Prevalence of measles IgG antibodies in adults aged 18-34 years in Ireland, 2022

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Key Points

- Using residual sera sourced from primary care between October and December 2022, the proportion of adults aged 18-34 years negative for measles IgG antibodies (seronegativity rate) is 10.7%. Using seronegativity as proxy for potential susceptibility to measles infection, this indicates that 10.7% of adults in this age range may be susceptible.

- Measles seronegativity:
  - overall is similar in males (10.6%) and females (10.7%).
  - is inversely associated with age group, with the highest seronegativity (14.7%) observed in the 18-19-year age group.
  - in males ranges from 17.9% for those aged 18-19 years (2003-2004 birth cohort) to 5.7% for males aged 30-34 years (1988-1992 birth cohort). This variation is not seen in females.

- The proportion positive for measles IgG antibodies, indicating exposure to either vaccination or infection (seroprevalence rate), is 89.3% overall.

  - For all birth cohorts, except for the 1997, 2000, and 2003 birth cohorts, (aged 25, 22 and 19 years respectively) the rates are below the WHO elimination target of 95%.

HSE Health Protection Surveillance Centre. Measles IgG seroprevalence in adults 18-34 years in Ireland, May 2023

- Seroprevalence rates are generally higher than the national measles vaccination uptake rates at 24 months, except for the youngest cohort aged 18-19 years (birth cohort 2003-2004). Noting:
  - Available national primary vaccination uptake data does not capture booster vaccination, late first doses > 24 months of age, or second doses for the selected age groups.
  - Large outbreaks of measles occurred during 1993, 2000, and 2003 and smaller outbreaks occurred since then, which may have boosted seroprevalence.

- There are some limitations with this data that need to be taken into consideration:

  - The residual sera are sourced from primary care at six acute hospital laboratories throughout Ireland, therefore they may not be representative of the general population. The dataset available for analysis is limited to age, sex and the participating laboratory where specimens were collected.
  - The assay is primarily designed for the detection of measles IgG post infection. It may not be as accurate at detecting measles IgG generated following measles vaccination, which is often a lower titre and declines more rapidly. It cannot distinguish between antibodies due to natural infection or vaccination.
  - As there is no "gold standard" measles IgG assay, the results may not be directly comparable to results generated in other studies using different tests. There was no independent evaluation of the assay, and the results were adjusted using the manufacturer's stated sensitivity and specificity, which was based upon a relatively small panel of samples.

Conclusions

Since 2018, Ireland is considered to have eliminated measles, having demonstrated interruption of endemic measles transmission for more than 36 months, although outbreaks may still occur, often associated with imported measles infection. These data, using the absence of measles IgG as a proxy, show potential susceptibility to infection in 10.7% of young adults, complementing and adding to information available from primary measles vaccination uptake data. A measles vaccination catch-up programme, particularly for younger males with suboptimal protection, should be considered.

This estimate was made possible by the existence of the National Serosurveillance Programme, established in response to COVID-19. It shows both the value of that infrastructure and some limitations due to restricted identifier data associated with each sample.

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Background

The National Serosurveillance Programme (NSP) is led by the HPSC Seroepidemiology Unit (SEU), working in partnership with the University College Dublin (UCD) National Virus Reference Laboratory (NVRL) Serosurveillance Unit and the acute-hospital Laboratory Surveillance Network (LSN). It is overseen by a national multi-disciplinary and multi-sectoral Steering Committee. The NSP conducts systematic sampling of residual specimens with the aim of estimating the proportion of people who have antibodies to infectious diseases in the general population, either from vaccination or previous infection, and to see if this changes over time. Residual sera specimens are anonymised blood samples that were originally collected for clinical testing and are now due to be discarded.

The World Health Organization (WHO) has identified measles as a priority disease for elimination due to the high morbidity and mortality associated with measles infections among susceptible populations globally (1). In June 2018, the European Regional Verification Commission for Measles and Rubella Elimination (RVC) concluded that Ireland had demonstrated interruption of endemic measles transmission for 36 months and is considered to have 'eliminated' measles (2). However, outbreaks can still occur following importation of the virus in particular from areas where there is ongoing endemic transmission. This, in combination with gaps in vaccination uptake in displaced populations, older persons without exposure to the wild virus who may have been missed in catch up campaigns, vaccine hesitancy worldwide, and the impacts of the COVID-19 pandemic on primary immunisation programmes, also raise concern about the risk of measles outbreaks. In 2019, the RVC expressed concerns about the threat to measles elimination due to low vaccination coverage, especially in Dublin, and recommended implementation of strategies to close immunity gaps in the population (3).

History of measles incidence, outbreaks, vaccination policies and uptake rates in Ireland

In 1985, Ireland introduced the mono-component measles vaccine, followed by the combined Measles, Mumps, Rubella Vaccine (MMR) vaccine in 1988, and the second MMR dose in 1992. Prior to the introduction of the first measles vaccine, the notified incidence of measles nationally had reached 280 cases per 100,000 population (4). The implementation of the measles vaccination schedule is shown in Table 1, and demonstrates that vaccination uptake contributed to the rapid and substantial reduction of measles incidence to 6 per 100,000 by 2002. Figure 1 shows measles case numbers between 1948 and 2022, and includes information on the timing of primary and mop up campaigns undertaken.

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Table 1. Introduction of measles vaccines and incident cases in Ireland, 1985-2002

Measles Vaccine	Year	Eligible Age Group	Incidence of measles (cases /100,000)
Primary Measles Vaccine			
Monocomponent Measles Vaccine	1985	15 mos. - 5 years	280/100,000
Combined Measles, Mumps, Rubella Vaccine (MMR)	1988 2002	15 mos. – 2 years 12-15 mos.	26/100,000 6/100,000
Second Dose Measles Vaccine			
Combined Measles, Mumps, Rubella Vaccine (MMR)	1992 1999	10-14 years 4-5 years	5/100,000 4/100,000

Source: Health Protection Surveillance Centre, European Health for All database
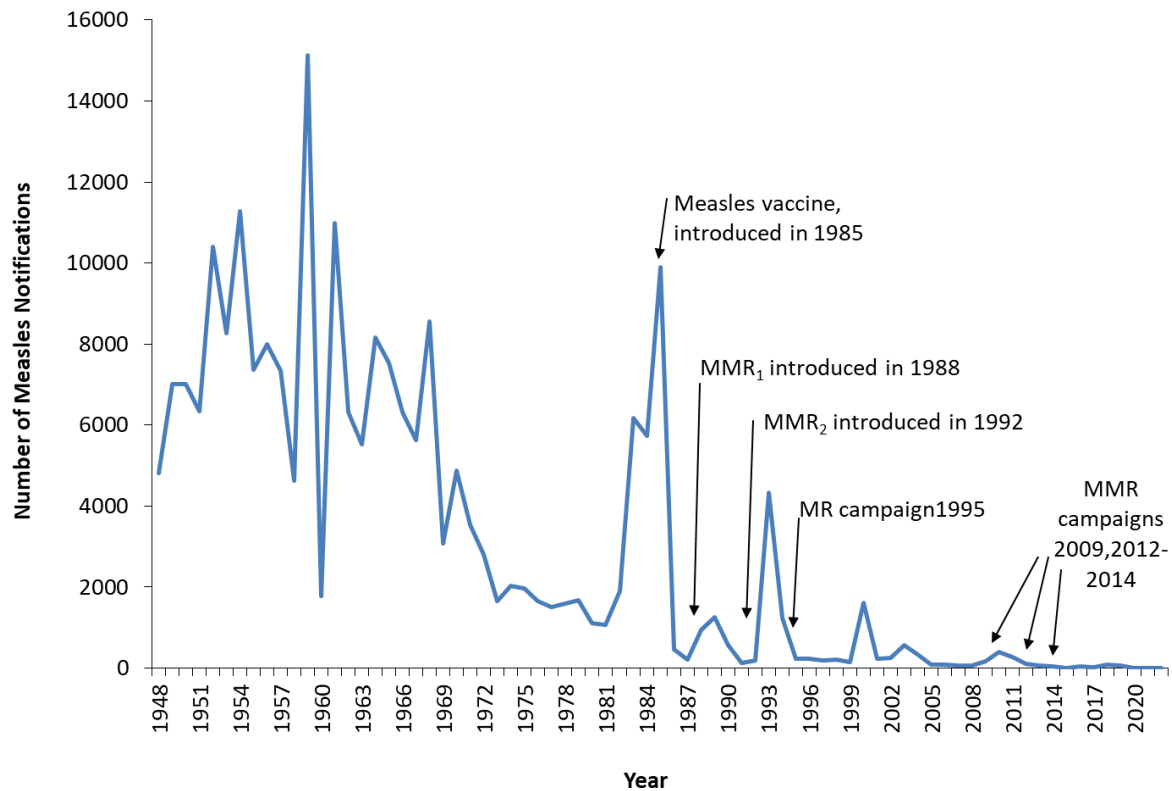
Source: HPSC Vaccine Preventable Diseases team

Figure 1: **Number of measles cases notified, 1948-2022, with vaccination schedule and mop up campaigns highlighted.**

The WHO advises that a vaccine coverage rate of at least 95% with two doses of the MMR vaccine is required to produce herd immunity, halt endemic measles transmission, and maintain elimination status (5). In Ireland, the uptake of the first dose of the MMR vaccine at 24 months peaked at 93% in 2013, and has consistently remained below the WHO European Region's average uptake rate. At present, Ireland does not have a national population vaccination register and MMR second dose national uptake rates among children 4-5 years of age are unavailable prior to 2011. National uptake data are also not available for MMR catch-up vaccination campaigns administered throughout the 1990's.

In addition, there is no unique health identifier in use across the system which would enable all medical interventions such as vaccination to be linked. Without a comprehensive view of measles immunisation uptake in Ireland, there is the risk of pockets of potential susceptibility forming or broadening, without the ability to identify and investigate the populations that are currently under vaccinated. In addition, health data generally lacks robust information on equity, that would allow us to identify pockets

of low coverage among underserved populations. Under these circumstances, seroprevalence data has the potential to capture all vaccination doses administered to individuals, and can provide insight to the current landscape of immunity and patterns across age and sex, although lacking ability to identify and assess immunity patterns across other population characteristics.

Since the introduction of the measles vaccine, there have been a number of large measles outbreaks in Ireland (table 2). The magnitude of these outbreaks has reduced over time, partly due to the speed at which potential cases are identified to reduce onward transmission. During the peak years of the most recent large outbreaks in 2003 and 2010, 61% and 77% of the measles cases notified, respectively, were reported as unvaccinated, where information on vaccination status was known. (6) (7). Case based notification of measles began in 2000, and data detailing measles outbreaks or cases prior to 2003 is not available.

Table 2. **Notified measles cases in Ireland during peak outbreak years, 1988-2010**

Year	Notified cases	Crude incidence rate	Unvaccinated cases	Hospitalised cases
1989	1,248	36/100,000	No data	No data
1993	4,328	121/100,000	No data	No data
2000	1,603	44/100,000	No data	No data
2003	584	15/100,000	61% (182/300)	120
2010	443	10/100,000	77% (257/332)	108

Source: HPSC, European Health for All database

The European Sero-Epidemiology Network 2 (ESEN2) serological study of measles conducted from 1996-2004 was the most recent serological study of measles in Ireland. In 2003, Ireland provided measles IgG antibody results for 2,590 residual sera specimens in persons aged one year and older. The study used the total seronegative sample proportion to define potential susceptibility, and subsequently the susceptible proportions within five discrete age groups were used to determine each participating country's susceptibility level.

In the results, Ireland was classified as having "higher susceptibility" as the WHO susceptibility target among the 5-9-year age group in particular was not achieved, however the susceptibility targets were not met for four of the five age groups overall (Table 3) (8).

Table 3. WHO measles susceptibility targets and Irish ESEN2 results by age group, 2003

Age Group (years)	WHO Susceptibility Target (%)	Ireland's Susceptibility Results (2003)
2-4	<15%	14.2%
5-9	<10%	11.8%
10-19	<5%	8.6%
20-39	<5%	7.8%
40+	<5%	7.6%

Source: ESEN2

Methods

In 2022, the NSP undertook a measles IgG seroprevalence study to identify the proportion of adults who may be susceptible to measles infection, in order to inform the assessment of Ireland's national measles elimination status, and to supplement current public health strategies required to maintain this goal.

Between 17 October 2022 and 2 December 2022, 2,197 specimens from adults aged 18-34 years (birth cohorts 1988-2004) tested in primary care were obtained from six LSN participating acute-hospital clinical chemistry laboratories; Letterkenny University Hospital, St. Vincent's University Hospital, University Hospital Limerick, Galway University Hospital, Beaumont Hospital, and Tallaght University Hospital. Sample distributions were requested based on the 2021 estimates of the Irish national age distribution for the age groups 18-19, 20-24, 25-29, and 30-34 years.

As seroprevalence is a core surveillance activity for which the HPSC is legally mandated, no individual patient consent was required.

Sera were tested for IgG antibodies to measles virus at the NVRL using the DiaSorin LIAISON® XL Measles IgG assay, which uses chemiluminescence immunoassay (CLIA) technology for the semi-quantitative determination of specific IgG antibodies to measles virus in human serum or plasma samples (9). This method reports measles virus IgG concentrations as arbitrary units (AU/mL). As shown in Table 1, specimens with a result ≥16.5 AU/mL are considered positive. Specimens with a result < 13.5 AU/ml are considered negative (not detected) and generally indicate no exposure to measles virus or no vaccination, but may also indicate waning immunity, in particular post vaccination. In this analysis, equivocal results are treated as positive results.

Table 4. DiaSorin LIAISON® XL Measles IgG assay result categorisation

Result	IgG concentrations
Negative	<13.5 AU/mL
Equivocal	13.5 – 16.4 AU/mL
Positive	≥16.5 AU/mL

Denominator population profiles were taken from CSO 2021 population estimates provided by the HSE National Health Intelligence Unit ('April 2021/H1') (10). Data were aggregated into the following age groups for analysis: 18-19 years, 20-24 years, 25-29 years, and 30-34 years.

The seroprevalence was adjusted for the misclassification or imperfect sensitivity and specificity in the application of the diagnostic testing using the manufacturers stated sensitivity and specificity values and the Rogan Gladen-estimator, see Technical Notes for further details (11). Unless stated otherwise, adjusted results are presented. Seroprevalence results are presented overall, by age group, and by sex, with 95% confidence intervals. Quantitative antibody concentrations are presented by age group and sex. A linear model was fitted to explore the relationship between the proportion seronegative and age and sex. A model with interaction between sex and age was also considered with the interaction term retained in the model if significant at the 5% level.

Results
Sample characteristics

Of 2,197 specimens collected, twelve specimens were omitted from the final dataset as they did not meet inclusion criteria, and two specimens were not tested due to insufficient volume, leaving a final dataset of 2,183 observations. In total, 2,183 adult residual sera specimens were available for analysis: 1200 females and 983 males. The median age was 27 years, the mean age was 26 years, and approximately half were between the ages of 22 and 31 years (table 5).

Table 5. Demographic characteristics of adult measles residual specimens, 10 October – 2 December 2022

Characteristic		Birth Cohort	Number	Percent
Sex	Male		983	55.0
	Female		1200	45.0
Age	Median age (years)		27	-
	Mean age (years)		26	-
	Age range (years)		18-34	-
	18-19	2003-2004	233	10.7
	20-24	1998-2002	618	28.3
	25-29	1993-1997	637	29.2
	30-34	1988-1992	695	31.8
County of residence	Dublin		1,485	68.0
	Donegal		187	8.6
	Galway		167	7.7
	Limerick		132	6.0
	Wicklow		102	4.7
	Other		111	5.0
Total			2,183	100.0

Measles seroprevalence results

The overall unadjusted measles seronegativity (potential susceptibility to measles) was 15.1%, (95% Confidence Interval 13.7, 16.7), and after adjustment this decreased to 10.7% (95% CI 9.1, 12.4). Seronegativity was similar for males and females, at 10.6%, (95% CI 8.3, 13.2) and 10.7%, (95% CI 8.6, 13.0) respectively.

Table 6: Seronegativity for measles antibodies by age and sex

Characteristic		Birth cohort	N seronegative	Total	% seronegative	CI lower	CI Upper	Unadjusted %
All			330	2183	10.7	9.1	12.4	15.1
Sex	Female		182	1200	10.7	8.6	13.0	15.2
	Male		148	983	10.6	8.3	13.2	15.1
Age group (years)	18-19	2003-2004	44	233	14.7	9.9	20.7	18.9
	20-24	1998-2002	99	618	11.6	8.7	15.0	16.0
	25-29	1993-1997	93	637	10.1	7.4	13.3	14.6
	30-34	1988-1992	94	695	8.9	6.4	11.9	13.5

Seronegativity decreased with increasing age-group; it was 14.7%, 11.6%, 10.1%, and 8.9% for the age groups 18-19 years, 20-24 years, 25-29 years, and 30-34 years respectively. The seronegative proportions by age group, stratified by sex are displayed in table 7.

Table 7. **Seronegative proportion by age group, stratified by sex**

Age group (years)	Birth cohort	Sex	N seronegative	Total	% seronegative	CI lower	CI Upper
18-19	2003-2004	Female	22	132	12.3	6.5	20.2
		Male	22	101	17.9	10.4	27.7
20-24	1998-2002	Female	45	343	8.5	5.1	12.8
		Male	54	275	15.6	10.9	21.1
25-29	1993-1997	Female	55	351	11.3	7.5	15.8
		Male	38	286	8.7	4.9	13.5
30-34	1988-1992	Female	60	374	11.7	8.0	16.1
		Male	34	321	5.7	2.6	9.9

Fitting a linear model to the proportion seronegative by age with an interaction term for sex, we find a difference in trends by age for males and females.

There is no evidence of an association between age and seronegativity for females; the fitted line had a slope of 0.12% (95% CI -0.38, +0.63). For males there was evidence of an inverse relationship between age and proportion seronegative, the fitted line had a slope of -0.90% (95% CI -1.40, -0.39) indicating an average drop of almost 1% in seronegativity for a one-year increase in age, for males 18-34 years (figure 2a and 2b and appendix A).
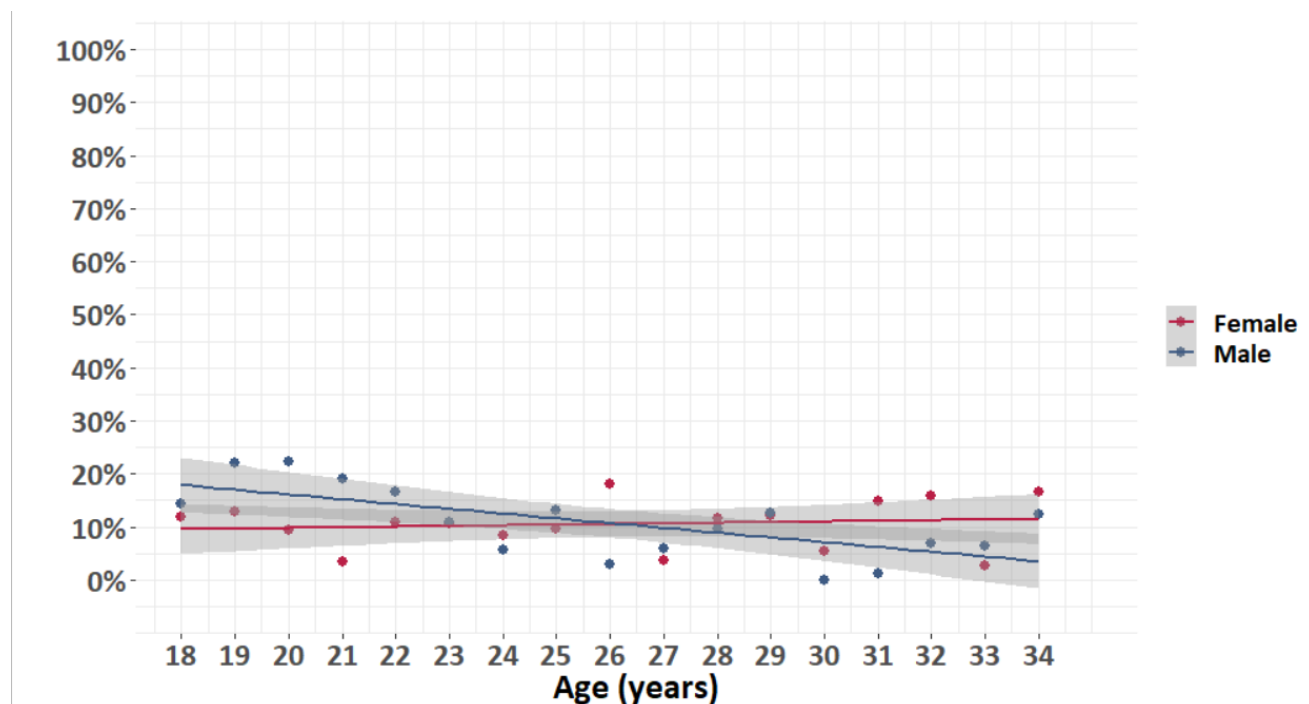

Figure 2a: **Seronegativity of measles antibodies by single year of age, stratified by sex**
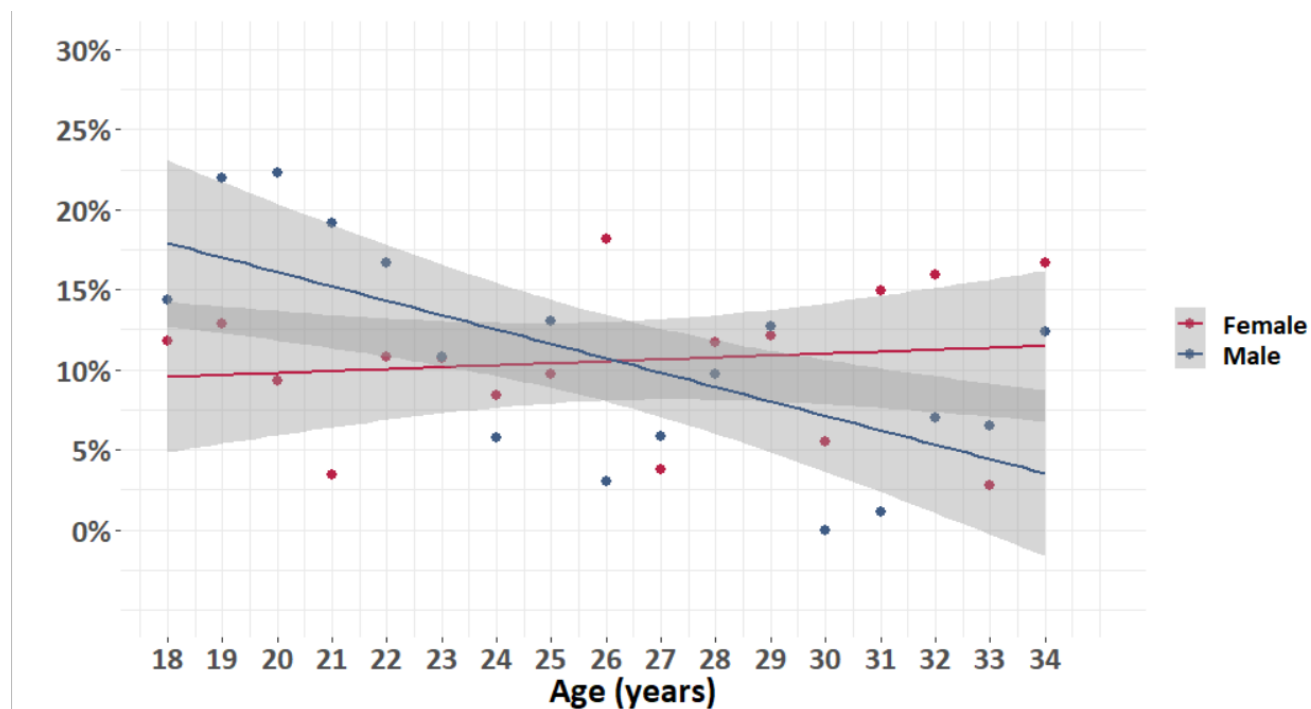
Figure 2b: **Seronegativity of measles antibodies by single year of age, stratified by sex (zoning in on details)**

Quantitative antibody levels in the total sample ranged from 4.9 AU/mL to 300 AU/mL, with a median of 84.1 AU/mL and an inter-quartile range of 27.4 AU/mL to 211 AU/mL. The lowest median antibody levels were seen in the youngest age groups (18-19-year-olds) among both males and females, 59.8 AU/mL and 63 AU/mL respectively, (table 9, figure 3).

Table 9: **Median, lower and upper quartile antibody levels by age group and sex**

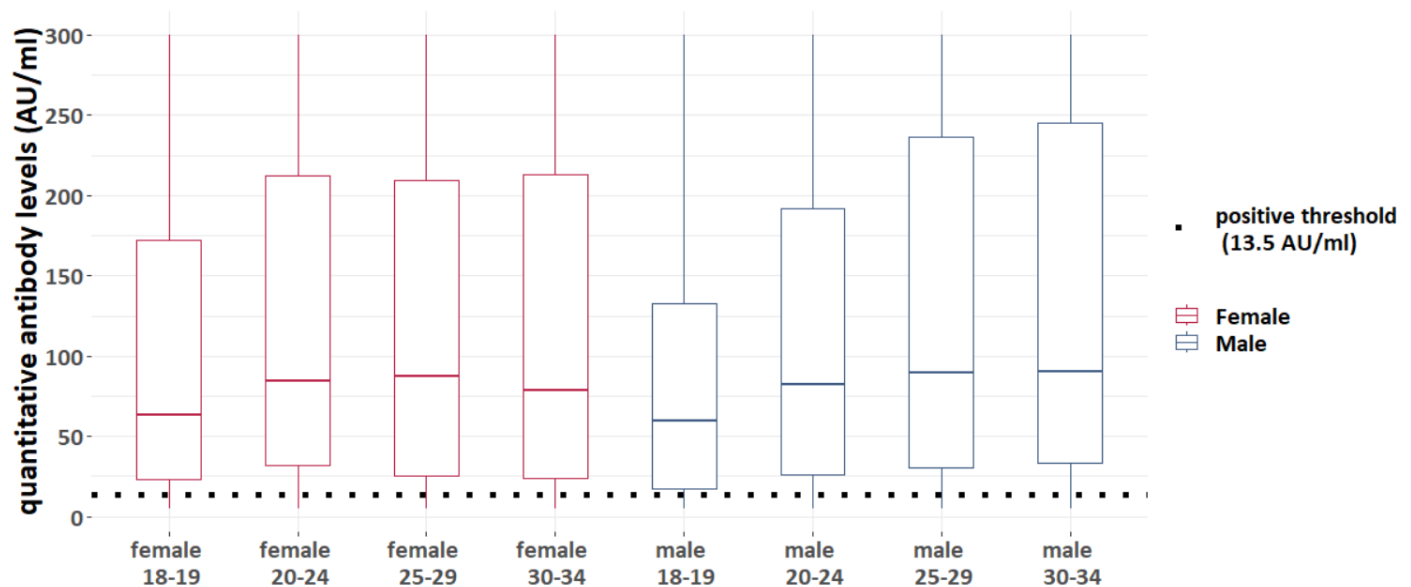| Sex	Age	Median antibody level	Lower quartile	Upper quartile
Female	18-19	63.0	23.0	172.0
Female	20-24	84.8	31.6	212.0
Female	25-29	87.5	25.4	209.5
Female	30-34	78.3	23.7	213.2
Male	18-19	59.8	17.5	133.0
Male	20-24	82.1	26.1	192.0
Male	25-29	89.7	30.5	236.2
Male	30-34	90.6	33.6	245.0

Figure 3: Measles Antibodies by age-group and sex (AU/mL)

Vaccination Uptake and Seroprevalence

National vaccination uptake rates at 24 months among those aged 18 to 34 years (birth cohorts 1988-2004) range from 72.5% to 86.1%, below the 95% vaccination uptake target, noting that available uptake data for this age group just includes information on uptake at 24 months, and doesn't capture second MMR or booster vaccination doses. Current seroprevalence estimates in this age group (18-34 years) range from 83.3% to 97.5% (figure 4). For all birth cohorts, except for the 1997, 2000, and 2003 birth cohorts, (aged 25, 22 and 19 years respectively) the rates are below the WHO elimination target of 95%.

Seroprevalence estimates are consistently higher than reported measles primary vaccination uptake rates at 24 months, except for the 2004 birth cohort where they are very similar. Seroprevalence rates rose in 2000, when primary vaccination rates dropped to 72%. It is possible that this may have been related to both an increase in the measles incidence rate in 2000 during an outbreak, and more importantly increased efforts to promote vaccination as an outbreak response measure.
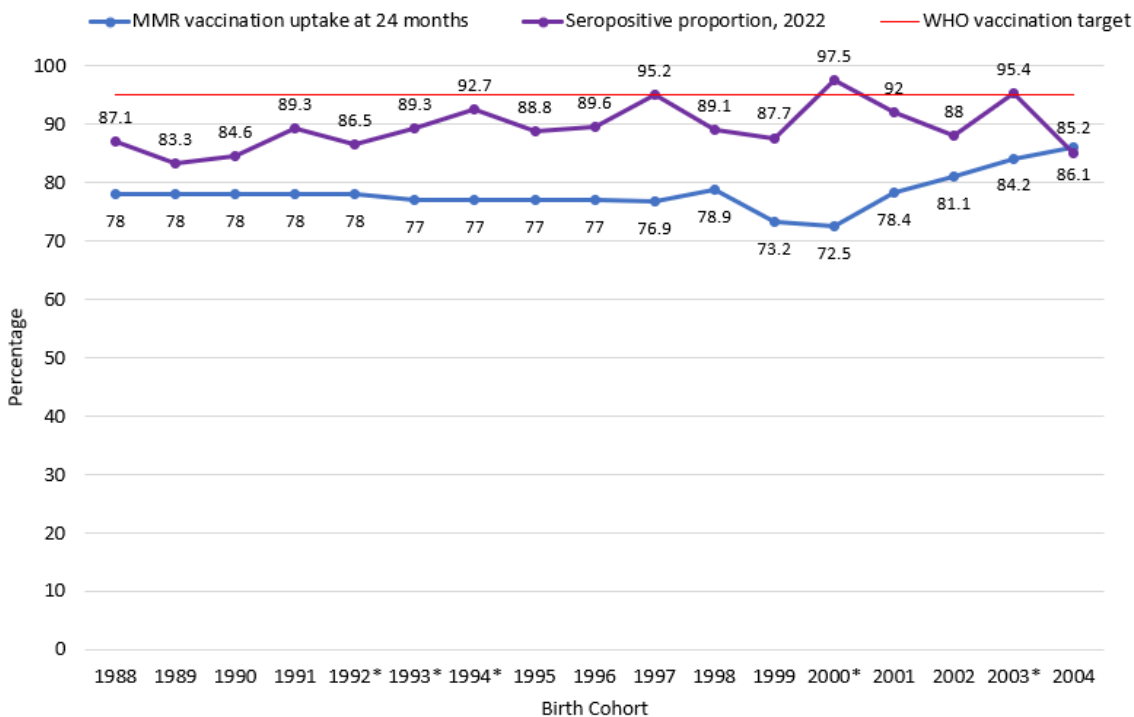
Source: Health Protection Surveillance Centre, European Health For All database

Figure 4: **Measles vaccination uptake rates at 24 months from 1988 to 2004 and current seroprevalence of measles IgG in persons born between 1998 and 2004 by year.**

Discussion

Measles seroprevalence analysis provides us with additional information to supplement that available using current primary immunisation uptake data. It adds to the scientific evidence base that informs risk analysis and proactive, targeted public health interventions and vaccination policy. It complements data from other surveillance systems, and can be used to estimate the proportion of the population that could be susceptible to infection.

In this sample, 10.7% of adults aged 18-34 years have no evidence of exposure to either measles vaccination or natural infection. Most cases of measles occur in inadequately vaccinated individuals; nearly two thirds of the reported measles cases occurring in 2003 and 2010 in Ireland were reported as unvaccinated.

Overall, seroprevalence estimates show susceptibility higher than the WHO measles elimination target of <5% susceptibity in those aged 18-34 years of age in all of the birth cohorts except 1997 (4.8%%), 2000 (4.5%%), and 2003 (4.4%); however, antibodies can wane over time, and seronegativity may not necessarily reflect susceptibility to infection.

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Adults from birth cohorts 1988-2004 became eligible for primary vaccination against measles virus between the ages of 12-24 months, and for secondary vaccination at ages 4-5 or 10-11 years depending on the vaccination schedule at the time. However, national secondary vaccination and catch up vaccination uptake information is unavailable for this population, and medical interventions are not currently linked via a unique health identifier. As seroprevalence estimates reflect not only primary vaccination, but also second dose vaccination, catch-up vaccination campaigns, and natural exposure to measles virus during periods of virus circulation in Ireland, it is not surprising that the estimates are higher than reported measles vaccination uptake for all but the youngest cohort in the sample, where the vaccination rates and seroprevalence rates were very similar. Given limitations with currently available national uptake data, seroprevalence rates may better estimate population protection and potential susceptibility. While seroprevalence studies provide valuable health intelligence, a unique health identifier used for all health interventions at primary, secondary, and tertiary care across public, private, and voluntary sectors in Ireland would improve the current deficits in health information and reporting abilities (12).

Quantitative antibody levels are lowest among the youngest age group, which may indicate younger cohorts are not receiving all recommended doses to complete the full measles vaccine schedule. Secondary vaccination uptake data are unavailable for these cohorts to investigate this further, which underscores the need for development of the national lifetime immunisation register in Ireland. Planning for this system is underway. Despite this, median antibody levels for all age groups in the study are above the serological threshold of at least 120mIU/mL that the WHO considers the most reliable correlate of protection (13). It is important to note that whilst the presence of measles IgG probably indicates clinical protection from the serious complications associated with measles infection, absence of antibody does not necessarily mean the individual is susceptible to infection or illness.

There is an inverse relationship between measles IgG seronegativity and age, where the highest proportion of seronegativity was within the 18-19-year age group at 14.7% (95% CI 9.9, 20.7). Anecdotally, the discredited research in the late 1990's that linked the measles vaccine and Autism Spectrum Disorder may have resulted in widespread vaccination hesitancy affecting vaccination uptake similar to the UK experience (14)(15), or this may be an effect of inward migration of unvaccinated individuals to Ireland (16). Methodologically dubious associations between measles vaccination and Crohn's disease and ulcerative colitis introduced in the mid to late 1990's may also have contributed to vaccine hesitancy during this period, although the available evidence does not support a link between the vaccines and inflammatory bowel disease (17).

The proportion of seronegative males was higher in younger birth cohorts, ranging from 17.9% for those born in 2003-2004 to 5.7% for those born in 1988-1992, while among females the seronegativity was relatively stable and ranged from 8.5% to 12.3% with no discernible trend. The stability among females could be associated with an awareness of congenital rubella syndrome, the tendency of parents or guardians to prioritise vaccination of girls with the MMR vaccine as a preventative measure against adverse

outcomes of pregnancy, and screening for rubella immunity in pregnancy, with MMR vaccination if not immune. In boys, it may be that parental behaviours regarding MMR immunisation of their children differed for males than females, as they may have been influenced by public perceptions of overall autism risk being higher in males. However, immunisation uptake data is unavailable by sex in Ireland to investigate this further. The trend in younger males was found to be statistically significant, and it is known that males experience both weaker antibody responses to measles vaccinations (18) and experience more measles antibody waning than females (19). A measles vaccination catch-up programme, particularly for younger males with suboptimal protection, should be considered.

At present, potential gaps associated with socio-economic, ethnic, or migrant status in Ireland cannot be explored with this anonymised data. Additional work is required to further understand vaccine coverage, barriers to vaccination and risk of infection in underserved and minority populations, with incorporation of standard health equity stratifiers in routinely collected health datasets (20). A national immunisation register would also facilitate repeated investigations to track attitudes toward vaccination and uptake over time (21).

As part of the HPSC's ongoing remit to protect the health of the Irish people as the national centre for surveillance of communicable diseases, the National Serosurveillance Programme facilitates identification of changes in measles seroprevalence at a community level. The data generated by the NSP and participating partners helps to identify variance in population susceptibility in an attempt to inform public health measures and can identify populations that may be at increased risk of infection. Serosurveillance is independent of changes in policy that affect the comprehensiveness of surveillance data being collected, and in tandem with traditional case-based surveillance it may provide knowledge on the pockets of potential susceptibility in the community.

Limitations

The limitations of this surveillance study include the use of residual, anonymised sera, which prohibits the collection of information on vaccination status, infection history, country of birth or underlying conditions of the individuals from whom the specimens were sourced. Sera were sourced from hospitals in Dublin, Donegal, Limerick, and Galway, and therefore the data may not be representative of the situation in other areas of Ireland, and may limit the generalisability of the results. This study thus shows both the strengths of the current NSP to support public health monitoring, and highlights the potential for greater benefits if more detail were available regarding the patients from whom serum has been taken. The sample targets were chosen to mimic the population age distribution; however, these were not achieved in the younger age groups, and population weighting has not been undertaken. This may have biased the results and led to an over or underestimation of seroprevalence in the population. This is however more feasible to undertake and less resource intensive than community surveys.

It is not possible to distinguish between vaccine and infection derived measles seropositivity in the data, and immune response varies from person to person. Although most people develop antibodies against measles after vaccination or infection, there are some who do not seroconvert and may not be detected by serosurveillance. In addition, due to lower titres generated following vaccination, detectable antibody wanes more rapidly in this group.

Humoral immunity as described in this study is only part of the overall immune response. As such, the results may not reflect immune protection at the site of infection, or T-cell mediated responses which play a vital role in virus clearance and may be maintained even if serum antibodies are not measurable. Immune response is not as robust after vaccination as after natural infection, and antibodies that are the result of vaccination can wane whereas those that are a result of previous infection do not (22).

There is no gold-standard commercial assay for measles, and the results of this study may not be directly comparable to previous or future studies using different tests. The assay used in this study is designed to detect antibodies associated with measles infection, and as a result the cut-offs used to determine a positive result may not be as applicable when used in a vaccinated cohort. This may introduce bias into the results where vaccine responses are not being captured accurately.

The data were adjusted for the manufacturer's stated sensitivity and specificity of the test; however, no independent verification was undertaken to ensure that the corrections applied were robust or accurate. As a result, there is a risk that negative results are attributable to either the lack of antibody response, or the inaccuracy of the test used. In alignment with the methodology from the ESEN2 study, equivocal results have been recoded as positives in the analysis in an effort to capture potentially lower vaccination immune responses, however this may lead to an overestimation of positive results and an underestimation of seronegativity or potential susceptibility. Equivocal results were not subjected to confirmatory testing or retesting on a separate assay.

Acknowledgements

Technical notes
Adjustments for sensitivity and specificity of the test

The seroprevalence was adjusted for the misclassification or imperfect sensitivity (the proportion of true positives that have been correctly identified) and specificity (the proportion of true negatives that have been correctly identified) in the application of the diagnostic testing. If the sensitivity and specificity of a test is known, we can get an approximately unbiased estimate of the true prevalence using the Rogan Gladen-estimator . Thus, the adjusted prevalence is estimated by:

$$prev_{adj} = (prev + sp - 1)/(se + sp - 1)$$

Where $prev$ is the unadjusted seroprevalence, sp is the specificity of the test and se is the sensitivity of the test. The associated confidence interval is similarly adjusted. The confidence interval is approximate because it assumes that the values of the sensitivity and specificity are known rather than estimated. If they are estimated, then this can be taken into account using the methods of Greiner & Gardner.

The Diasorin LIAISON® XL Measles IgG assay has a manufacturer's stated sensitivity of 94.7% (95% CI 91.7, 96.9), and a specificity of 97.4% (95% CI 94.1, 99.2).

Further information

Information on measles epidemiology in Ireland can be accessed on the HPSC website here.

The WHO measles and rubella elimination profile for Ireland is available here.

Bibliography

1. Measles [Internet]. [cited 2023 Apr 6]. Available from: https://www.who.int/news-room/fact-sheets/detail/measles

2. WHO-EURO-2020-1421-41171-55983-eng.pdf [Internet]. [cited 2023 May 31]. Available from: https://apps.who.int/iris/bitstream/handle/10665/337779/WHO-EURO-2020-1421-41171-55983-eng.pdf?sequence=2&isAllowed=y

3. WHO-EURO-2021-4369-44132-62279-eng.pdf [Internet]. [cited 2023 Apr 11]. Available from: https://apps.who.int/iris/bitstream/handle/10665/350211/WHO-EURO-2021-4369-44132-62279-eng.pdf

4. WHO European health information at your fingertips. [Internet]. [cited 2023 May 31]. Available from: Incidence of measles per 100 000 - European Health Information Gateway (who.int): https://gateway.euro.who.int/en/indicators/hfa_326-2080-incidence-of-measles-per-100-000/visualizations/#id=19257

5. Nearly 40 million children are dangerously susceptible to growing measles threat [Internet]. [cited 2023 Apr 6]. Available from: https://www.who.int/news/item/23-11-2022-nearly-40-million-children-are-dangerously-susceptible-to-growing-measles-threat

6. Measles, 2003 [Internet]. [cited 2023 Apr 6]. Available from: https://www.hpsc.ie/a-z/vaccinepreventable/measles/surveillancereports/annualreportsonmeaslesinireland/File,2449,en.pdf

7. Measles, 2010 [Internet]. [cited 2023 Apr 6]. Available from: https://www.hpsc.ie/a-z/vaccinepreventable/measles/surveillancereports/annualreportsonmeaslesinireland/File,13118,en.pdf

8. Andrews N. Towards elimination: measles susceptivility in Australia and 17 European countries. Bull World Health Organ. 2008 Mar 1;86(3):197–204.

9. mmrv_schede_unite.pdf [Internet]. [cited 2023 Apr 6]. Available from: https://www.diasorin.com/sites/default/files/allegati_prodotti/mmrv_schede_unite.pdf

10. Atlas Finder [Internet]. [cited 2023 Apr 6]. Available from: https://finder.healthatlasireland.ie/

11.	scheda_measles_igg.pdf [Internet]. [cited 2023 Apr 6]. Available from: https://www.diasorin.com/sites/default/files/allegati_prodotti/scheda_measles_igg.pdf

12.	Unique_Health_Identifier_Report (1).pdf [Internet]. [cited 2023 Apr 25]. Available from: https://www.hiqa.ie/sites/default/files/2017-02/Unique_Health_Identifier_Report%20(1).pdf

13.	World Health Organization - 2009 - The Immunological Basis for Immunization Series, Module 7: Measles - u.pdf. Available from: https://apps.who.int/iris/bitstream/handle/10665/44038/9789241597555_eng.pdf?sequence=1&isAllowed=y

14.	Thompson, G. Measles and MMR statistics. House of Commons Library. SN02581.pdf [Internet]. [cited 2023 Apr 25]. Available from: https://researchbriefings.files.parliament.uk/documents/SN02581/SN02581.pdf

15.	Rao TSS, Andrade C. The MMR vaccine and autism: Sensation, refutation, retraction, and fraud. Indian J Psychiatry. 2011;53(2):95–6.

16.	Low vaccination rates among refugees mean a measles outbreak is a real threat [Internet]. The Irish Medical Times. [cited 2023 May 31]. Available from: Low vaccination rates among refugees mean a measles outbreak is a real threat (imt.ie)

17.	Davis RL, Bohlke K. Measles vaccination and inflammatory bowel disease: controversy laid to rest? Drug Saf. 2001;24(13):939–46.

18.	Green MS, Schwartz N, Peer V. Gender differences in measles incidence rates in a multi-year, pooled analysis, based on national data from seven high income countries. BMC Infect Dis. 2022 Apr 11;22(1):358.

19.	Quach H, Ovsyannikova I, Grill D, Warner N, Poland G, Kennedy R. Seroprevalence of Measles Antibodies in a Highly MMR-Vaccinated Population. National Library of Medicine. 2022 Nov 3; 10(11): 1859. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9698789/

20.	Carroll C, Evans K, Elmusharaf K, et al. A review of the inclusion of equity stratifiers for the measurement of health inequalities within health and social care data collections in Ireland: BMC Public Health 21, 1705 (2021). https://doi.org/10.1186/s12889-021-11717-5

21.	Larson et al. - 2014 - Understanding vaccine hesitancy around vaccines an.pdf [Internet]. [cited 2023 Apr 25]. Available from: https://www.hse.ie/eng/health/immunisation/news/16-louise-marron-a-national-survey-of-parents-views-on-childhood-vaccinations-in-ireland1.pdf

22.	Bolotin S, Osman S, Hughes SL, Ariyarajah A, Tricco AC, Khan S, et al. In Elimination Settings, Measles Antibodies Wane After Vaccination but Not After

Infection: A Systematic Review and Meta-Analysis. J Infect Dis. 2022 Sep 28;226(7):1127–39.

Appendix A

Table A1: **Linear regression model output. The outcome is the proportion seronegative in the sample. Independent variables are age (in years) and sex.**

Variable	Coefficient	Standard error	CI lower	CI Upper
Intercept	0.07	0.065	-0.060	0.207
Age (years)	0.001	0.002	-0.004	0.006
Sex	0.27	0.093	0.078	0.456
Age*sex	-0.01	0.003	-0.017	-0.003

The model suggests that there is variation in the effect of age on seronegativity by sex. The interaction explains 18.7% of the outcome proportion seronegative, corresponding to an increase in the R-squared of 11.4% for the model without interaction to 30.1% for the model with interaction.