systems, should not receive the vaccine.

Following the introduction of the measles vaccine its impact on cases numbers was rapidly apparent. Reported case numbers declined from 10,000 in 1985 to 201 cases in 1987. In 1998, Andrew Wakefield published fraudulent data proposing a link between the MMR vaccine and autism. There followed widespread alarmist dissemination of the information such that confidence in the vaccine fell resulting in significant decline in vaccine uptake to 77% – well below the levels needed for herd immunity and prevent the transmission of the virus. There followed a measles outbreak in Ireland in 2000 with 1500 reported cases and 3 deaths.

Measles is a disease that relies on human to human transmission and thus is an ideal target for erradication. The projected eradication of measles by 2015 was derailed as consumer confidence in the vaccine plummeted. Although much in this regard has been reversed and MMR vaccine uptake rates in Ireland although significantly restored, reaching 93% in 2015, remain just short of the 95% threshold to prevent transmission. Every effort must be made to reach and to maintain vaccination rates > 95%.

MENINGOCOCCAL VACCINATION:
The introduction of the meningococcal C vaccine has dramatically reduced the incidence of meningococcal disease in children (Fig 1. Men C data shown in the lighter shade). Meningococcal B disease remains a problem but with the addition of the meningococcal B vaccine to the National schedule similar declines can be anticipated. In the UK meningococcal

[1] Adapted from HSE. MMR Vaccine discussion Pack. https://www.hpsc.ie/a-z/vaccinepreventable/measles/publications/File,1242,en.pdf accessed 5.5.2017

B vaccine has been found to be extremely effective. When compared with the group who were not included in the vaccination campaign, the rates were halved in vaccine eligible children within 10 months of its introduction[2]

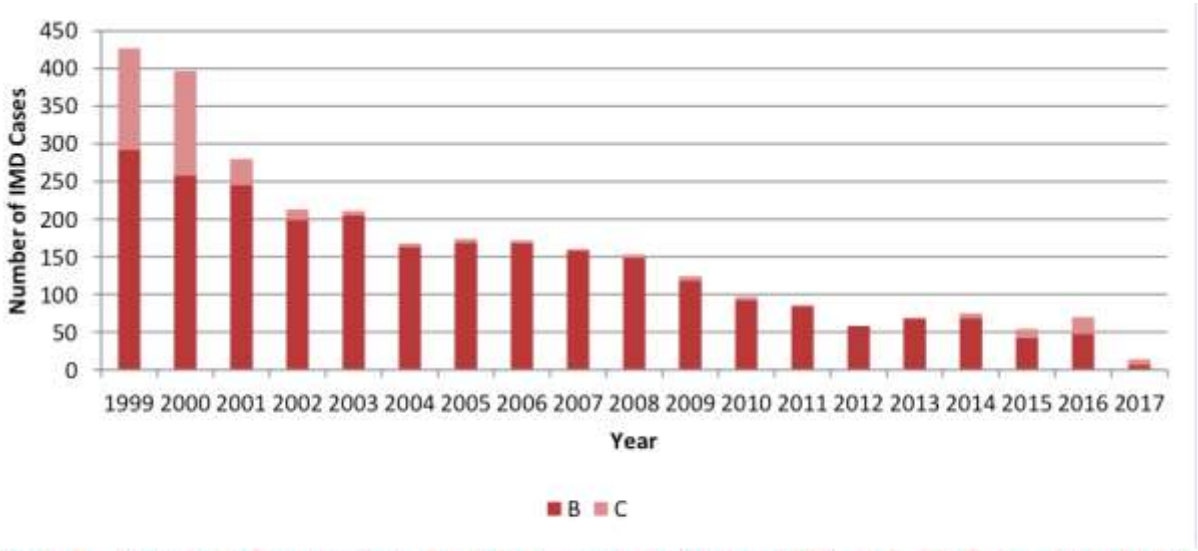


Figure 1. Number of serogroup B and C cases between 1999 and 2017 to date (CIDR, 01/March/2017)

HPV (HUMAN PAPILLOMA VIRUS VACCINE).
The HPV vaccine was introduced for all 12 to 13 year old girls in 2010. In Ireland a 4 valent vaccine, Gardasil® is in current use. Following initial good uptake, concerns re possible vaccine related side effects has led to a marked decline in uptake. These concerns have proved unfounded but the continued dissemination of alarmist information has undermined public confidence in the vaccine.

WHY USE THE VACCINE?
There are more than 100 different types of HPV, most of which infect the skin, causing common skin warts (verrucae). Some 40 types can infect the genital tract, where infection is associated with genital warts and multiple cancers, of which cancer of the cervix is the most significant. Cervical cancer is the fourth most common cancer in women with over half a million cases and 270,000 deaths globally in 2012. HPV infection causes almost all cervical cancers and pre-cancers and approximately 90% of anal, 70% of vaginal, 50% of penile, 40% of vulvar and 13 – 72% of mouth and throat cancers. The types of HPV that infect the genital tract are categorized into low-risk (types 6 & 11) and high-risk (types 16 & 18) cancer types. Types 16 and 18 are high risk types for cancer and types 6 and 11 cause about 90% of genital warts. Gardasil® vaccine provides protection against these four types. A newer vaccine, now in use in the US, targets 9 different types of HPV thus providing even greater breath of protection against cancer inducing infection.

"On average, 538 cases of HPV-associated cancers were diagnosed per year in Ireland during 2010-2014, of which 393 (3 in 4) were in women, 145 (1 in 4) in men. Cervical carcinomas were the most frequent (on average 292 cases per year). Next most frequent were SCCs (squamous cell cancers) of oropharyngeal sites (133 per year), vulva (38), anus and rectum (36), penis (32) and vagina (10). In total, these cancers accounted for about 2.6% (1 in 38) of all invasive cancers (excluding non-

[2] Parikh SR et al. Lancet 2016;388:2775-82

melanoma skin cancer) diagnosed in Ireland during 2010-2014, or 4.1% (1 in 24) for females, 1.3% (1 in 77) for males." (National Cancer Registry Ireland 2017).

It is estimated that HPV infection causes up to 420 cancer cases and 130 cancer deaths each year, most of which can be prevented by the HPV vaccine. In Ireland, the lifetime risk of developing cervical cancer is 1% and of having a pre- cancer is 8.7% (National Cancer Registry (http://www.ncri.ie/sites/ncri/files/factsheets/FACTSHEET_cervix_2.pdf , accessed 6.5.2017). HPV vaccine can prevent most of these cases. The evidence of benefit is very strong.

Garland et al. in a systematic review of the experience of Gardasil® vaccine in a real world (not in a clinical trial) setting showed that, over the last decade, where HPV vaccines have been used infections with HPV 6/11/16/18 have decreased by 90% with 90% reduction in genital warts, 45% reduction in low grade precancers, and 85% reduction for high grade cervical abnormailities – the imminent precursor of cervical cancer.[3] Countries included Australia, Belgium, Canada, Denmark, France, Germany, New Zealand, Sweden and the US. Similar results have been reported by Kahn et al[4]. In their report the benefit of the vaccine was shown not only to the vaccine recipients, with a 90% reduction in HPV infections but also in the unvaccinated in the community with a 30% reduction in the unvaccinated showing evidence of herd immunity.

These vaccines are very very effective at preventing HPV infection and thus will prevent cervical cancer and a range of other cancers.

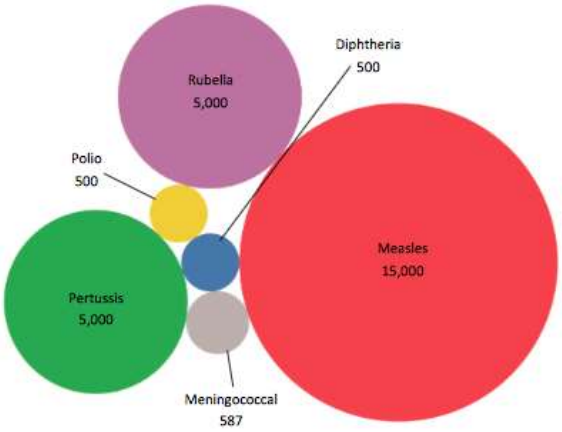
[3] Garland et al. CID2016:63:519-528
[4] Kahn et al. CID 2916:63; 1281-1288

Vaccines Work in Ireland

These bubbles are sized according to the annual number of cases in Ireland during the pre-vaccine era versus 2015. It is clear that significant progress has been made. However, we must not become complacent. We need to keep vaccine uptake at 95% to stop outbreaks of these serious infectious diseases.

Then

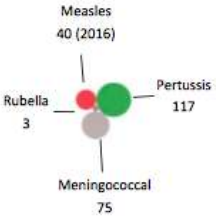
(annual disease cases in Ireland pre-vaccine)



* The figure refers to number of diphtheria cases in 1948 as pre-vaccine data are not available

Now

(disease cases in Ireland in 2015)



Diphtheria 0
Polio 0

Reference:
http://www.hpsc.ie/
http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/

www.immunisation.ie
@HSEImm
#VaccinesWork

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[5] From https://hse.ie/eng/health/Immunisation/vaccineswork/

MYTHS NOT FACTS:

Myth: The diseases are extinct or no longer a threat

The diseases that vaccines prevent remain a threat.
Serious diseases will come back if we do not vaccinate and maintain vaccine uptake rates:

To date just one human disease, smallpox, has been successfully eradicated though vaccination. Once the threat of infection was definitively removed vaccination programs against smallpox were no longer needed and withdrawn. Similarly, polio and measles were targeted for eradication.

The very real possibility of polio eradication, with its curtailment to isolated areas of Nigeria and Afganistan was achieved when interruption of vaccination programs led to its resurgence spreading not just within those countries but also to others. As long as one person remains infected with polio the threat of epidemic spread remains.

If the level of vaccination in our community drops then it could take just one returning emigrant from an area with polio still in circulation to bring it back and cause an outbreak. Over the last years this has been evidenced by measles, travellers infected in a country with a measles outbreak return only to develop measles in transit or on their return. Fever and rash is frequently not recognised as measles thus providing th eopportunity for further spread. Only vigilance in maintaining vaccine uptake rate will protect the individual and the community.

In the mid 1970's a scare in relation to pertussis vaccine resulted in dramatic declines in vaccine uptake (Figure). This was followed by a prompt rise in cases. Infections rates were brought under control only following vaccination. Sadly many infants suffered during this time. Some of whom will have resulting chronic lung disease

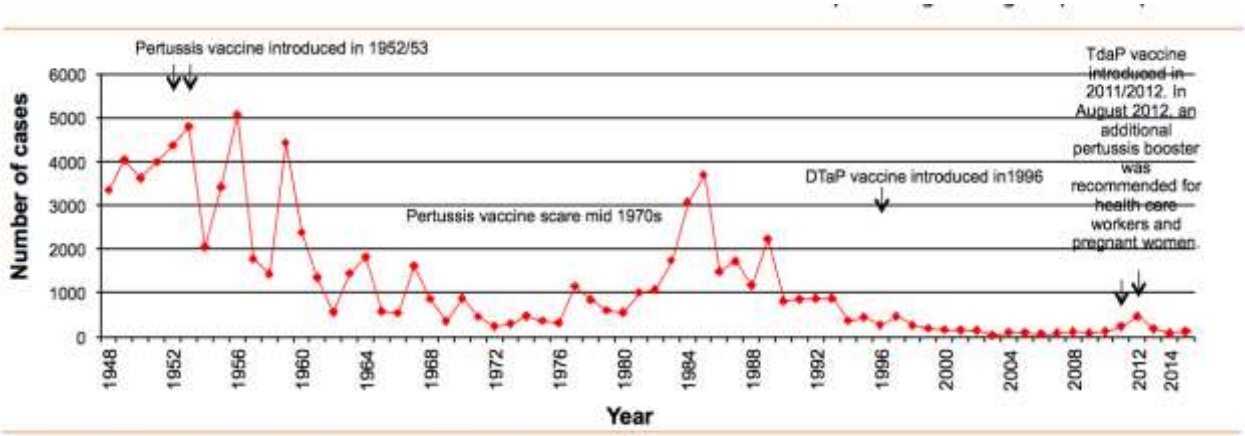

Figure 1. Number of notified pertussis cases in Ireland by year, 1948-2015
1948-June 2000 data collated by DoHC
July 2000-2015 data collated by HPSC

Myth: MMR vaccine causes autism

This myth arose from the fraudulent reports of Andrew Wakefield. The original paper was retracted but the damage of the misinformation was done. Families suffered fearing that their choice to vaccinate may have cause autism in their child. Families suffered because losing confidence in vaccines they avoided all vaccines – some to endure the pain of seeing their child contract a vaccine preventable disease. This did untold damage to children and their families.

Myth: HPV vaccine causes POTS/CFS/ME
Myth: HPV vaccines causes CRS (Chronic regional pain syndrome)

A number of vaccine recipients had reported a very wide range of symptoms which have been temporally related to the vaccine and which they fear are causally related. The symptoms attributed are very extensive; headache, persistent sore throat, dizzyness, fainting, chronic fatigue, muscle weakness, pain, joint pain numbness, thyroiditis, rheumatoid arthritis, seizures, heart palpitations, changes in menstrual cycle, breathing problems and abdominal pain (https://www.regret.ie/images/UnexplainedPoster.png).
The complex of symptoms, while unique to the individual have similarity with significant overlap with those symptoms associated with chronic fatigue syndrome (CFS)/myalgic encephalitis (ME) and POTS.

Prompted by the reports in 2015 a careful review was carried out by the European Medicines Agency - Pharmocovigilance risk assessment committee (PRAC) looking for evidence of these diagnosis or of suggestive symptoms in patients who were enrolled in any of the clinical trials and in the post marketing surveillance. At that stage over 65 million doses of HPV vaccines had been used Gardasil had been trialed in 60,594 subjects with197,983 person-years follow-up. They also extensively reviewed the incidence and prevalence of these conditions in the unvaccinated population.

EMEA- PRAC concluded:

" Symptoms of CRPS and POTS may overlap with other conditions, making diagnosis difficult in both the general population and vaccinated individuals. However, available estimates suggest that in the general population around 150 girls and young women per million aged 10 to 19 years may develop CRPS each year, and at least 150 girls and young women per million may develop POTS each year. The review found no evidence that the overall rates of these syndromes in vaccinated girls were different from expected rates in these age groups, even taking into account possible underreporting. The PRAC noted that some symptoms of these syndromes may overlap with chronic fatigue syndrome (CFS, also known as myalgic encephalitis or ME). The results of a large published study showed no evidence of a link between HPV vaccine and CFS. As many of the reports considered in the review have features of CFS and some patients had diagnoses of both POTS and CFS, these results were considered relevant for the current evaluation. Taking into account the totality of the available information the PRAC concluded that the evidence does not support that HPV vaccines (Cervarix, Gardasil, Gardasil 9, Silgard) cause CRPS or POTS. The benefits of HPV vaccines continue to outweigh their risks".

(http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/HPV_vaccines_20/Opinion_provided_by_Committee_for_Medicinal_Products_for_Human_Use/WC500197129.pdf)

HPV vaccines represent a major step forward in combatting cancer. They are safe. It is inevitable various symptoms or diseases, for which there is no identified medical explanation, will be attributed to vaccinations when the timing of symptom onset coincides with the timing of vaccination. Such occurred with pertussis vaccines and encephalopathies in the 1970's, with MMR and autism in the 1990's and now with HPV vaccine and POTS/CFS/CRS. It is inevitable that some young people who receive the vaccine will develop constellation of symptoms, such as those described, around the time of vaccination as even in

the unvaccinated population the symptom onset coincides with the age range when vaccination is targeted[6],[7].

THE FUTURE

The current immunisation program targets, Diphtheria, Tetanus, Pertussis (whooping cough), polio, hepatitis B, Rotavirus, *Haemophilus influenza* type B, Meningococcus types B and C, pneumococcal infections, Measles, Mumps, Rubella, influenza and Human papillomaviruses. ALL of these vaccines have proven effectiveness and are safe. THEY SAVE LIVES and protect the health of our community and the wellbeing of our families. The risk of an adverse event related to a vaccine is overwhelming outweighed by the benefit afforded.

THERE IS MORE TO DO.

Varicella Zoster Virus (VZV) (Chicken pox/shingles):

Varicella vaccine is urgently required as part of our National Program. This is not just to protect the children from chicken pox – which although it can be a relatively mild illness for some, it is the leading infectious cause of stroke in children, can cause pneumonia, hepatitis and encephalitis and importantly is a most common cause of serious life threatening secondary invasive bacterial infection with *Group A streptococcus* (GAS) (the so called flesh eating bacteria in the media) and *Staphylococcus aureus*. In 2016 in Temple Street Children's Hospital 70% of the cases of invasive GAS were associated with preceding chickenpox.

Shingles, a painful eruption of the virus that lies dormant in our systems after chicken pox. It can cause persisting chronic pain in the affected area. Our risk increases as we age. Approximately 1 in 3 people will develop shingles in their lifetime. It is a vaccine preventable disease.

There has been an upsurge in the cases of meningococcal infection with types W and Y in the UK. We are beginning to see a similar rise in cases. These are also preventable through vaccination and adjustments to our current program may be needed.

Whooping cough (pertussis) has never gone away completely– however vaccination has protected the most vulnerable young infants from disease and resulted in a milder, if bothersome cough in adolescents and adults. The bacteria remain a real threat to newborns. In 2016 there were 214 cases notified, including one death. The highest attack rates are in infants under 1 year. Infants less than 6 months of age and preterm infants are at particular risk for severe disease. Of those hospitalized 50% will have episodes where they stop breathing, 20% have pneumonia, 3% develop convulsions, and 1 – 4% die. Providing a booster vaccination to women during pregnancy has proved very effective in preventing infection in the youngest infants (those at risk from death) and protecting them until they are old enough to receive their own vaccines. Unfortunately, while this benefit is recognised and National recommendations include whooping cough booster vaccines in pregnancy, no clear pathway has been developed whereby women can easily access the vaccine. Pathways to ensure provision of vaccines to pregnant women (as recommended for flu and whooping cough) must be developed urgently if further deaths are to be avoided

Group B streptococcal infection passes to newborn infants causing bloodstream infections, meningitis and infection of bones, joints and other organs. Newborn infants are most

[6] Heyer G. Pediatric Annals, 2017;46:e145

[7] Assessment report, EMA/762033/2015

vulnerable and their vulnerability lasts for the first few months of life. Vaccination of mothers during pregnancy has the ability to provide enough protective antibodies to the infant to get them safely through the first months of life. Such a vaccine is in development and we anticipate its availability in the next 3 – 5 years.

Influenza Vaccines: While not the perfect vaccines in terms of guaranteed protection, influenza vaccines save lives. Currently targeted at our senior population, health care workers and immunocompromised patients and their contacts, there is a clear health and economic benefit to increasing the breath of influenza immunisation programs.
Influenza vaccines, given to healthy children also saves lives – not just among the vaccinated but amongst their elderly contacts. It must be acknowledged that some young people are suffering from narcolepsy, which was likely triggered in susceptible individuals by the pandemic flu vaccine in 2009, an undoubted tragedy for the families, yet the roll out of the pandemic response saves innumerable lives.
It behoves us to ensure that those who genuinely suffer an adverse consequence from a vaccine should be supported – and to ensure that there are robust mechanisms in place to promptly recognize such events. The issue of narcolepsy can be contrasted to that of POTS/CFS/CRS and the HPV today. With narcolepsy, the concerns were raised, investigation commenced and a real difference in frequency of narcolepsy cases among the vaccinated compared to the unvaccinated found – strengthening the link. With POTS/CRS/CFS, the issue arose, was investigated and no difference in incidence between vaccinated and unvaccinated found. With Narcolepsy, cases were rare before the vaccine and there was a sudden surge in incidence following the vaccination program. With POTS/CRF/CFS the symptom complex was frequently seen before introduction of the HPV program.

LIMITATIONS OF THIS SUBMISSION:
This is not a comprehensive paper on vaccines. It will however hopefully serve to highlight the benefits of vaccination, the need for robust surveillance systems to detect vaccine related adverse events, the potential for misinformation to derail vaccination programs with serious consequences for the health and economic welfare of the population, and reaffirm the importance of maintaining a strong, dynamic, National Immunisation Programme.

Conclusions:

- Vaccines have changed for the good the lives of infants, children and adults in Ireland.
- No medicine or therapy can be 100% safe for 100% of the population (nor was walking or driving to this meeting today), but any balancing of risks in relation to vaccines in our National Program shows that the benefits far outweighs any very small risk.
- Misinformation dangerously undermines the public confidence in vaccines resulting in decreased uptake
- Decreased uptake will lead to disease resurgence, illness, death and economic loss
- Every effort must be made to strengthen the National Immunisation Program
- The vaccines in our National Immunisation Program are safe and effective