Invasive Pneumococcal Disease in Ireland

A Bi-annual report by the Health Protection Surveillance Centre
and the Irish Pneumococcal Reference Laboratory at the Department of Clinical Microbiology,
Royal College of Surgeons in Ireland, Education and Research Centre,
Beaumont Hospital and the Children's University Hospital, Dublin

Quarters 1-2, 2018 Provisional Figures

5th November 2018

SUMMARY

Number of confirmed cases Q1-Q2, 2018: 312
Number of confirmed cases Q1-Q2, 2017: 245

Increase in IPD cases compared with Q1-Q2, 2017: **27%**

Decline in IPD in Q1-Q2, 2018 compared with the same period in 2008 by:

- 100% in children < 5 years due to PCV7
- 88% in all ages due to the PCV7
- 98% in children < 5 years due to the PCV13
- 58% in all ages due to the PCV13

Increase in IPD:

- 178% (2.8 times) in all ages due to non-PCV13

Predominant serotypes Q1-Q2, 2018: 8, 19A and12F

BACKGROUND

Streptococcus pneumoniae, the causative organism for invasive pneumococcal disease (IPD) is a notifiable disease in Ireland. IPD notification data are collated on the Computerised Infectious Disease Surveillance (CIDR) system. Enhanced surveillance of IPD notifications is undertaken by Departments of Public Health (DPH).

Surveillance of *S. pneumoniae*, from the perspective of antimicrobial resistance, is undertaken by the European Antimicrobial Resistance Surveillance Network (EARS-Net), a collaboration involving microbiology laboratories and Health Protection Surveillance Centre (HPSC). Some participating laboratories also collect additional information as part of the enhanced surveillance of bloodstream infections. These data are reported to the HPSC in Ireland. Quarterly EARS-Net reports by the HPSC are available at http://www.hpsc.ie .

Ireland (HPSC) is participating in a European Centre for Disease prevention and Control (ECDC) and European Commission (EC) funded projects, SpIDnet (since 2012) and I-Move plus (since 2015). Included in the aims of these projects is strengthening or setting up long term active population based IPD surveillance to estimate the impact of the pneumococcal conjugate vaccines in Europe.

Since April 2007, the Irish Pneumococcal Reference Laboratory (IPRL) has been offering a typing service to Irish laboratories for all invasive *S. pneumoniae* isolates submitted. This is a collaborative project involving RCSI Education and Research Centre, Beaumont Hospital, the Children's University Hospital, Temple Street and HPSC but is funded on a year-to-year basis only.

In September 2008, the 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in Ireland to the infant schedule at 2, 6 and 12 months of age. A catch-up programme was also implemented at the time for children <2 years of age. In December 2010, PCV13 replaced PCV7 in the infant immunisation schedule. Due to the introduction of Men B vaccine in to routine immunisation the third dose of PCV 13 was shifted to 13 months of age in December 2016 for children born on or after 1st October 2016.

PCV7 vaccine covers the following serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F. The additional six serotypes included in PCV13 are: 1, 3, 5, 6A, 7F and 19A.

The IPD case definition for IPD has been revised a number of times (January 2012, July 2015) since IPD was first specified for the purpose of notification in 2003. (SI No. 707 of 2003). In the original 2003 case definition, cases were classified as possible, probable, or confirmed based on laboratory criteria for diagnosis and whether the sample was from a sterile or non-sterile site. In January 2012, with the first case definition revision; cases where *S. pneumoniae* antigen was detected in a normally sterile site (e.g. blood, CSF) were classified as confirmed rather than probable cases and (www.hpsc.ie) where *S. pneumoniae* antigen was detected in urine, such cases were classified as possible cases. In order to make meaningful comparisons by case classification, the 2012 case definition was applied to the historical (2004-2011) IPD data presented in this report.

In addition, since July 1 2015, the IPD case definition was changed; possible cases (*S. pneumoniae* antigen detected in urine only) are no longer notifiable. Only confirmed IPD cases have to be reported to Departments of Public Health www.hpsc.ie since that date.

For this report, in line with changes in case definition in 2015, we focus only on confirmed IPD cases. Possible cases were excluded from data analysis.

This report focuses on the epidemiology of confirmed IPD based on notification data for Q1-Q2, 2018. These data were extracted from CIDR on 5th November 2018 and are provisional. Data from the IPRL are also presented.

RESULTS

Notification Data – Q1-Q2, 2018

In Q1-Q2, 2018, 312 cases of IPD were notified in Ireland. All notified IPD cases were classified as confirmed compared to 245 in Q1-Q2 2017; (fig. 1). Slightly more cases occurred in females (n=170/312). Cases ranged in age from 1 month to 95 years, with a median age of 67 years.

There was a 27% increase in IPD notifications in Q1-Q2, 2018 compared to the same period in 2017 (n=245 cases) (fig. 1).

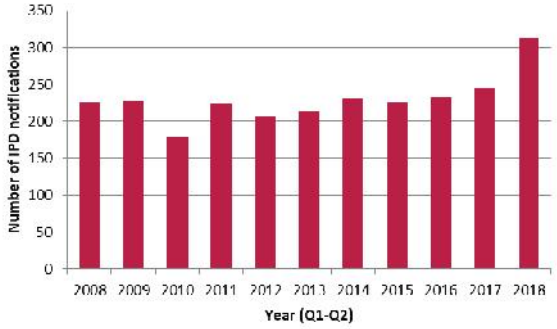

Figure 1. Number of confirmed IPD notifications in Ireland in Q1-Q2, 2008-2018
*as per IPD case definition 2015

The increase in IPD cases in the first two quarters of 2018 compared with the same period in 2017 was associated with the increase in notifications of confirmed cases in those aged 65 years and older and also in those aged 55-64 years (fig. 2). The numbers of cases in other age groups for Q1-Q2 2018 remained largely unchanged when compared with the same period of previous year (fig. 2). However compared with Q1-Q2, 2008 (pre-vaccine period), IPD is now almost half of what it was amongst children <5 years of age (fig. 2).

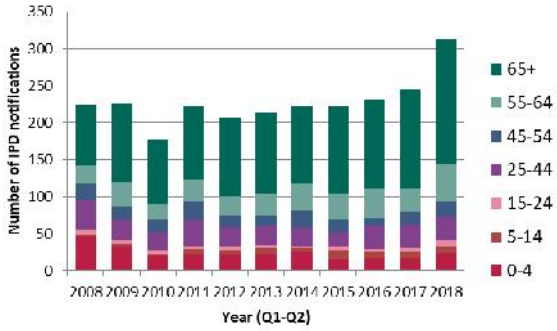

Figure 2. Number of confirmed IPD notifications in Ireland by age group in Q1-Q2, 2008-2018*
*as per IPD case definition 2015

Sixty one of the IPD cases notified were reported to have died. For eleven of these deaths, IPD was excluded as the cause of death. For the remaining fifty deaths, 36 were female and 14 were male, ranging in age from 16 to 95 years. There was one reported death in a teenager. Serotype information was available for 38 of 50 deaths. Most common serotypes were 19A and 3 (6 case each serotype), 8 (5 cases), 20 and 35B (3 cases each serotype). Twenty eight IPD-related deaths were notified during the same period in 2017.

Notifications with typing data

Of the 312 confirmed IPD notifications in Q1-Q2, 2018, 303 (97%) were confirmed by culture and therefore an isolate was available for analysis. Of these isolates, 85% (n=257) were serotyped. Thirty-two different serotypes were identified in the first six months of 2018. Serotype 8 and 19A were the predominant serotypes, followed by 12F, 9N, 22F and 3 (fig. 3). In Q1-Q2, 2018 there was a marked increase in serotype 8 almost double that notified during the equivalent period in 2017. All except one case of serotype 8 (serotype 8 n=49) occurred in adults. An increase in serotypes 19A, 22F, 9N and 3 was also seen in Q1-Q2, 2018. (fig. 3). The number of serotype 12F decreased in Q1-Q2, 2018 compared with the same period in 2016 (fig. 3). None of the serotypes covered by PCV7 were ranked in the top six in Q1-Q2, 2018 (fig. 3).

In children <5 years of age, serotypes 12F, 15B/C, 22F and 23B (two cases occurred for each) were the predominant serotypes, followed by serotypes 10A, 11A, 15A, 24F, 33F, 8 and 9N (one case for each serotype).

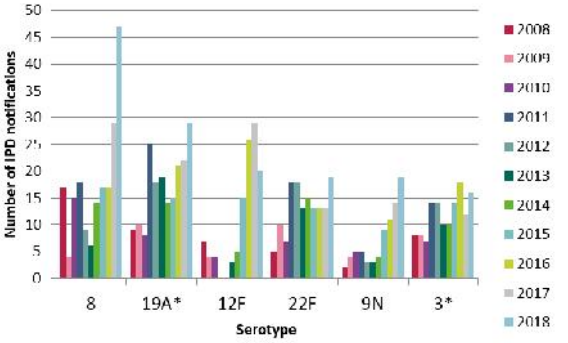

Figure 3. Number of confirmed IPD notifications by serotype, Q1-Q2 of 2008-2017, based on the six most common serotypes notified in Q1-Q2, 2018
* Denotes serotypes in PCV13 but not PCV7

Impact of pneumococcal conjugate vaccines (PCVs)

Based on the typing data from the IPRL, by June of 2018, the numbers of cases of IPD due to the PCV7 serotypes has declined by 100% in children aged <5 years, by 82% in those ≥5 years of age and by 88% in all age groups overall when compared with the same six-month period in 2008.

The introduction of PCV13 has also had an impact in children <5 years of age, with the number of IPD cases covered by this vaccine declining by 98% (fig. 4). A reduction (91%) in the number of cases in age group <5 years due to the additional six serotypes included in PCV13 has also been seen.

The overall number of IPD cases due to PCV13 serotypes in those ≥5 years of age has declined by 43%. This decline can be attributed predominantly to a fall in the number of cases due to the serotypes in PCV7 and not due to a reduction in the additional six serotypes covered by PCV13. The number due to the additional six serotypes in PCV13 has increased by 26% in this age group (fig. 5). Overall, since 2008, there has been a 2.8 times (70 cases in 2008 versus 195 in 2018) increase in IPD cases due to the non-PCV13 serotypes. Some of these serotypes are covered in the 23-valent pneumococcal polysaccharide vaccine (PPV23)

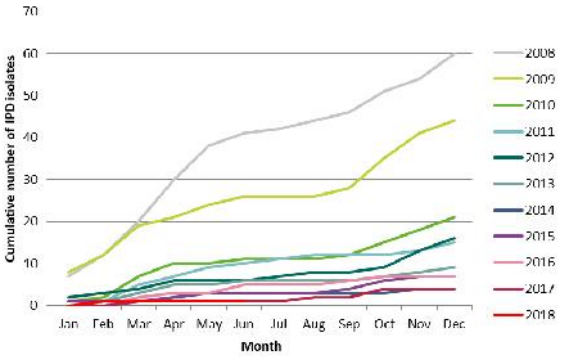

Figure 4. Cumulative number of IPD isolates due to serotypes covered by PCV13 in children <5 years of age, by month and by year, 2008-2018
Data Source: CIDR and IPRL database

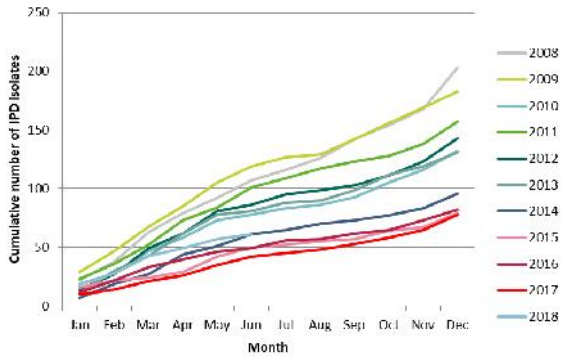

Figure 5. Cumulative number of IPD isolates due to the additional six serotypes covered by PCV13 in those ≥5 years, by month and by year, 2008-2018
Data Source: CIDR and IPRL database

Enhanced Surveillance

Since 2000 enhanced surveillance of IPD cases has been undertaken in children and adolescents <15 years of age. It was expanded to all age groups in most areas of the country after 2015. In Q1-Q2, 2018 there were 312 confirmed IPD cases. Bloodstream infection (bacteraemia) was the most common clinical presentation (n=251, 80%), with 207 (82%) of these cases also presenting with pneumonia. Twenty three cases presented with meningitis, ten of them had also bacteraemia and the clinical diagnosis was not reported for the remaining 38 cases.

Two hundred and fifteen (69%) cases were reported as having underlying medical conditions/risk factors predisposing them to IPD infection. In 57 cases there was no recognised risk factor; risk factor data was not known in three cases, for seven cases risk factor was under investigation, and none were specified (missing) for the remaining 32 cases.

According to currently available information, no vaccine failures occurred in the first six months of 2018.

DISCUSSION

The number of confirmed IPD cases was higher in Q1-Q2, 2018 than the number reported in Q1-Q2, 2017 (312 versus 245, respectively). An increase of 27% in IPD notifications was observed. The increase in IPD cases in Q1-Q2 2018, particularly in those >65 years, may be partly explained by the very high influenza incidence during this time.

When compared with the pre-vaccine period (Q1-Q2, 2008), the number of cases in children <5 years of age has declined by 73% due to all serotypes. Serotype 8 was the predominant serotype in Q1-Q2, 2018.

There has been a major reduction in IPD due to PCV7 serotypes, with the number of cases in Q1-Q2, 2018 declining by 88% overall and by 100% in those <5 years of age when compared with the pre-vaccine period. The introduction of PCV13 also has an impact in this age group, with the number of IPD cases due to the additional six serotypes declining by 91%.

In patients aged 5 years and older an increase in IPD cases has been seen due to the additional six serotypes in PCV13. In addition, a marked increase in the number of cases due to non-PCV serotypes has also been observed, indicating serotype replacement.

Information sought as part of enhanced surveillance, such as clinical symptoms or underlying conditions were missing in around 10% of all confirmed cases. However, this is an improvement in comparison to the previous year when only around 25 % had such data reported. Improvements in enhanced surveillance reflect increased efforts to collect these data by Departments of Public Health as well as support provided to some HSE areas though EU project funding (SpIDnet and I-Move+).

Continued good quality IPD surveillance including the monitoring of invasive *S. pneumoniae* serotypes is crucial in identifying any epidemiological changes in the disease and assessing the impact of PCV in Ireland. It is also vital that laboratories send all invasive *S. pneumoniae* isolates for typing. In addition, enhanced surveillance needs to be continued, and both expanded and strengthened in all areas in the country.

ACKNOWLEDGEMENTS

Sincere thanks to microbiology laboratories, clinicians and Departments of Public Health for providing data for this report and for contributing to the surveillance of IPD in Ireland.

Notes regarding the Surveillance of Invasive Pneumococcal Disease

Laboratories

1. All cases of IPD diagnosed are notified in a timely manner using CIDR to the relevant Department of Public Health
2. All invasive *S. pneumoniae* isolates are submitted to the Children's University Hospital (Temple Street) for typing
3. Data on antimicrobial resistance profiles of invasive *S. pneumoniae* isolates (blood and CSF) are reported via the EARS-Net project and the latest data are available at http://www.hpsc.ie/A-Z/MicrobiologyAntimicrobialResistance/EuropeanAntimicrobialResistanceSurveillanceSystemEARSS/EARSSSurveillanceReports/2014Reports/

Departments of Public Health

1. All IPD cases notified are inputted to CIDR
2. An enhanced surveillance form is completed for each notification of IPD Enhanced surveillance in all IPD
3. cases is also encouraged. The latest version of this form is available at http://www.hpsc.ie/hpsc/A-Z/VaccinePreventable/PneumococcalDisease/SurveillanceForms/File,3206,en.pdf
4. Enhanced data should is inputted to CIDR for all IPD events where information is available
5. The vaccination status of all IPD cases (PCV and PPV) is ascertained and details entered on CIDR. Determining vaccination status is essential for cases where infection is due to a serotype covered by PCV13 (i.e. 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F), so that any potential vaccine failures can be identified.

Appendix 1

Table A1.1. Number of confirmed IPD events by year, quarter and age group (years), Q1-2008 to Q2-2018

Age groups	2008				2009				2010				2011				2012				2013				2014				2015				2016				2017				2018	
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
0-4	23	23	8	17	22	11	2	17	8	13	2	12	12	11	3	15	13	9	8	13	7	16	5	10	12	13	1	11	10	5	6	14	6	11	13	12	8	9	6	18	15	9
5-9	1	0	1	0	2	0	1	7	0	0	0	2	4	1	1	4	2	2	1	4	4	3	0	1	3	2	1	8	4	7	0	3	4	3	0	3	4	3	3	0	4	0
10-14	1	0	2	2	1	0	2	2	1	0	0	0	0	1	1	0	1	0	0	2	0	0	0	0	1	0	1	0	1	1	1	1	1	1	0	2	1	2	0	0	3	2
15-24	3	4	0	4	4	1	1	7	4	1	1	2	1	2	2	1	4	2	0	2	1	4	1	1	1	2	1	1	3	1	0	0	2	1	3	0	1	4	0	3	4	4
25-34	5	8	1	4	7	7	5	1	5	6	0	4	6	3	1	5	8	4	1	1	6	5	2	4	7	3	0	5	2	4	2	5	4	3	0	2	9	2	3	4	6	11
35-44	17	10	12	15	9	5	2	8	3	10	3	5	19	9	4	3	6	8	4	6	9	6	6	1	8	7	3	7	8	6	8	6	17	7	8	8	11	9	3	11	10	5
45-54	10	13	3	6	10	9	4	8	11	7	8	8	11	13	5	4	8	7	2	6	6	8	5	5	10	13	3	6	9	8	3	5	6	6	3	9	13	4	7	7	8	13
55-64	13	11	12	15	16	15	4	9	13	9	4	12	13	18	10	6	19	8	7	13	21	7	14	15	20	15	4	13	18	17	12	9	21	19	5	14	17	16	10	20	25	26
65+	40	42	36	42	62	45	26	23	50	37	21	39	46	52	31	31	57	48	26	45	64	46	19	42	56	49	25	37	63	56	33	37	72	47	21	47	78	54	23	52	102	65
All ages	**113**	**111**	**75**	**105**	**133**	**93**	**47**	**82**	**95**	**83**	**39**	**84**	**112**	**110**	**58**	**69**	**118**	**88**	**49**	**92**	**118**	**95**	**52**	**79**	**118**	**104**	**39**	**88**	**118**	**105**	**65**	**80**	**133**	**98**	**53**	**97**	**142**	**103**	**55**	**115**	**177**	**135**

Table A1.2. Number of confirmed IPD events by year, quarter and gender, Q1-2008 to Q2-2018

Gender	2008				2009				2010				2011				2012				2013				2014				2015				2016				2017				2018	
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
Male	66	70	44	58	83	46	31	42	57	49	24	36	60	67	30	36	59	50	28	45	68	50	23	38	53	55	27	47	58	54	39	43	72	55	31	49	65	59	31	52	74	68
Female	47	41	31	47	50	47	16	40	38	34	15	48	52	43	28	33	59	38	21	47	50	45	29	41	65	49	12	41	60	51	26	37	61	43	22	48	77	44	24	62	103	67
Total	**113**	**111**	**75**	**105**	**133**	**93**	**47**	**82**	**95**	**83**	**39**	**84**	**112**	**110**	**58**	**69**	**118**	**88**	**49**	**92**	**118**	**95**	**52**	**79**	**118**	**104**	**39**	**88**	**118**	**105**	**65**	**80**	**133**	**98**	**53**	**97**	**142**	**103**	**55**	**115**	**177**	**135**

Table A1.3. Number of confirmed IPD events by year, quarter and case classification, Q1-2008 to Q2-2018

Case classification	2008				2009				2010				2011				2012*				2013				2014				2015**				2016				2017				2018	
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
Confirmed	113	111	75	105	133	93	47	82	95	83	39	84	112	110	58	69	118	88	49	92	118	95	52	79	118	104	39	88	118	105	66	80	133	98	53	97	142	103	55	115	177	135
Probable	1	0	0	0	1	0	1	0	1	0	0	2	1	1	3	3	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*
Possible	13	19	7	20	34	12	8	21	23	28	13	23	21	17	12	18	26	17	14	23	81	113	41	58	124	102	46	59	110	70	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*	NA*
Total	**127**	**130**	**82**	**125**	**168**	**105**	**56**	**103**	**119**	**111**	**52**	**109**	**134**	**128**	**73**	**90**	**144**	**105**	**63**	**115**	**199**	**208**	**93**	**137**	**242**	**206**	**85**	**147**	**228**	**175**	**66**	**80**	**133**	**98**	**53**	**97**	**142**	**103**	**55**	**115**	**177**	**135**

*Note: From January 2012, the IPD case definition was revised and cases diagnosed on the basis of the detection of *S. pneumoniae* antigen from a normally sterile site and, previously classified as probable cases, were now included under the confirmed case classification. Since July 2015 possible cases are not notifiable.

Table A1.4. Number of confirmed IPD events by year, quarter and HSE area, Q1-2008 to Q2-2018

HSE area	2008				2009				2010				2011				2012				2013				2014				2015				2016				2017				2018	
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
E	42	49	22	39	49	35	21	40	30	31	14	31	41	34	23	31	36	21	18	34	43	21	22	32	45	33	20	26	44	40	32	27	55	41	25	32	56	37	23	41	69	57
M	3	4	3	4	8	3	3	1	9	7	0	5	5	5	1	3	7	5	2	6	7	3	0	1	8	7	2	9	5	8	4	4	7	9	1	4	10	14	3	8	13	12
MW	14	8	6	12	11	9	1	5	8	8	5	11	11	11	4	8	12	8	9	11	12	8	6	6	10	9	4	7	8	12	4	7	14	5	4	8	12	8	2	11	15	12
NE	14	7	2	4	7	4	1	7	7	2	1	6	10	7	5	2	8	12	4	4	15	11	4	6	11	15	1	9	11	9	4	6	10	6	6	7	9	9	7	15	15	13
NW	10	5	5	6	5	8	4	0	6	3	1	2	2	10	5	6	8	6	4	5	8	8	4	7	6	8	0	6	7	3	2	7	2	5	1	9	12	4	2	10	6	6
SE	12	15	11	13	15	12	5	11	14	12	4	11	8	12	4	5	20	17	6	12	13	11	7	10	15	10	5	9	13	9	5	14	18	14	7	12	18	6	6	9	22	7
S	13	12	6	14	20	12	6	13	9	14	11	12	24	17	12	7	13	12	4	10	10	24	5	7	14	14	4	10	19	16	11	11	20	11	6	15	21	15	7	13	20	18
W	5	11	20	13	18	10	6	5	12	6	3	6	11	14	4	7	14	7	2	10	10	9	4	10	9	8	3	12	11	8	3	4	7	7	3	10	4	10	5	8	17	10
Total	**113**	**111**	**75**	**105**	**133**	**93**	**47**	**82**	**95**	**83**	**39**	**84**	**112**	**110**	**58**	**69**	**118**	**88**	**49**	**92**	**118**	**95**	**52**	**79**	**118**	**104**	**39**	**88**	**118**	**105**	**65**	**80**	**133**	**98**	**53**	**97**	**142**	**103**	**55**	**115**	**177**	**135**