Report on invasive Group A streptococcal (iGAS) infections in Ireland

Updated 23rd January 2024

This report contains the latest iGAS data reported to public health in Ireland by:

- notification date (when public health was first informed about the cases) and
- epidemiological date (when the cases actually occurred)

The aim of this report is to provide an epidemiological review of the iGAS upsurge that occurred between October 2022 and August 2023 and an ongoing review of cases to date (up to and including Week 52 2023 which ended on Saturday 30th December).

The report will be published monthly during the usual peak season for iGAS and/or during periods of increased activity.

Background

Between October 2022 and August 2023, Ireland experienced an unusual upsurge in invasive Group A Streptococcus (iGAS) disease, particularly in children aged under 18 years.

Similar increases in iGAS activity were reported in other European countries, including Denmark, France, the Netherlands and the United Kingdom.
iGAS infections in Ireland typically peak during the first six months of the year. The increase observed towards the end of 2022 is the first time a peak has been reported outside this usual period of seasonal increase. This may, in part, be explained as being as a consequence of the COVID-19 pandemic when normal social mixing

patterns were interrupted leading to changes in transmission of diseases such as iGAS.

Data from 2023 indicate that the number of iGAS cases are 4.2-times higher than expected, with 533 cases notified between January and December compared with an average of 126 cases during the pre-pandemic years of 2017-2019.

Between 2nd October 2022 and 30th December 2023, 599 cases of iGAS were notified in Ireland. Of these, 239 (or 40%) were in children aged <18 years, of whom 211 were aged 0-9 years. This contrasts with the pre-pandemic years when approximately 25% of iGAS infections were in children aged <18 years.

Among cases notified since October 2022, there have been 12 deaths in children (10 in children aged under 10 years old and two in children aged 10-17 years) and 21 in adults (age range, 46-96 years). One of these 21 adult deaths was a case notified in October 2022 but occurred in September 2022.

So far in 2023, there have been 12 adult and 8 paediatric deaths reported. The most recent death was in an adult and occurred in November 2023.

This report is based on data available as of 23rd January 2024 and presents year-to-date data up to 30th December 2023 (the end of week 52).

Between August and October 2023, total cases of iGAS returned to expected levels for the same time of year as in pre-pandemic years. Since July 2023, paediatric cases of iGAS have returned to baseline levels. This is similar to the picture being observed in England and Scotland.

Towards the end of 2023, iGAS numbers have been provisionally increasing, based on the 5-week moving average and epi date. This recent activity has been mostly in adults and is in line with the slight increase expected for the usual end-of-year period. As there is a close association between iGAS and winter respiratory viruses, close monitoring and scrutiny of iGAS activity is continuing during the winter.

Key definitions

iGAS case definition

iGAS is statutorily notifiable in Ireland under S.I. No. 707/2003 of Infectious Diseases Regulations. The iGAS surveillance case definition was updated on the 23rd of December 2022. This is available in Appendix A1.

CIDR

CIDR, or Computerised Infectious Disease Reporting, is an information system developed to manage the surveillance and control of infectious diseases in Ireland.

For more information on CIDR, see https://www.hpsc.ie/cidr/

Notification date versus Epidemiological date

When looking at the data, it is important to distinguish between two key dates associated with each case.

The **notification date (or Noti-date)** is the date when public health become aware of the case (i.e., the date when the case is reported to public health and an iGAS disease event is created on CIDR).

The **epidemiological date (or Epi-date)** is the date that most closely corresponds to when the iGAS disease episode occurred. For the purpose of examining trends, the epidemiological date is used. As some recent cases may be notified at a later date, the numbers presented in this report may change as new data becomes available.

The epi-date for a case is based on the earliest of dates available on the case and taken from date of onset of symptoms, date of diagnosis, laboratory specimen collection date, laboratory received date, laboratory reported date, or event creation date/notification date on CIDR. Usually there is very little difference between these two dates, but occasionally there may be a lag in reporting to Departments of Public Health, such as when there is a surge in cases (as seen in December 2022). Using this date, rather than event creation/ notification date, adjusts for any delays in testing/notification.

Invasive group A streptococcal infection

Data by notification date

A total of 533 notifications of iGAS infection have been reported through the Computerised Infectious Diseases Reporting (CIDR) system up to the end of week 52 2023 (week ending Saturday 30th December) (Table 1).

Of these 533 notifications, 518 have an epidemiological date in 2023. Thus, for the remainder of this report, data will be displayed using epidemiological date, or Epi-date, in order to examine the trends based on the timeframe when the cases occurred (Figures 1 and 2).

Table 1. iGAS cases reported in Ireland by notification date and epidemiological date, 2017-2023.

Year	Noti-date Weeks 1-52	Epi-date Weeks 1-52
2017	130	139
2018	136	131
2019	108	104
2020	43	40
2021	34	33
2022	99	123
2023	533	518

*The notification date refers to the approximate date when the case was first reported to public health; while the epidemiological date refers to the closest date to when the case actually occurred (i.e., the earliest of onset date, specimen date, date of diagnosis, etc).

Data by epidemiological date

With 518 cases of iGAS infection for the year-to-date (week 1 to 52 2023; **data based on the Epi-week**), the numbers are significantly higher than recorded for the equivalent period last year (123 cases) and over the three years immediately prior to the pandemic, 2017-2019 (average 125; range 104 to 139 cases) (Table 1).

The iGAS case definition was updated at the end of December 2022 (see Appendix 1 for the new and old case definitions) in order to ensure that all potential iGAS cases were captured by routine iGAS surveillance. As a consequence, the overall numbers of cases would be expected to be higher than with the previous case definition. Analysis of the cases notified so far in 2023 has revealed that the new

case definition has resulted in an additional 20% of cases being reported that would not have been classified as iGAS by the previous case definition.

The latest data (up to 30th December 2023) provisionally show signs of an increasing trend, with the number of iGAS cases reported on a weekly basis in Ireland slightly above what would be expected at this time of the year (Figure 2).

Note: The iGAS case definition was updated on 23/12/2022 **(Appendix 1A)**.

Figure 1. Timeline of iGAS cases by Epi-month, 2017-2023.

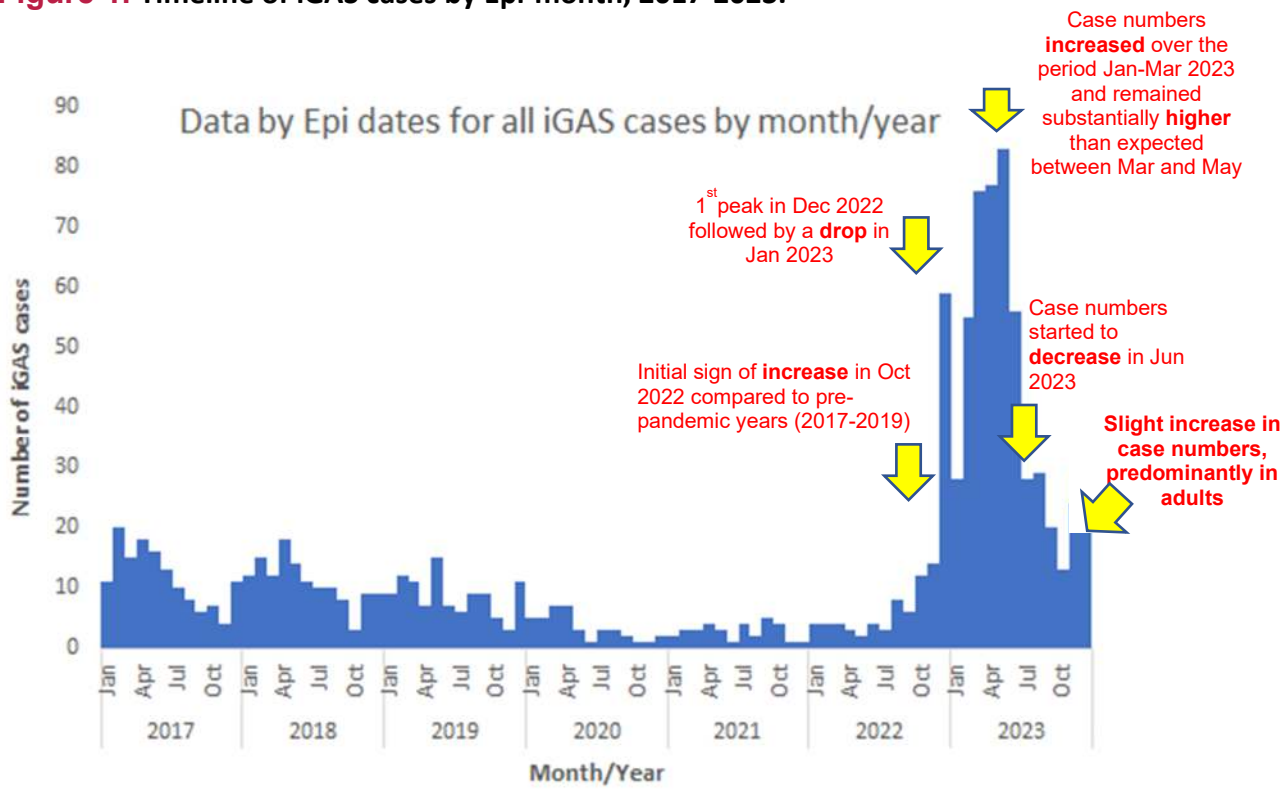
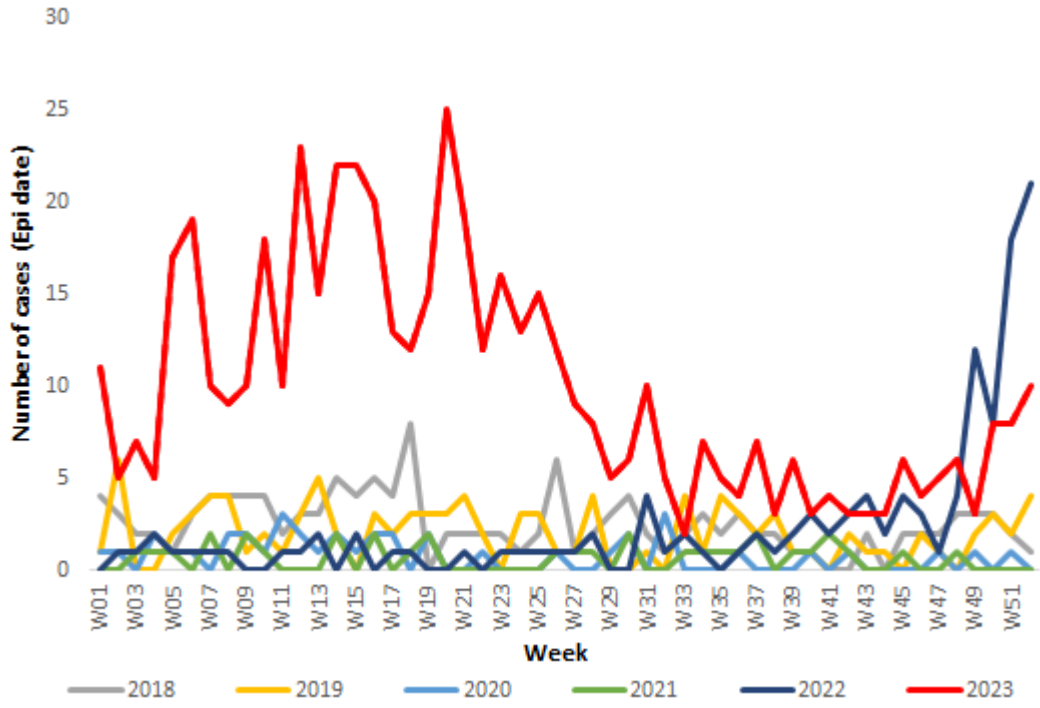


Figure 2. **iGAS cases in Ireland by Epi-week and year, 2018-2023.**

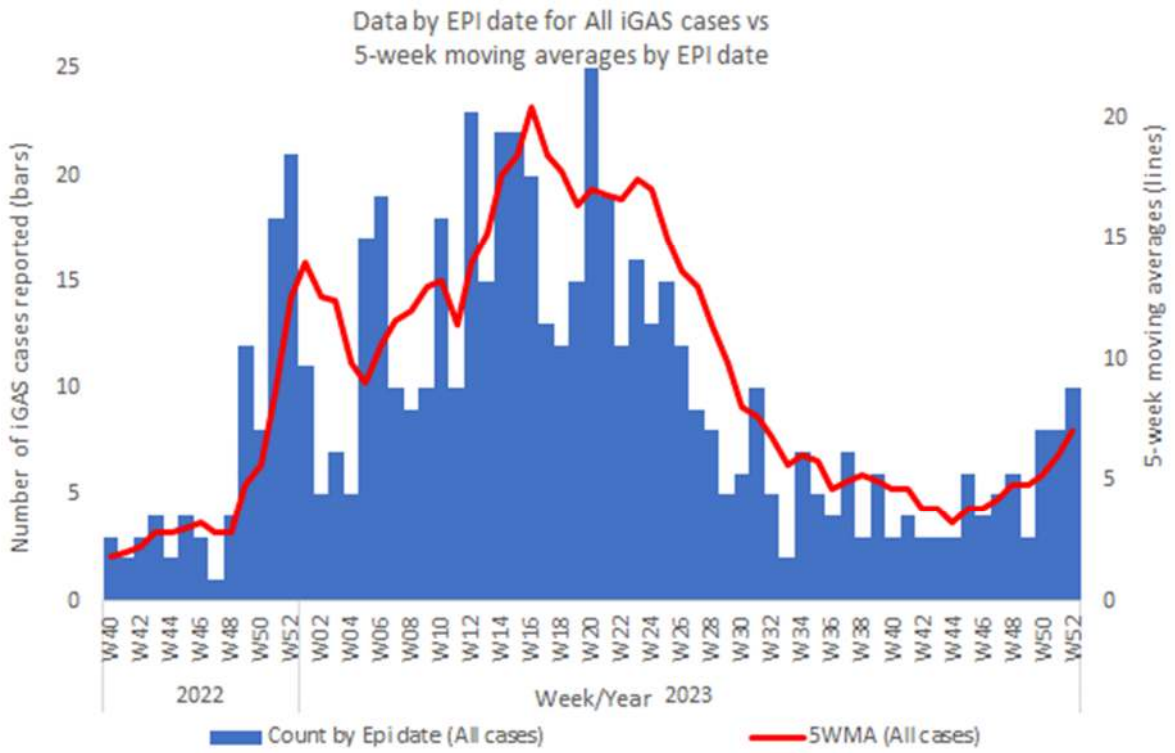


Trend analysis

As there is a lot of week-to-week variation in the number of cases being reported, use of a moving average provides a more reliable picture of the underlying trend. This smooths the data removing any temporary rises and falls when looking at the raw weekly numbers, as observed with the blue bars below in Figure 3.

The 5-week moving average of cases is calculated as the average of the latest complete week and the previous 4 weeks.

Figure 3. iGAS cases by Epi-date compared with the 5-week moving average of cases during the course of the current upsurge, Week 40 2022 – Week 52 2023.



5WMA, 5-week moving average

Breakdown by age

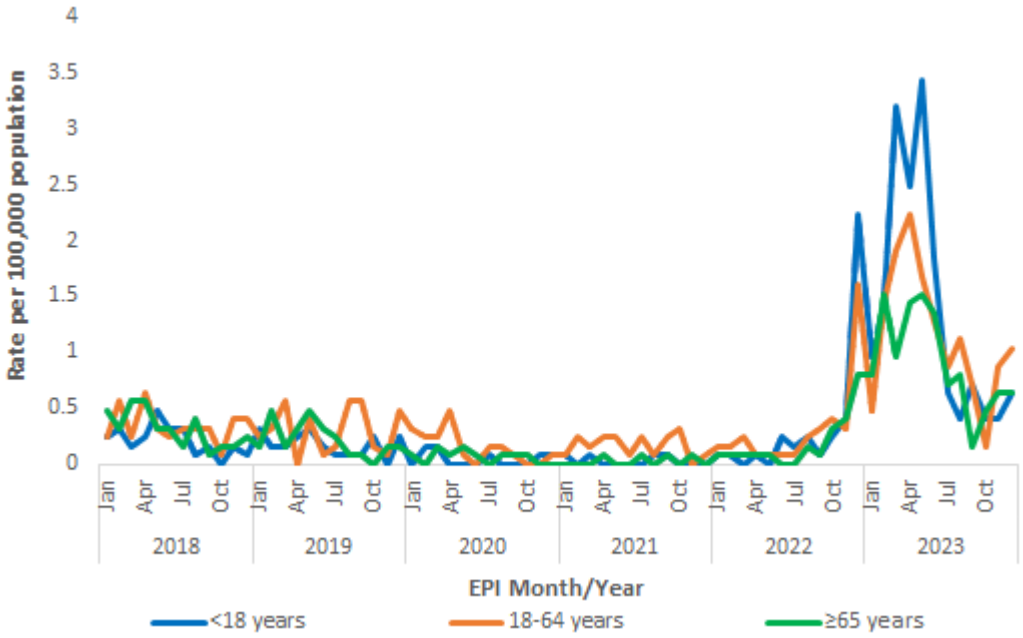
The median age of patients with iGAS infection in 2023 was 37 years (range, <1 year to 99 years).

The data are broken down by three broad age groups: children aged <18 years; adults aged 18-64 years; and older adults aged ≥65 years.

Since October 2022, increases were reported across the three age groups, especially in children (Figure 4). In the years prior to the COVID-19 pandemic, children accounted for approximately 25% of all iGAS cases. Since the 2022-2023 upsurge, the proportion that are children rose to 41% during 2023.

The latest monthly data show an increasing trend for both adult age groups (18-64 years and 65 and over) with a slight increase for children aged <18 years (Figure 4).

Figure 4. iGAS rates per 100,000 population in Ireland by age group and Epi month and year, 2018-2023.



Breakdown by Health Region

For the year-to-date, the highest rate was reported in the HSE South-West region (16.6 per 100,000 population) while the lowest rate was in the HSE Dublin and South-East region (7.4) (see Table 2).

Table 2. iGAS cases (number and crude incidence rate) by Health Region, 2023.

Health Region	N	CIR
HSE Dublin & NE	111	9.5
HSE Dublin & M	85	7.8
HSE Dublin & SE	71	7.4
HSE SW	121	16.6
HSE MW	48	11.9
HSE W & NW	82	11.1
Total	**518**	**10.2**

N, number of cases; CIR, crude incidence rate per 100,000 population; See appendix 2 with map showing health regions.

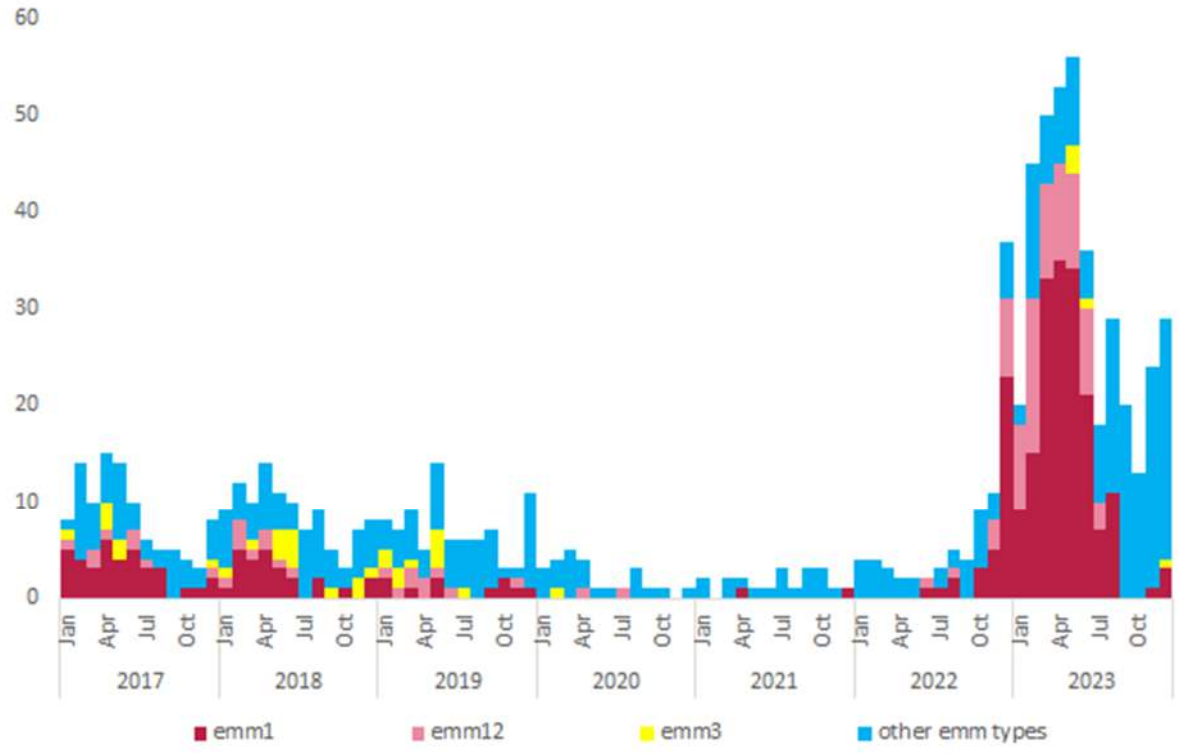
Typing data

Analysis of iGAS isolate typing data indicates that two *emm*-types have predominated since the start of the upsurge with emm1 accounting for the majority of cases (55% of referrals), followed by *emm*12 (21%) and *emm*28 (4%). This compares with 14%, 11% and 7%, respectively, in the last pre-pandemic year of 2019 when emm3 also comprised 13% of all referrals (<1% in 2022/2023 upsurge).

Figure 5 below shows the relative contribution of emm-types 1, 12 and 3 amongst iGAS isolates that were referred to IMSRL* since 2018.

*typing data available up to end December 2023

Figure 5. Distribution of three important *emm* types – *emm*1, *emm*12 and *emm*3 – causing invasive iGAS disease in Ireland, by month 2017-2023.



Outcome

As of 2nd December, 20 deaths have been reported in 2023 where iGAS infection was determined to be the main or contributary cause of death. Eight of the deaths were in children <18 years (CFR, 3.9%).

The overall case fatality rate (CFR) was higher in 2022 (10.6%) than to date in 2023 (3.9%) reflecting the sudden upsurge in iGAS during the last 3 months of 2022.

Of the 33 deaths in cases notified since October 2022, 29 were due to three emm-types that are known to be associated with more severe disease: emm-type 1 (n=18; 59%); emm-type 12 (n=10, 28%) and emm-type 28 (n=1, 3%).

Table 3. All deaths due to iGAS, including breakdown for all adults (aged ≥18 years) and children (aged 0-17 years), 2017-2023.

	All age groups			All adults			Children		
Year	N cases	N deaths*	CFR	N cases	N deaths*	CFR	N cases	N deaths*	CFR
2017	139	5	3.6%	102	5	4.9%	37	0	0.0%
2018	131	8	6.1%	98	6	6.1%	32	2	6.3%
2019	104	6	5.8%	78	4	5.1%	26	2	7.7%
2020	40	4	10.0%	33	4	12.1%	7	0	0.0%
2021	33	1	3.0%	29	1	3.4%	4	0	0.0%
2022	123	13	10.6%	74	9	12.2%	48	4	8.3%
2023**	518	20	3.9%	311	12	3.9%	207	8	3.9%

N, number; CFR, case fatality ratio

* Where iGAS is indicated as the main or contributary cause of death; ** Data up to 30th December 2023

Association with respiratory virus and varicella (chickenpox) infections

Co-infections with respiratory viruses, especially seasonal influenza, are known to be risk factors for development of invasive Group A streptococcus (iGAS). Respiratory viruses (especially influenza) are thought to produce epithelial damage that increases the likelihood of bacteria such as GAS and pneumococcus becoming invasive.

Varicella infection, or chickenpox, is also a known risk factor for development of iGAS. Only hospitalised cases of chickenpox are notifiable in Ireland, so it is not possible to determine the effects of wider chickenpox infection in the community; however, clinicians are asked to report on the presence or absence of varicella infection as a potential risk factor as part of the enhanced surveillance of iGAS infection.

Adults

Amongst adults, the first peak in iGAS infections in late December 2022/early January 2023 mirrored increases in both COVID-19 and seasonal influenza (Figure 6). Through the remainder of January 2023, all three diseases saw a dramatic decrease in this age group. However, in first half of February iGAS numbers increased again while those of the two respiratory virus infections remained low. A third iGAS peak in April was preceded by a smaller (compared with the previous) COVID-19 peak.

In the five weeks of data since the last report (Weeks 48 to 52), there has been an expected increase in seasonal influenza while the number of COVID-19 notifications has also started to rise. Between Weeks 48 and 52, there has been a slight increase in adult iGAS cases (Figure 6).

Varicella infection did not appear to have an association with iGAS infection in adults (Figure 7). Additional data from CIDR indicated that as of Week 52, no adults had a co-infection with iGAS and hospitalised varicella, while only one adult (aged 18-64 years) with iGAS reported varicella as a risk factor (<1% of adult iGAS cases).

Children

Amongst children, the first peak of iGAS infection in late December 2022/early January 2023 mirrored increases in seasonal influenza and to a lesser extent COVID-19 (Figure 6). Respiratory syncytial virus (RSV) peaked in early November 2022 but no correlation with iGAS infection in children was identified (data not shown). As in adults, paediatric cases of respiratory viral infection fell markedly

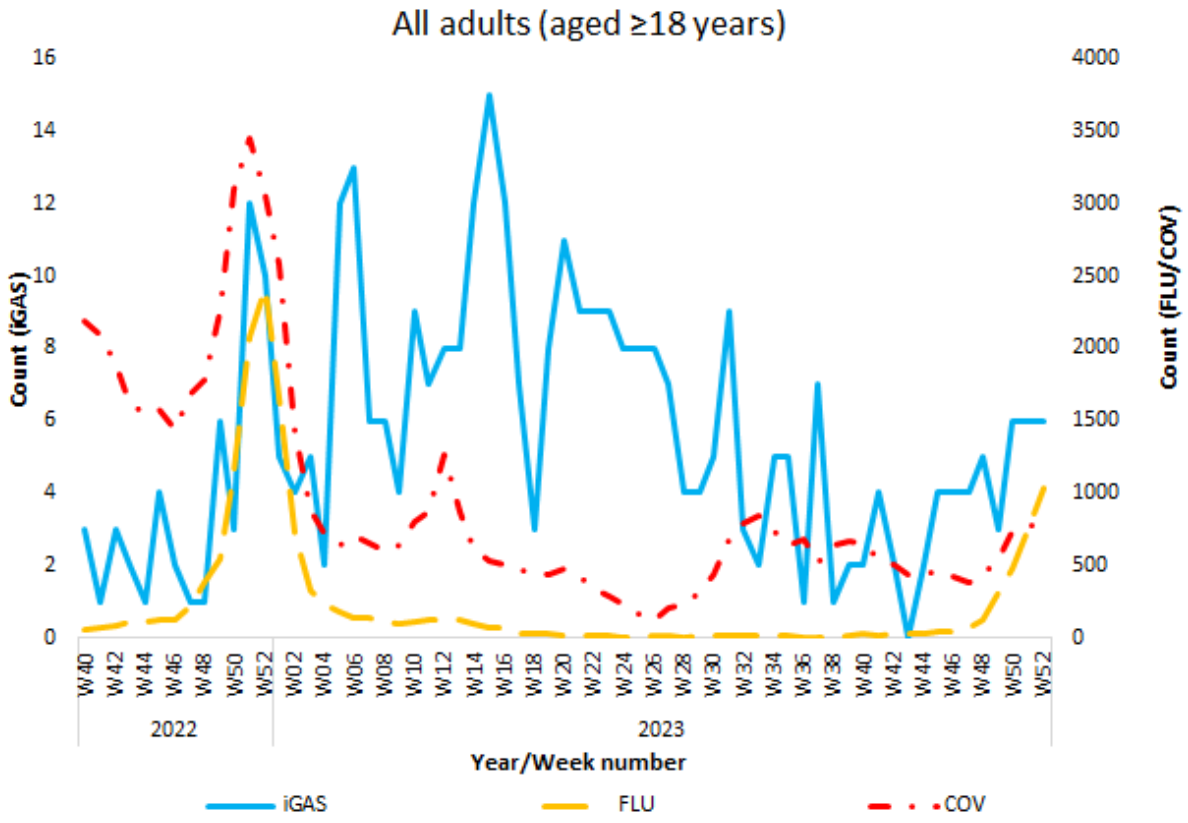
during January 2023. The second major iGAS peak in children occurred in early April, coinciding with a smaller peak in influenza.

In the five weeks of data since the last report (Weeks 48 to 52), COVID-19 and influenza cases have started to increase while cases of iGAS remain in line with what we would expect to see at this time of year (Figure 6).

During the summer months, there was an increase in cases of hospitalised chickenpox. A third iGAS peak in late May/early June also followed a period of relatively high hospitalised chickenpox activity.

There is a firmly established relationship between varicella infection and subsequent development of iGAS – numerous studies report that iGAS infection is preceded by varicella in about 20% of cases. There is no such clear relationship in adults. In this current upsurge, a clear relationship between paediatric iGAS and varicella was evident, most especially during the second major peak (Figure 7). Additional data from CIDR indicated that as of Week 52 2023, 30 children (28 aged 0-9 years and 2 aged 10-17 years) in 2023 had a co-infection with both iGAS and varicella (17% of all children); while 49 children (32 aged 0-4 years, 14 aged 5-9 years and three aged 10-17 years) with iGAS reported varicella as a risk factor (23% of all children).

Figure 6. **iGAS comparison with Influenza and COVID-19 for all adults (aged ≥18 years) and children (aged 0-17 years) by EPI week, Week 40 2022 - Week 52 2023.**



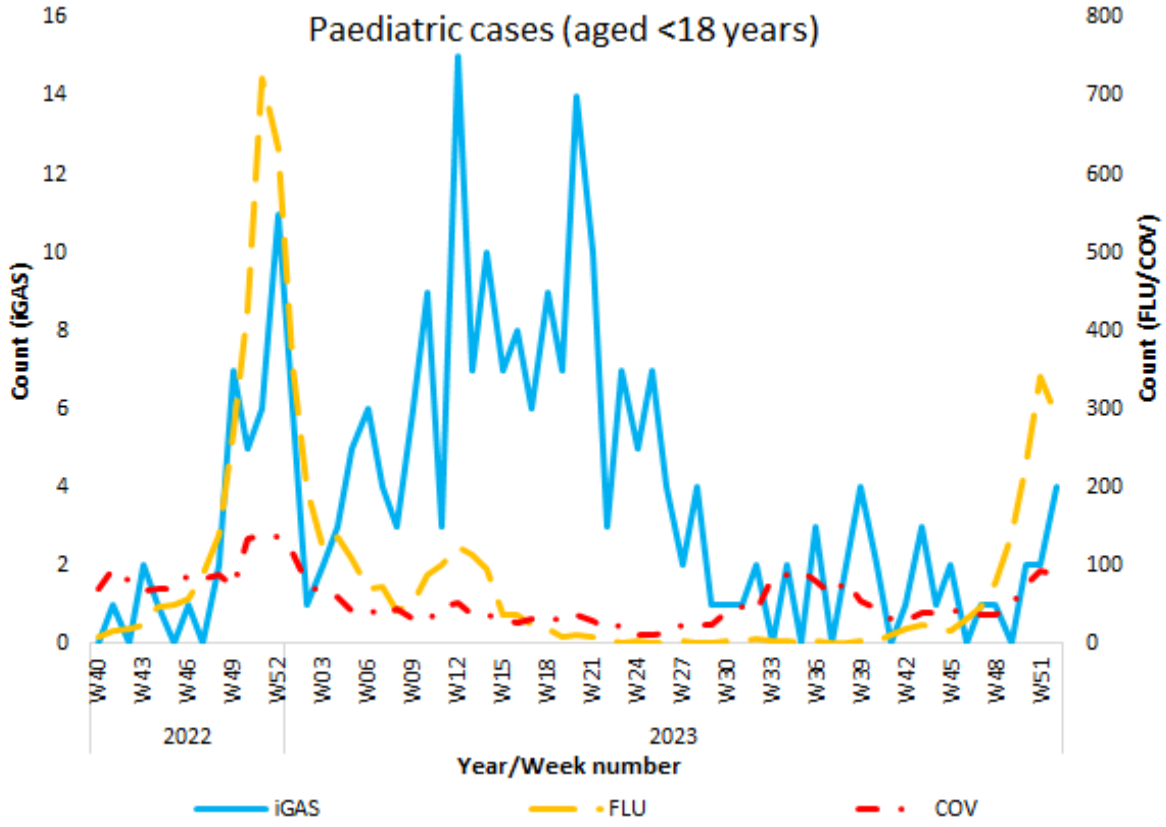
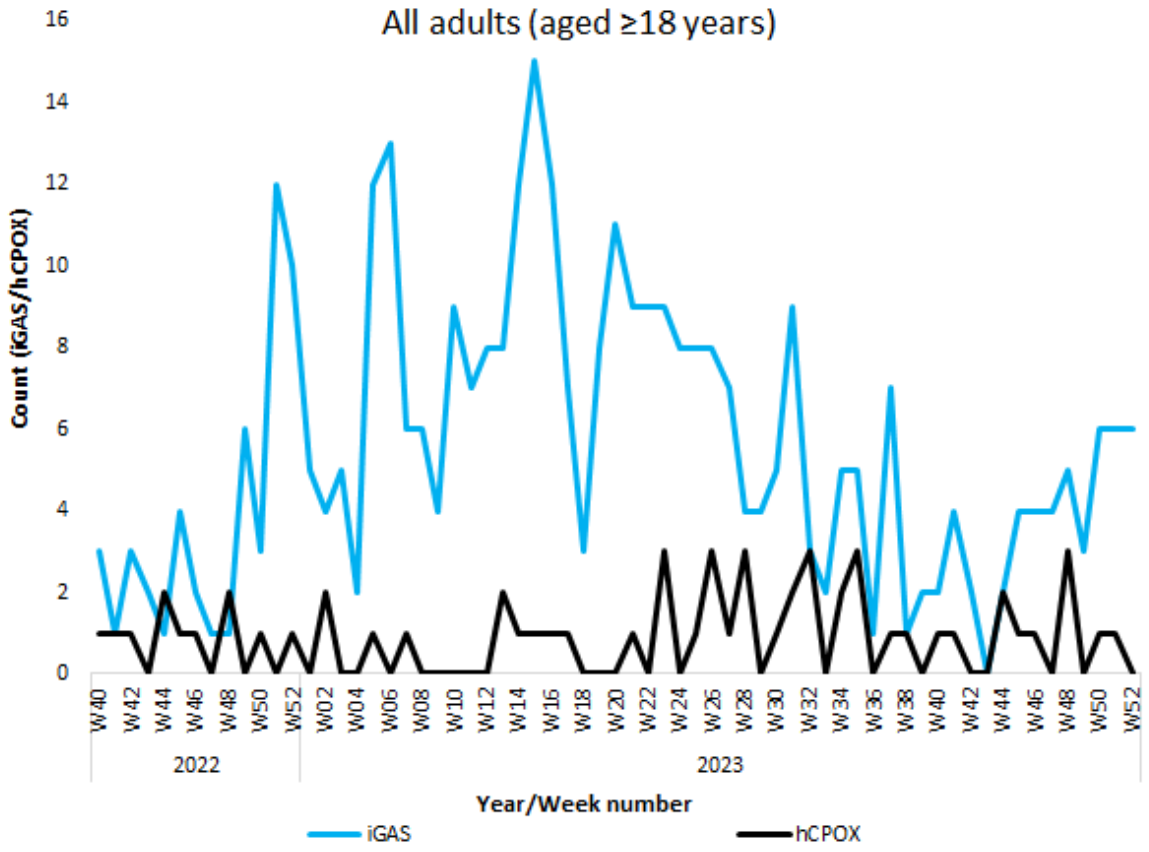
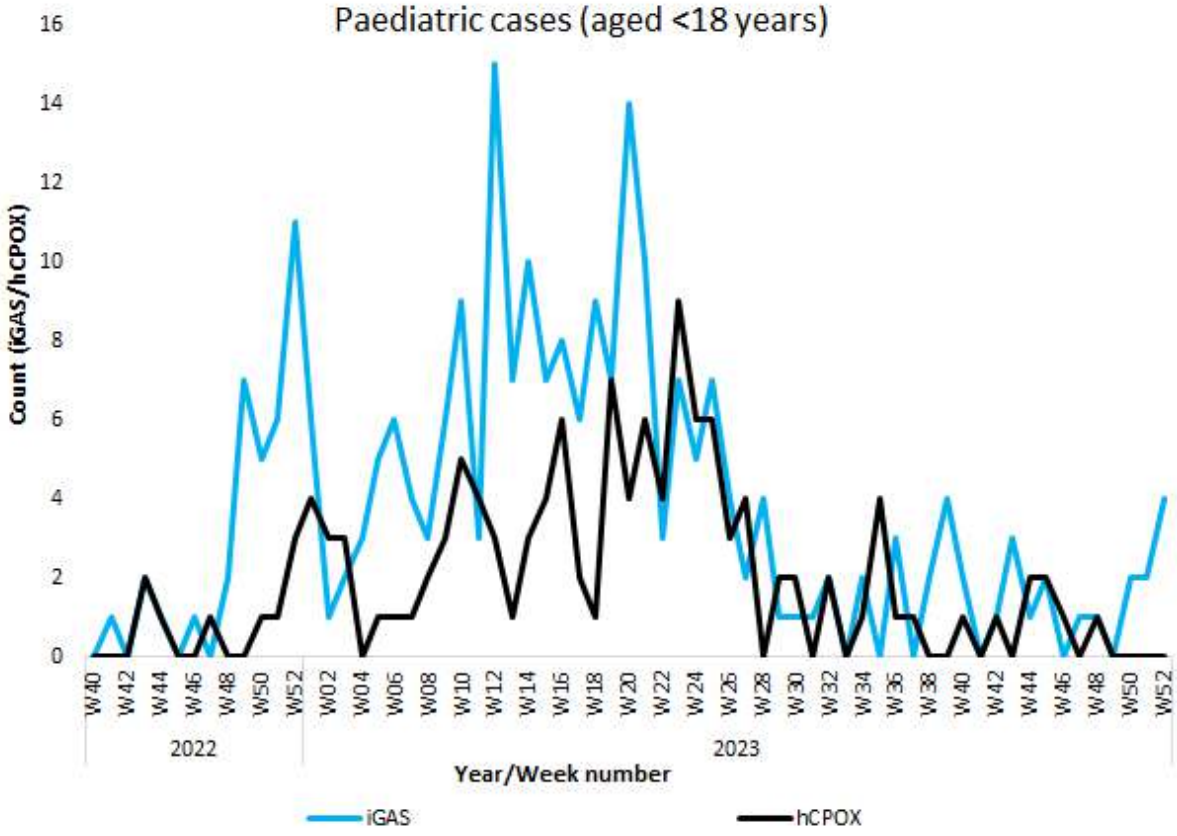


Figure 7. **iGAS comparison with and hospitalised chickenpox for all adults (aged ≥18 years) and children (aged 0-17 years) by EPI week, Week 40 2022 - Week 52 2023.**





Effect on data due to change in the case definition

The case definition for iGAS was updated at the end of December 2022 in order to increase its sensitivity (i.e., to ensure that all potential cases of iGAS were identified). As expected, this has resulted the case definition becoming less specific (i.e., resulting in additional cases being reported that would not have met the previous case definition).

Of the 518 cases notified so far in 2023, it is estimated that 103 (19%; or almost one-in-five) of these are as a result of the updated case definition. However, when the data are adjusted to look at only cases meeting the old case definition, the trends observed in 2023 are similar to those reported throughout this report.

Discussion

Following the unseasonal upsurge in iGAS infection that occurred in Ireland in late 2022 to summer 2023, iGAS cases returned to more normal levels during autumn 2023. A slight increase in cases, primarily in the adult population, was observed in November 2023. It is too early to predict the trajectory of iGAS over this coming winter but HPSC will continue to closely monitor iGAS infections, alongside respiratory viral and hospitalised chickenpox cases.

An unseasonal upsurge of iGAS infection was first identified in the UK in November 2022. HPSC identified a similar increase in iGAS activity in Ireland, following shortly after that in the UK. An alert was initially sent to the health system in December 2022.

The features of this upsurge included that:

- It followed a period of very low iGAS activity during the pandemic period, mirroring the situation with many other bacterial and viral infections (e.g., seasonal influenza)
- It was preceded by increased respiratory virus activity at the end of 2022, especially influenza (and COVID-19) as society began to fully re-open with the lifting of restrictions imposed during the pandemic
- There was a re-emergence of *emm*1 and *emm*12:
    - emm1 increased from 14% in 2019 to 41% in 2022
    - emm1 increase continued into 2023 (55%) with emm12 also seeing an increase (22%; up from 11% in 2022 and 11% in 2019)
- An increase in varicella activity was reported in 2023: hospitalised chickenpox, especially amongst children aged 0-17 years [Epi-date 2023: accounting for 116 of 158 cases reported on CIDR (data up to 08/11/2023), or 73% vs Epi-date 2022: 23 of 82 cases, or 28%]. This increase in varicella drove – in part – the period of iGAS upsurge in the first and second quarters of 2023

The first major spike in activity occurred in December 2022 following on closely from the increases in respiratory viruses, including influenza, COVID-19 and respiratory syncytial virus (RSV), as well as invasive pneumococcal disease (IPD) and invasive *Haemophilus influenzae* disease.

Although iGAS activity started to drop off in January 2023 at the same time that respiratory viruses were decreasing, a second major iGAS spike occurred in February 2023, which was sustained through the following months. This second spike was related – in part – to an increase in varicella activity in the community, especially in children aged 0-9 years.

iGAS activity started to ease off in late May but remained at a slightly higher level than would be expected for the time of year.

Since late November, iGAS has provisionally increased to levels typical for the time of year compared with previous pre-pandemic years (based on the 5-week moving average and epi date), although still below levels seen at the peak of the upsurge in December 2022 and data for the most recent weeks may be revised upwards as additional cases are notified.

The M protein, encoded by the *emm* gene, plays a major role in the pathogenesis of iGAS infections, and is also used as an epidemiological marker to characterise GAS clones. Certain emm types, such as *emm*1, *emm*3 and *emm*12, are known to be associated with more severe disease and therefore with poorer outcomes. Emm-typing data show that the predominant emm types vary from year-to-year.

In the 2015/2016 season, the UK experienced a large increase in both scarlet fever and iGAS infection to an extent not seen previously. This increase coincided with the emergence of a new sub-lineage of emm1, $M1_{UK}$, that overtook the previous successful epidemic emm1 strain, $M1_{global}$, as the predominant strain. More recently, another sub-lineage of emm1, $M1_{DK}$, has emerged recently in Denmark and its spread has partly led to an increase in iGAS there, although other factors associated with the pandemic (as outlined below) are considered to have played a role.

During the pandemic, a number of measures were implemented to control the spread of COVID-19, including closures of schools and workplaces with the advice to work at home where possible; social distancing; the wearing of masks; importance of good hand hygiene; and advice not to travel. As a consequence, very low iGAS infection levels (among a range of other communicable diseases) occurred between March 2020 and September 2022. Reduced exposure to GAS during the pandemic is likely to have contributed to increased susceptibility to infection in the general population, with particularly sever effects in the most vulnerable subjects.

Relevant information and updated guidance on the management of close contacts of iGAS cases in various settings, including households; nurseries, schools and other childcare facilities; and hospitals, is available on the HPSC website:

https://www.hpsc.ie/a-z/other/groupastreptococcaldiseasegas/factsheets/

https://www.hpsc.ie/a-z/other/groupastreptococcaldiseasegas/guidance/

All invasive disease GAS isolates, and also non-invasive isolates from suspected clusters or outbreaks, should be submitted for typing to:

Dr Mary Meahan

Irish Meningitis and Sepsis Reference Laboratory (IMSRL)

Temple Street Children's University Hospital

Temple Street

Dublin 1

For further details:

- email Mary.Meehan@cuh.ie or
- call 01-8784854
- information on IMSRL and the IMSRL Request Form can be found at:

  https://www.cuh.ie/healthcare-professionals/departments/irish-meningitis-sepsis-reference-laboratory-imsrl/

Data sources and methods

Data were extracted from CIDR on **22nd January 2024**.

Population rates are calculated per 100,000 population using the CSO census for 2022.

Emm typing data is provided by IMSRL. The M protein gene (emm) encodes the cell surface M virulence protein.

The most recent peak years for iGAS in Ireland were 2017 (with 139 cases) and 2018 (with 131 cases).

References

1. Guy R, Henderson KL, Coelho J, Hughes H, Mason EL, Gerver SM and others (2023). Increase in invasive group A streptococcal infection notifications, England, 2022. Eurosurveillance: volume 28, issue 1.

Acknowledgements

We would like to thank all our colleagues in public health departments and microbiology laboratories across Ireland.

Thanks also to IMSRL for providing emm-typing data.

Feedback and specific queries about this report are welcome via amr@hpsc.ie

Appendix 1A. Case Definition for Invasive Group A Streptococcal Infection (iGAS)

Current case definition as of: 22 December 2022

Clinical criteria

Severe clinical presentation consistent with iGAS or severe GAS infection such as.

- streptococcal toxic shock syndrome (STSS)
- necrotising fasciitis
- pneumonia
- septic arthritis
- meningitis
- peritonitis
- osteomyelitis
- myositis
- puerperal sepsis
- cellulitis

accompanied by a systemic presentation necessitating hospitalisation.

Laboratory criteria

1. Isolation of group A streptococcus (GAS), **by culture or molecular methods** (such as PCR), from a normally sterile body site (blood, cerebrospinal fluid, pleural-peritoneal-pericardial fluids, joint aspirate, bone, or deep tissue or abscess at operation or post-mortem)
2. Isolation of GAS from a non-sterile site (e.g., throat, sputum, vagina)

Epidemiological criteria

Suspected case has an epidemiological link to a confirmed case of iGAS

Case classification

1. **Confirmed case**
    1. Any person meeting the laboratory criteria of (1) above
    OR

2. Any person meeting the laboratory criteria of (2) above PLUS the clinical criteria described above

2. **Probable case**
    1. Any person meeting the clinical criteria above
       PLUS
        - the epidemiological criteria above
          OR
        - the clinician considers that GAS is the most likely cause

Appendix 1B. Case Definition for Invasive Group A Streptococcal Infection (iGAS)

2012 Version 1.8 (old case definition)

Streptococcus group A infection (invasive)

(*Streptococcus pyogenes* (blood, CSF or other normally sterile site))

Clinical criteria

Streptococcus group A infection (invasive) comprises three clinical syndromes:
a) Streptococcal Toxic Shock Syndrome (STSS), which is characterised by hypotension (fifth percentile of systolic blood pressure in children, or <90mmHg systolic pressure in adolescents and adults) and two or more of the following:

a. Renal impairment (creatinine greater than twice upper limit of normal for age)
b. Coagulopathy (platelets <100,000x106/l or evidence of disseminated intravascular coagulation)
c. Liver dysfunction (ALT, AST or bilirubin more than twice upper limit of normal for age)
d. Adult respiratory distress syndrome (pulmonary infiltrates and hypoxaemia without cardiac failure or generalised oedema)
e. Generalised erythematous rash that may desquamate
f. Soft tissue necrosis (necrotising fasciitis, myositis, gangrene)

b) Necrotising fasciitis
c) Sepsis syndrome, or systemic inflammatory response syndrome, with or without an identifiable focus of infection (such as meningitis, pneumonia, cellulitis, peritonitis, puerperal sepsis, septic arthritis, myositis)

Laboratory criteria

Laboratory criteria for a confirmed case

- Isolation of group A streptococcus, or detection of group A streptococcus nucleic acid, from a normally sterile site (blood, cerebrospinal fluid, pleural fluid, peritoneal fluid, pericardial fluid, joint aspirate, bone, or deep tissue or abscess at operation)

Laboratory criteria for a probable case (STSS or necrotising fasciitis only)

- Isolation of group A streptococcus from a non-sterile site (e.g., throat, sputum, vagina)

Laboratory criteria for a possible case (STSS or necrotising fasciitis only)

- Serological evidence of recent group A streptococcal infection

- Presence of streptococci on Gram stain of tissue or pus (necrotising fasciitis only)

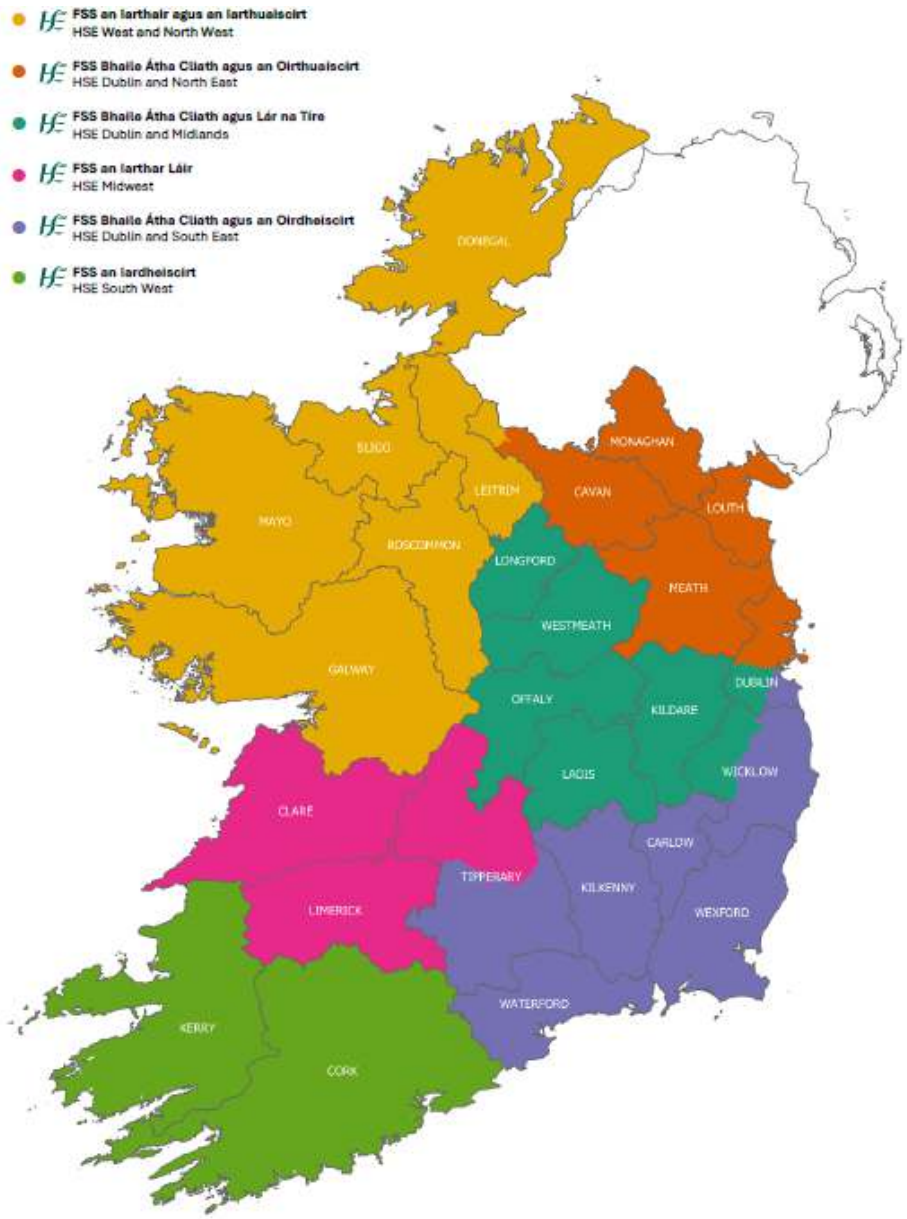
Epidemiological criteria

NA

Case classification

A. **Possible case**
Any person meeting the clinical criteria for STSS, or with necrotising fasciitis, and the laboratory criteria for a possible case
B. **Probable case**
Any person meeting the clinical criteria for STSS, or with necrotising fasciitis, and the laboratory criteria for a probable case
C. **Confirmed case**
Any person meeting the laboratory criteria for a confirmed case

Appendix 2. Map of the new HSE health regions



[1] West county Wicklow continues to be aligned with Kildare for health services, and a small portion of west county Cavan continues to be aligned with Sligo/Leitrim for health services, in recognition of existing patient flow patterns.