# 2.3 Invasive Group A Streptococcal Disease


## Summary

Total number of cases, 2014 = 164
Crude incidence rate, 2014 = 3.57 per 100,000 population


**Notifications**

In 2014, 164 cases of invasive group A streptococcal (iGAS) disease were notified, which corresponds with a rate of 3.57 iGAS cases per 100,000 population [95% confidence interval (CI): 3.05 – 4.17 per 100,000]. The 2014 iGAS rate was slightly lower than in 2013 (3.57 versus 3.66 [95% CI: 3.13 – 4.26 per 100,000]). However, the increase is not considered to be statistically significant as the confidence intervals overlap.

*Case classification*

The majority (n = 160; 98%) were classified as confirmed cases: patients with group A streptococcus (GAS; *Streptococcus pyogenes*) isolated from a sterile site. However, one of these cases did not meet the case definition for a confirmed case as the case presented with an abscess and GAS was isolated from a non-sterile site (throat swab) only. Three cases were classified as probable iGAS cases: patients with streptococcal toxic shock syndrome (STSS) or necrotising fasciitis and GAS isolated from a non-sterile site (e.g. throat, sputum, vagina). However, two of these cases did not meet the case definition for a probable case as neither presented with STSS or necrotising fasciitis and GAS was isolated from non-sterile sites only. One case was classified as a possible case, i.e. the case presented with STSS and there was serological evidence of recent GAS infection (high antibody titres to streptolysin O were detected).

*Patient demographics*

Of the 164 cases, 94 (57%) were male. The mean age of patients with iGAS was 44 years (range = 4 months – 99 years) and iGAS was more common in young children and older adults (Figure 1).

*Geographic spread and seasonal variation*

Table 1 displays the numbers and crude incidence rates (CIRs) of iGAS disease by HSE area from 2010 to 2014. While HSE East accounted for the highest number of reported cases in 2014 (n=65), HSE West had the highest CIR (4.94 per 100,000 population). In two of the HSE areas, HSE South and HSE West, both numbers of cases and CIRs increased, while in the other six HSE areas decreases were reported.

The peak months in 2014 were March (23 cases), April and July (21 cases each) and May (20 cases). As in

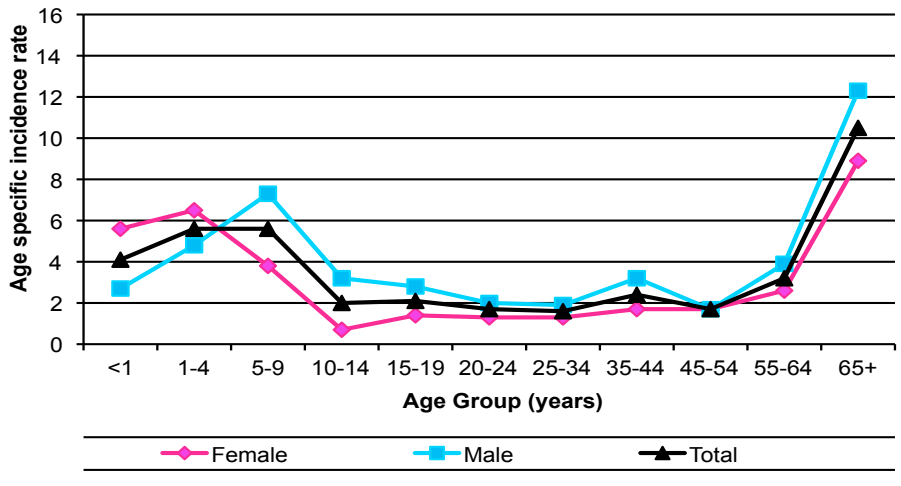


*Figure 1. Age and sex specific rates of iGAS disease in 2014*

previous years, the peak period occurred during the first half of the year (Figure 2). Upon annual review of cumulative monthly data, an increase in notifications was first noted from April 2012 (Figure 3). The increase was sustained throughout 2013 and into 2014 with the numbers starting to level off in the latter months of 2014. Data presented here are based on the date the case was notified to public health, not on the date the case was first detected.

*Isolate details*

Of 160 confirmed cases, GAS was isolated from a sterile site in 151 cases and a non-sterile site (throat) for one case (see earlier comment on this case classification), with a source site not reported for eight cases. GAS was isolated primarily from blood cultures (n=100; 66%), abscesses (n=21), deep tissue (n=12), joints (n=6), pleural fluid (n=3), bone (n=1) and peritoneal fluid (n=1). For four cases, GAS was isolated from another sterile site in addition to blood: abscess (n=2), bone (n=1) and joint (n=1).

Of the three probable iGAS cases notified, GAS was isolated from non-sterile sites, i.e. vaginal, perineal and thigh wound swabs. In two of these cases, the case definition for probable iGAS was not met as they did not have a clinical presentation that included STSS or necrotising fasciitis (see earlier comment under "case classification"). In the possible iGAS case, there was no isolate but high antibody titres to streptolysin O were detected in conjunction with a clinical presentation that included STSS.

Typing data, based on sequencing of the *emm* genes that encode the M protein (the major virulence factor), were available on 130 isolates submitted from 29 laboratories: *emm*-types 3 (n=47; 36%), 1 (n=21; 16%), 28 (n=12; 9%), 89 (n=8; 6%), 4 and 81 (n=7; 5% each) and 12 (n=6; 5%) comprised 86% of all the isolates typed. Twelve other *emm*-types (each represented by four isolates or less) were also detected. Of the 15 patients with STSS for whom *emm*-typing was undertaken, eight GAS isolates belonged to *emm*3 (53%) and three to *emm*1 (20%).

**Enhanced surveillance data**

Enhanced data were provided for 150 (91%) of the 168 iGAS cases, which is slightly lower than in 2013 (156 of 168 cases; 93%). The source laboratory could be ascertained for all cases. As in previous years, there

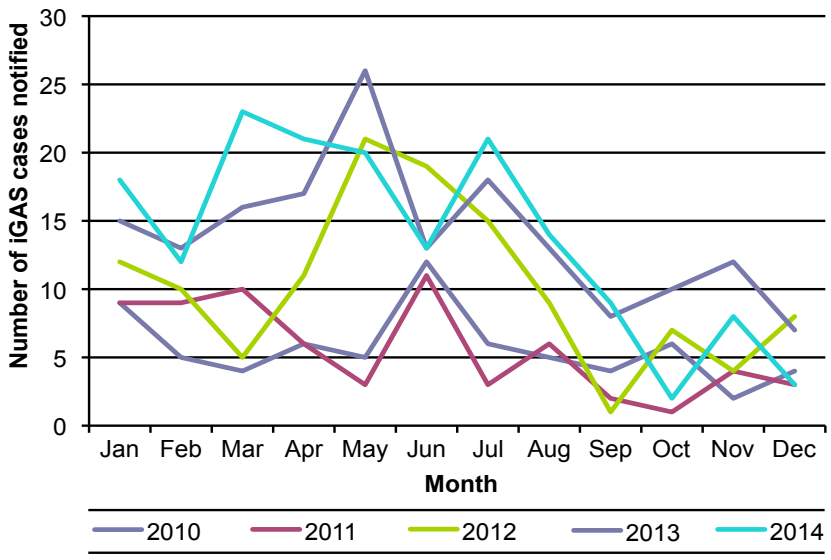


*Figure 2. Monthly distribution of iGAS cases, 2010-2014*

*Table 1. Numbers (n) and Crude Incidence Rates (CIRs) per 100,000 population of iGAS disease by HSE Area (2010-2014)*

| HSE Area | 2010 | | 2011 | | 2012 | | 2013 | | 2014 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | CIR | n | CIR | n | CIR | n | CIR | n | CIR |
| HSE E | 22 | 1.36 | 29 | 1.79 | 51 | 3.15 | 67 | 4.14 | 65 | 4.01 |
| HSE M | 2 | 0.71 | 5 | 1.77 | 7 | 2.48 | 7 | 2.48 | 4 | 1.42 |
| HSE MW | 6 | 1.58 | 6 | 1.58 | 8 | 2.11 | 16 | 4.22 | 13 | 3.43 |
| HSE NE | 7 | 1.59 | 1 | 0.23 | 11 | 2.50 | 14 | 3.18 | 12 | 2.72 |
| HSE NW | 8 | 3.10 | 2 | 0.77 | 5 | 1.94 | 6 | 2.32 | 3 | 1.16 |
| HSE SE | 5 | 1.00 | 7 | 1.41 | 16 | 3.22 | 21 | 4.22 | 18 | 3.62 |
| HSE S | 12 | 1.81 | 12 | 1.81 | 14 | 2.11 | 18 | 2.71 | 27 | 4.06 |
| HSE W | 6 | 1.35 | 5 | 1.12 | 10 | 2.25 | 19 | 4.27 | 22 | 4.94 |
| IRELAND | 68 | 1.48 | 67 | 1.46 | 122 | 2.66 | 168 | 3.66 | 164 | 3.57 |

*CIRs calculated using the 2011 census*

was wide variation in completeness of enhanced data reporting. Table 2 summarises characteristics of iGAS cases in Ireland from 2010 to 2014.

*Clinical details*
Clinical presentation data were provided for 132 cases (80%). As in previous years, bacteraemia (n=100 cases, including cases where bacteraemia was not specifically stated but GAS was isolated from blood) and cellulitis (n=58) were the commonest presentations, followed by STSS (n=21; seven of which were implied based on the information provided on the clinical presentation), pneumonia (n=14), septic arthritis (n=11), necrotising fasciitis (n=7), myositis (n=6), puerperal sepsis (n=4), erysipelas (n=2) and peritonitis (n=1). Note that an iGAS case could have more than one clinical manifestation of infection.

*Risk factors*
Risk factor data were provided for 126 iGAS cases (77%). Risk factors included: age ≥65 years (n=56), presence of skin or wound lesions (n=50), diabetes mellitus (n=11), malignancy (n=10), varicella infection (n=7), steroid use (n=6), alcoholism (n=5), injecting drug use (IDU) (n=5), recent childbirth (n=4), and non-steroidal anti-inflammatory drug (NSAID) use (n=2). Note that an iGAS case could have more than one risk factor. No risk factors were identified for 37 cases.

*Clinical management/Severity*
Surgical intervention was required for 41 patients (aged 14 months – 86 years). This included one patient with STSS, three patients with necrotising fasciitis and three patients with both STSS and necrotising fasciitis.

Among patients requiring surgical intervention, risk factor data were provided for 39 cases. Risk factors included: skin and wound lesions (n=16), age ≥65 years (n=5), varicella infection (n=2), alcoholism (n=1), malignancy (n=1), IDU (n=1) and NSAID use (n=1). Note that an iGAS case requiring surgery could have more than one risk factor. No risk factors were identified for 17 patients.

Thirty-six patients (aged 14 months – 99 years) required intensive care unit (ICU) admission. This included 12 patients with STSS, four patients with necrotising fasciitis and three patients with both STSS and necrotising fasciitis.

Among patients admitted to an ICU, risk factor data were provided for 32. Risk factors included: age ≥65 years (n=15), skin and wound lesions (n=13), diabetes mellitus (n=4), malignancy (n=3), alcoholism (n=2), IDU (n=1) and varicella infection (n=1). Note that an iGAS case requiring ICU admission could have more than one risk factor. No risk factors were identified for eight patients. Length of ICU stay was provided for 18 cases. The median length of ICU stay was three days (range = 1 – 7).

*Other epidemiological information*
Three cases were reported as hospital-acquired. There were no iGAS outbreaks reported.

*Outcome*
Outcome at seven-days following GAS isolation was reported for 102 cases:
- 92 were still alive
- 10 patients had died, where GAS was the main or contributory cause of death

The seven-day case fatality rate (CFR) for iGAS disease was 10%.

Of 21 STSS cases, outcome at seven-days was reported for 17. Of those, there were six deaths due to GAS (CFR = 35%).

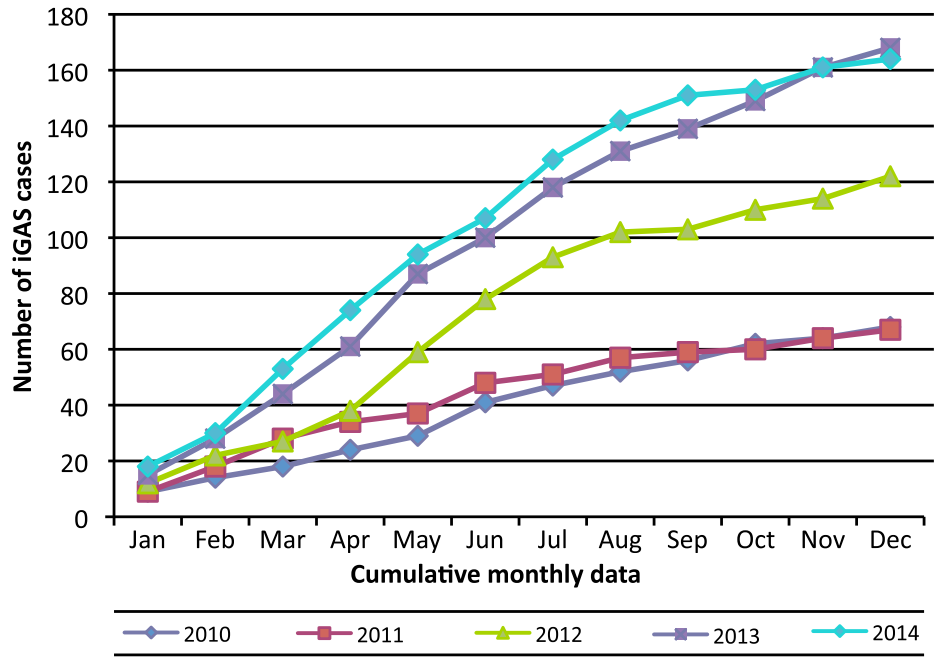


*Figure 3. Cumulative monthly numbers of iGAS cases, 2010-2014*

*Table 2. Characteristics of iGAS cases in Ireland, 2010-2014*

| | Year | | | | |
|---|---|---|---|---|---|
| | 2010 | 2011 | 2012 | 2013 | 2014 |
| **Notifications** | | | | | |
| Total iGAS cases notified | 68 | 67 | 122 | 168 | 164 |
| iGAS incidence rate per 100,000 population | 1.48 | 1.46 | 2.66 | 3.66 | 3.57 |
| Cases for which Enhanced data provided** (%) | 61 (90%) | 60 (90%) | 106 (87%) | 156 (93%) | 150 (91%) |
| | | | | | |
| **Patient Demographics** | | | | | |
| Male (%) | 36 (53%) | 28 (42%) | 59 (48%) | 95 (57%) | 94 (57%) |
| M:F ratio | 1.13:1 | 0.72:1 | 0.94:1 | 1.30:1 | 1.34:1 |
| Mean age | 49 | 43 | 44 | 41 | 44 |
| Median age | 49 | 39 | 42 | 40 | 44 |
| Age range | 0-97 | 0-97 | 0-92 | 0-93 | 0-99 |
| Paediatric cases (aged <18 years) (%) | 10 (15%) | 15 (22%) | 28 (23%) | 45 (27%) | 47 (29%) |
| Older cases (aged 65+ years) (%) | 22 (32%) | 22 (33%) | 42 (34%) | 50 (30%) | 56 (34%) |
| | | | | | |
| **Clinical Presentation†** | | | | | |
| Data on Clinical Presentation (%) | 60 (88%) | 58 (87%) | 103 (84%) | 142 (85%) | 132 (80%) |
| Streptococcal Toxic Shock-like Syndrome (STSS) without NF (%) | 7 (12%) | 4 (7%) | 22 (21%) | 28 (20%) | 18 (14%) |
| Necrotising fasciitis (NF) without STSS (%) | 2 (3%) | 1 (2%) | 2 (2%) | 6 (4%) | 4 (3%) |
| STSS and NF (%) | 2 (3%) | 2 (3%) | 4 (4%) | 4 (3%) | 3 (2%) |
| Bacteraemia with focal presentations (%) | 27 (45%) | 30 (52%) | 42 (41%) | 45 (32%) | 45 (34%) |
| Bacteraemia with no focal presentations (%) | 21 (35%) | 15 (26%) | 21 (20%) | 36 (25%) | 35 (27%) |
| Other focal presentations with no bacteraemia (%) | 1 (2%) | 6 (10%) | 11 (11%) | 23 (16%) | 28 (21%) |
| | | | | | |
| Bacteraemia (%) | 55 (92%) | 52 (90%) | 80 (78%) | 107 (75%) | 100 (76%) |
| Other focal presentations: | | | | | |
| Cellulitis (%) | 22 (37%) | 24 (41%) | 41 (40%) | 45 (32%) | 58 (44%) |
| STSS (%) | 9 (15%) | 6 (10%) | 26 (25%) | 32 (23%) | 21 (16%) |
| Pneumonia (%) | 10 (17%) | 8 (14%) | 17 (17%) | 24 (17%) | 14 (11%) |
| Septic arthritis (%) | 2 (3%) | 2 (3%) | 7 (7%) | 10 (7%) | 11 (8%) |
| Necrotising fasciitis (%) | 4 (7%) | 3 (5%) | 6 (6%) | 10 (7%) | 7 (5%) |
| Myositis (%) | 2 (3%) | 0 (0%) | 4 (4%) | 3 (2%) | 6 (5%) |
| Puerperal sepsis (%) | 4 (7%) | 5 (9%) | 6 (6%) | 6 (4%) | 4 (3%) |
| Erysipelas (%) | 0 (0%) | 0 (0%) | 3 (3%) | 3 (2%) | 2 (2%) |
| Peritonitis (%) | 1 (2%) | 3 (5%) | 1 (1%) | 4 (3%) | 1 (1%) |
| Meningitis (%) | 2 (3%) | 1 (2%) | 3 (3%) | 3 (2%) | 0 (0%) |
| | | | | | |
| **Risk Factors†** | | | | | |
| Data on Risk Factors (%) | 49 (72%) | 49 (73%) | 96 (79%) | 138 (82%) | 126 (77%) |
| Age 65+ years (%) | 22 (32%) | 22 (33%) | 42 (34%) | 50 (30%) | 56 (34%) |
| Skin lesions/wounds (%) | 16 (33%) | 20 (41%) | 34 (35%) | 56 (41%) | 50 (40%) |
| Diabetes (%) | 8 (16%) | 7 (14%) | 5 (5%) | 16 (12%) | 11 (9%) |
| Malignancy (%) | 6 (12%) | 6 (12%) | 10 (10%) | 23 (17%) | 10 (8%) |
| Varicella (%) | 2 (4%) | 2 (4%) | 9 (9%) | 5 (4%) | 7 (6%) |
| Steroid use (%) | 2 (4%) | 1 (2%) | 8 (8%) | 11 (8%) | 6 (5%) |
| Alcoholism (%) | 3 (6%) | 1 (2%) | 5 (5%) | 6 (4%) | 5 (4%) |
| Injecting drug user (%) | 6 (12%) | 3 (6%) | 6 (6%) | 5 (4%) | 5 (4%) |
| Childbirth (%) | 4 (8%) | 5 (10%) | 6 (6%) | 6 (4%) | 4 (3%) |
| Non-steroid anti-inflammatory drug use (%) | 6 (12%) | 1 (2%) | 2 (2%) | 4 (3%) | 2 (2%) |
| No identified risk factor (%) | 7 (14%) | 8 (16%) | 14 (15%) | 37 (27%) | 37 (29%) |
| | | | | | |
| **Outcome at 7 days** | | | | | |
| Data on outcome at 7 days (%) | 43 (63%) | 43 (64%) | 65 (53%) | 108 (64%) | 102 (62%) |
| RIP/GAS main cause or contributory (%) | 4 (9%) | 5 (12%) | 8 (12%) | 16 (15%) | 10 (10%) |
| STSS cases: Data on outcome at 7 days (%) | 8 (89%) | 5 (83%) | 17 (65%) | 26 (81%) | 17 (81%) |
| STSS cases: RIP/GAS main cause or contributory (%) | 2 (25%) | 1 (20%) | 6 (35%) | 10 (38%) | 6 (35%) |
| | | | | | |
| **Severity** | | | | | |
| Data on Admission to ITU (%) | 57 (84%) | 57 (85%) | 99 (81%) | 153 (91%) | 144 (88%) |
| Admitted to ITU (%) | 14 (25%) | 11 (19%) | 40 (40%) | 44 (29%) | 36 (25%) |
| Data on Surgical Intervention (%) | 49 (72%) | 45 (67%) | 86 (70%) | 136 (81%) | 127 (77%) |
| Surgical Intervention Required (%) | 12 (24%) | 8 (18%) | 26 (30%) | 39 (29%) | 41 (32%) |
| | | | | | |
| **Typing** | | | | | |
| iGAS isolates that were typed (%) | | | 109 (89%) | 140 (83%) | 130 (79%) |
| Emm-1 (%) | | | 53 (49%) | 41 (29%) | 21 (16%) |
| Emm-3 (%) | | | 4 (4%) | 33 (24%) | 47 (36%) |
| Other emm-types (%) | | | 52 (47%) | 66 (47%) | 62 (48%) |
| | | | | | |
| STSS cases: iGAS isolates that were typed (%) | | | 25 (96%) | 28 (88%) | 15 (71%) |
| Emm-1 (%) | | | 17 (68%) | 9 (32%) | 3 (20%) |
| Emm-3 (%) | | | 2 (8%) | 9 (32%) | 8 (53%) |
| Other emm-types (%) | | | 6 (24%) | 10 (36%) | 4 (27%) |

** Degree of completion of enhanced surveillance forms varies from case to case: information may not be available on all variables/ categories, thus calculations of percentages take into account only those cases for which data are provided
†Note: A patient may have more than one clinical presentation or risk factor

Of 41 cases requiring surgical intervention, outcome at seven-days was reported for 32. Of those, there were no deaths due to GAS.

Of 36 cases admitted to ICU, outcome at seven-days was reported for 26. Of those, there were six deaths due to GAS (CFR = 23%).

*Antimicrobial susceptibility*
Antimicrobial susceptibility data were reported on 94 GAS isolates (88 from blood and six from other specimens) by 25 laboratories via the European Antimicrobial Resistance Surveillance Network (EARS-Net). All isolates tested were susceptible to penicillin (n=84) and vancomycin (n=71). Resistance to erythromycin was reported in four (5%) of 85 isolates, to clindamycin in one (2%) of 42 isolates and to tetracycline in four (12%) of 33 isolates.

**CONCLUSION**
In 2014, 164 cases of iGAS infection were notified in Ireland, the second highest annual number reported to date after 2013 (n=168). The CIR decreased from 3.66 in 2013 to 3.57 per 100,000 in 2014, but this was not statistically significant. There were signs that the numbers of iGAS infections was levelling off towards the end of 2014.

Invasive GAS is a potentially life-threatening disease. In 2014, the CFR was 10% for all iGAS infections and even higher for patients admitted to ICU (23%) or presenting with STSS (35%). Since 2012, more patients have presented with STSS than in previous years: with 26 cases in 2012, 32 cases in 2013, and 21 cases in 2014 compared with 6-9 cases in each of the previous four years.

Typing of *emm* genes was undertaken on a national basis for the first time in 2012, with the establishment of a GAS typing service by the Epidemiology and Molecular Biology Unit (EMBU) at the Children's University Hospital, Temple St. In 2014, one *emm* type, *emm*3, predominated comprising 36% of all isolates typed. This is in contrast with the situation in 2012 when another *emm* type, *emm*1, was predominant comprising 49% of all isolates typed; while in 2013 both emm1 and emm3 were the dominant *emm* types. Certain *emm* types, including *emm*1 and *emm*3, are associated with STSS, and STSS in turn is strongly associated with increased mortality. The changes observed in the predominant *emm* types in circulation and in the clinical presentations over the last couple of years highlight the dynamic nature of iGAS infection.

Ongoing surveillance is essential, specifically completion of the enhanced data questionnaire, to gain a greater understanding of iGAS, to enable early detection of clusters/outbreaks, to ensure prompt implementation of infection prevention and control precautions and appropriate management of contacts. Epidemiological typing as provided by the EMBU is another vital element to increase insight into GAS infection in Ireland, as certain *emm* types are associated with greater morbidity and mortality.

Antimicrobial susceptibility data confirm that iGAS remains susceptible to penicillin and that penicillin should continue to be the treatment of choice for iGAS.

HPSC thanks participating microbiology laboratories and public health departments for their ongoing contribution to the iGAS enhanced surveillance scheme.

All microbiology laboratories are encouraged:

- to return enhanced iGAS surveillance forms for every patient with iGAS
- to submit all iGAS isolates to the Epidemiology and Molecular Biology Unit (EMBU), Children's University Hospital, Temple St for *emm*-typing
- to submit antimicrobial susceptibility data on all iGAS cases along with EARS-Net quarterly returns

The enhanced surveillance form can be downloaded from the HPSC web site at:
http://www.hpsc.ie/hpsc/A-Z/Other/GroupAStreptococcalDiseaseGAS/SurveillanceForms/

Further information on iGAS disease in Ireland, including factsheets for patients and contacts, national guidelines is available at: http://www.hpsc.ie/A-Z/Other/GroupAStreptococcalDiseaseGAS/

The figures presented in this summary are based on data extracted from the Computerised Infectious Diseases Reporting (CIDR) System on **1st October 2015.**