NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

Centre for Respiratory Diseases and Meningitis
National Institute for Communicable Diseases
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Cumulative invasive pneumococcal disease case numbers reported by the GERMS-SA surveillance programme, 1 January 2012 to 31 July 2023

GERMS-SA surveillance programme

- GERMS-SA is a national, active, laboratory-based surveillance system initiated in 2003.
- Invasive pneumococcal disease (IPD) cases defined as hospitalised individuals with *Streptococcus pneumoniae* detected from normally sterile-site specimens (e.g. cerebrospinal fluid, blood or joint fluid).
- Repeat isolates from the same individual within 21 days were excluded.
- ~190 laboratories each year send reports and isolates.
- Age, sex, date of specimen collection, and source of specimen were captured.
- Pneumococcal isolates were serotyped by Quellung reaction using specific antisera (2003-2016: Statens Serum Institute, Copenhagen, Denmark; 2017 onwards: SSI Diagnostica, Copenhagen, Denmark).
- Culture-negative/bacterial antigen detection test positive, or isolates that lost viability were confirmed positive using a real-time *lyt*A PCR[1] and serotyped using an adaption from the method described by Azzari *et al*.[2] This molecular assay includes targets for 38 serotypes (42 serotypes prior to 2014) and covers all serotypes included in PCV13. Only samples with an initial *lytA* PCR ct value of ≤35 were included. Where ct value was ≤35 but no serotype could be identified by including the 38 targets (42 targets prior to 2014), serotype was classified as non-vaccine type. Where *lytA* PCR ct value was ≥36, serotype was classified as unknown and was not included in graphs. Where the PCR target could not distinguish between vaccine and non-vaccine serotype, serotype was classified as unknown and not included in the figures (targets: 18ABC, 18ABCF, 7AF, 9ALVN and 9AV).
- From the 1st January 2023, the pneumococcal molecular serotyping method changed to the use of a TaqMan Array card (Spn TAC). The TaqMan Array Card (TAC) system, designed and validated by the Centers for Disease Control and Prevention (CDC) (Atlanta, USA) and manufactured by Life Technologies (New York, USA), is a semi-quantitative multi-target real-time PCR platform for the simultaneous detection of a range of targets (be it multiple pathogens or multiple serotypes) in a single specimen.[3] The cards consist of multiple singleplex and/or duplex PCR reactions in 1 µl reaction wells pre-spotted with the target-specific primers and probes on a 384-well array card. Nucleic acids and reagents are mixed and loaded onto the card through individual sample ports, centrifuged at high speed for distribution of the reaction mix into reaction wells and then loaded onto a dedicated block on a ViiA7 or QS7 real-time PCR instrument (Life Technologies). The TAC system was pioneered by the CDC and has subsequently been used in a number of studies for screening a variety of pathogens.[3] The Spn TAC card has 95 targets. The targets are able to identify *S. pneumoniae*, 99 *S. pneumoniae* serotypes and 5 antibiotic resistance genes.
- **Cumulative graph case numbers include viable isolates and those non-viable but characterised using molecular diagnostic techniques.**

- Figures 1 – 3 are for cases < 5 years, and Figures 4 – 6 for cases 5 years and older. Cases with unknown age were excluded from the figures.
- There are three graphs for each age group:
  - Disease caused by any of the seven serotypes in PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F)
  - Disease caused by any of the six additional serotypes in PCV13 but not in PCV7 (1, 3, 5, 6A, 7F, 19A)
  - Disease caused by any serotypes not in PCV13
- Figures showing number of viable isolates submitted to GERMS-SA from 2008 to 2012 can be found in the appendix at the end of this report.
- More information on the GERMS-SA system available at: https://www.nicd.ac.za/centres/division-of-public-health-surveillance-and-response/

PCV vaccine introduction in South Africa

- The 7-valent pneumococcal conjugate vaccine (PCV7) was introduced into the South African Expanded Programme on Immunisation in April 2009, with no catch-up vaccination campaign.
- There was a graded replacement of PCV7 by 13-valent pneumococcal conjugate vaccine (PCV13) in 2011. By June 2011 all provinces were using PCV13.
- There was a limited PCV13 catch-up campaign in 2011 and 2012.
- WHO/UNICEF vaccine coverage estimates for receiving a third dose of the PCV vaccine in South Africa are 10% in 2009, 58% in 2010, 62% in 2011, 75% in 2012, 77% in 2013, 85% in 2014, 85% 2015, 82% in 2016, 78% in 2017, 83% in 2018, 86% in 2019, 83% in 2020, and 87% in 2021.[4]
- The effect of the vaccine on IPD in South Africa has been described.[5,6]

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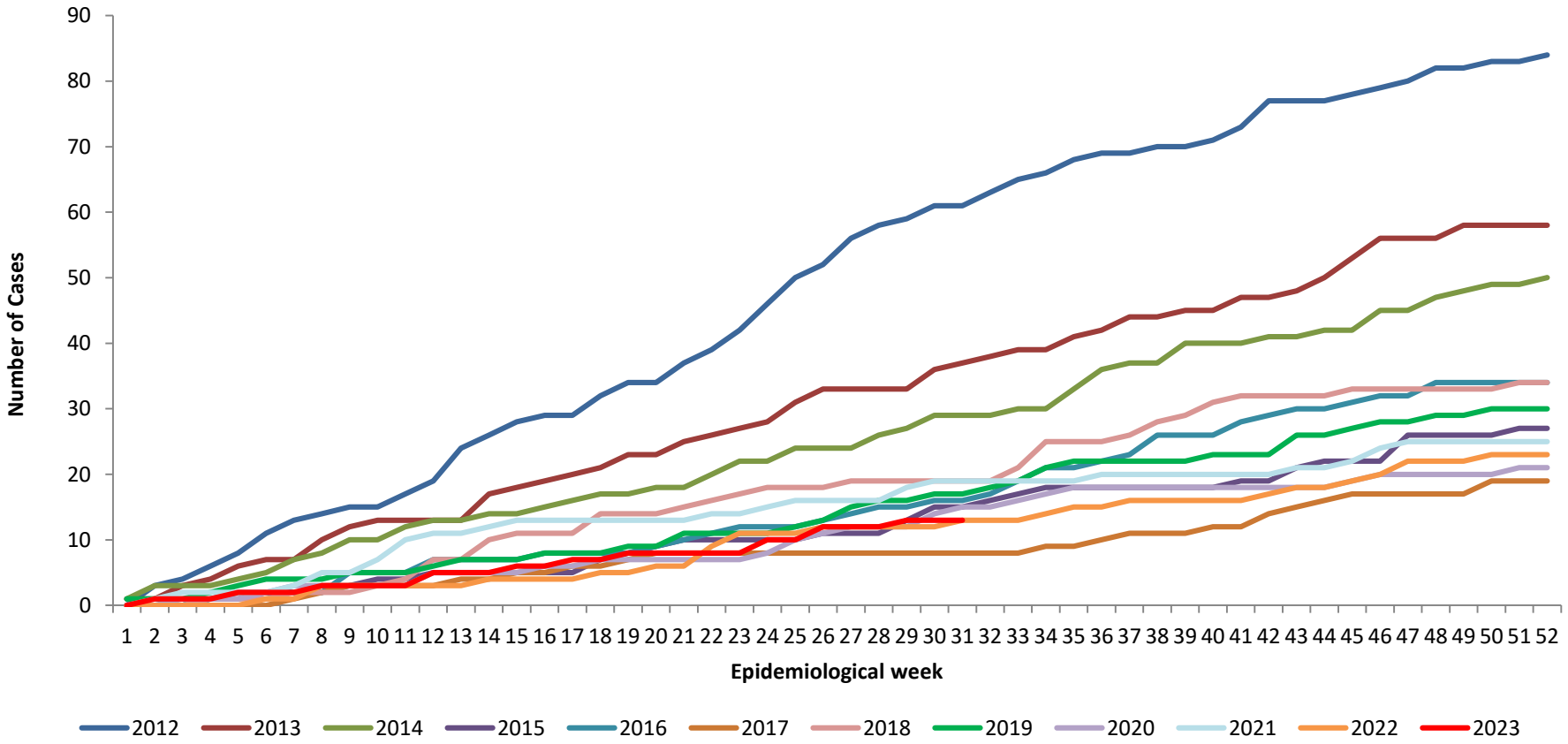

Figure 1. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the seven serotypes (4, 6B, 9V, 14, 18C, 19F and 23F) in PCV7: children <5 years of age in South Africa, from 2012 to date. Viable isolates and those serotyped using molecular techniques included.

Data are provisional as reported to date.

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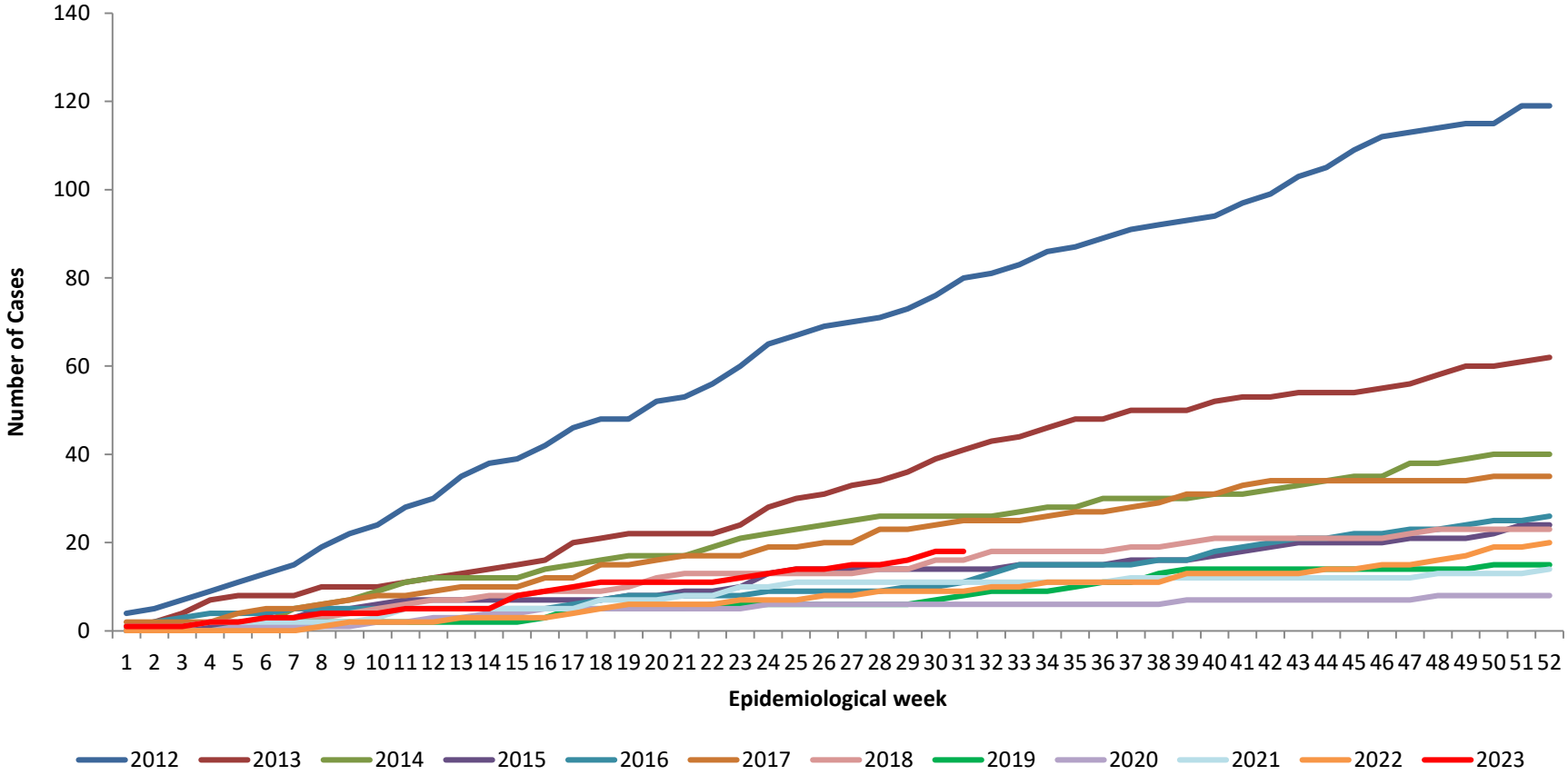

Figure 2. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the six additional (1, 3, 5, 6A, 7F, 19A) serotypes in PCV13 but not in PCV7: children <5 years of age in South Africa, from 2012 to date. Viable isolates and those serotyped using molecular techniques included. (Note: There is reported cross protection between 6A and 6B which is included in PCV7[7])

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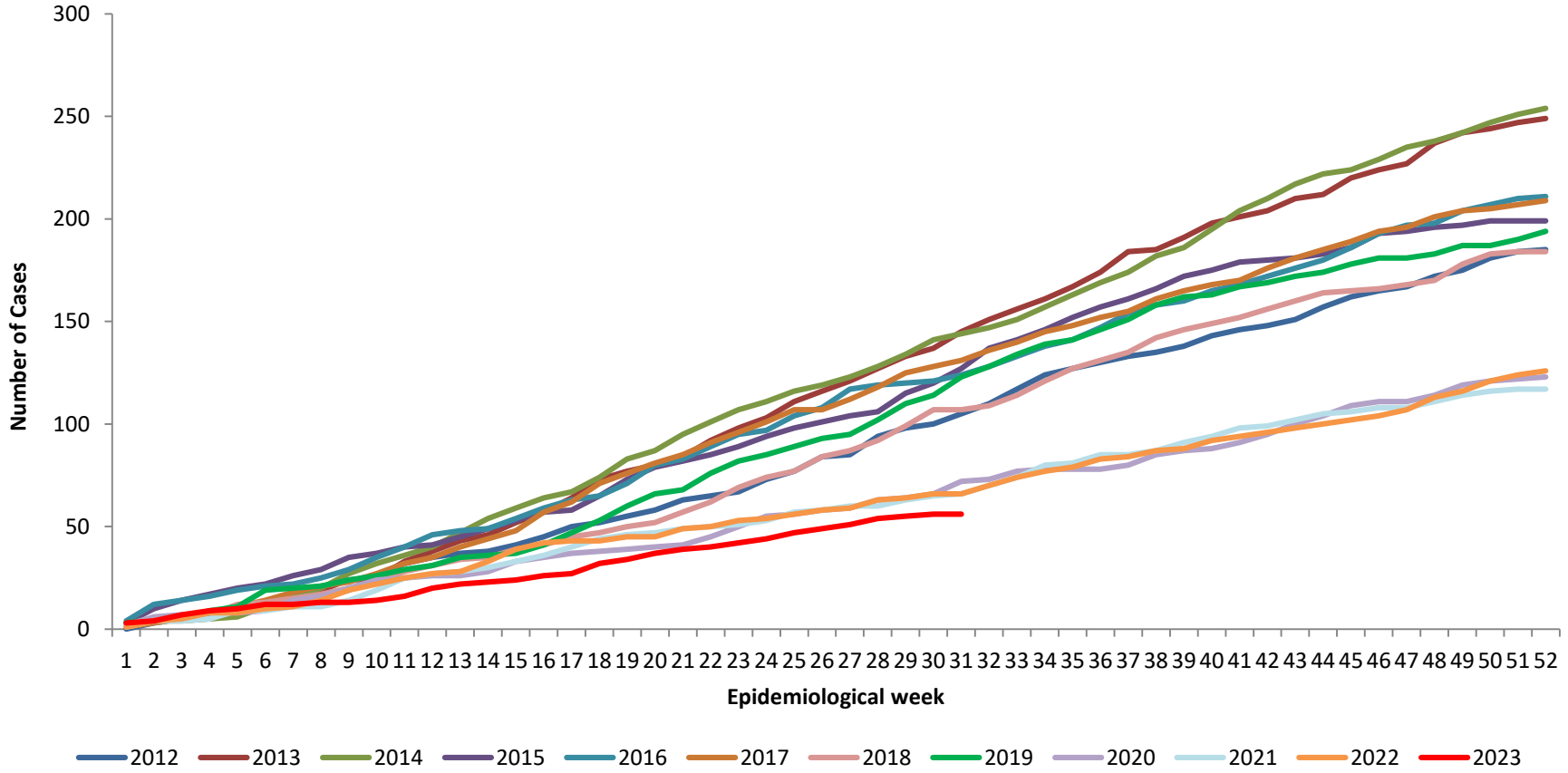

Figure 3. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the serotypes not in PCV13: children <5 years of age in South Africa, from 2012 to date. Viable isolates and those serotyped using molecular techniques included.

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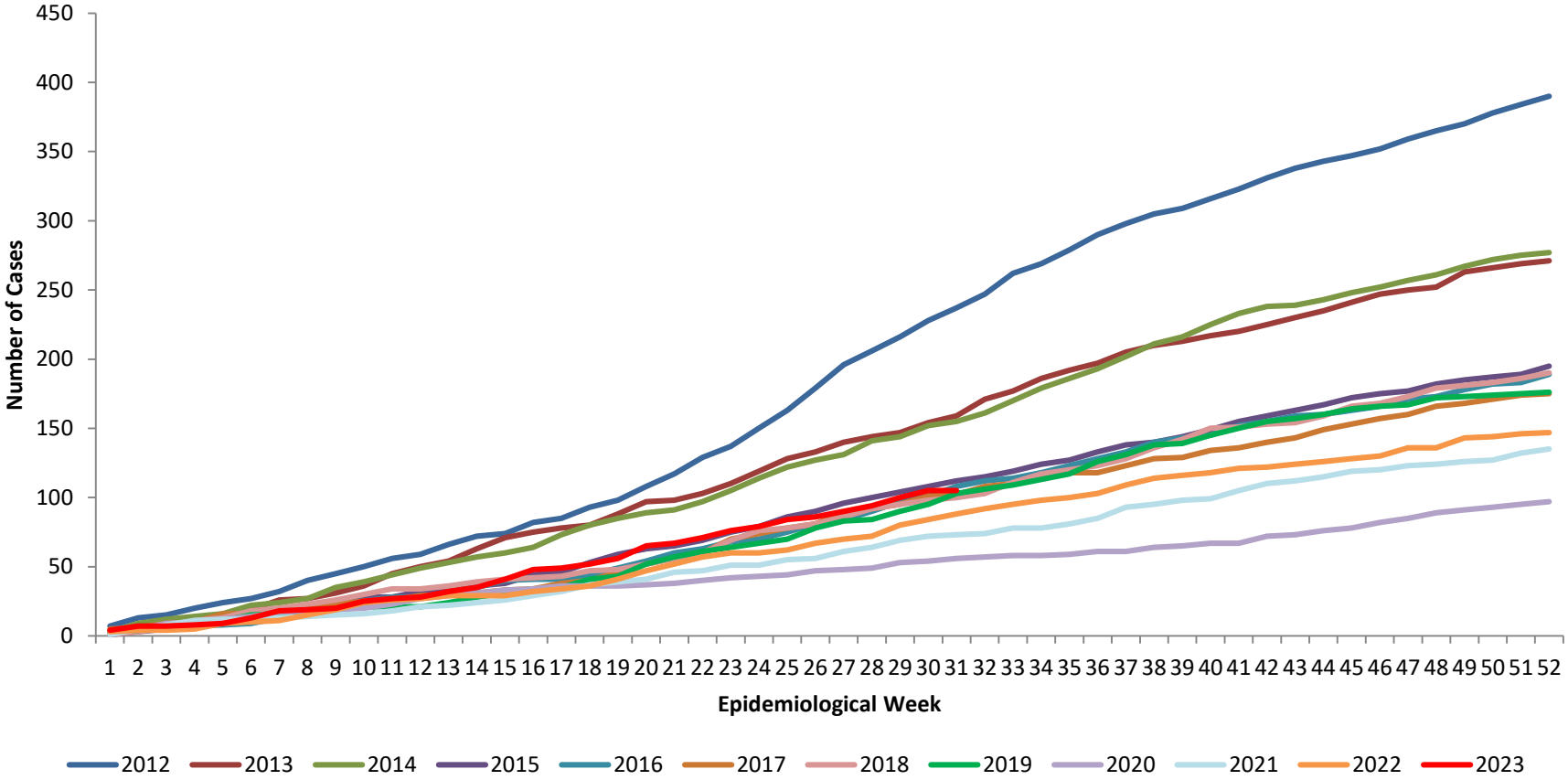

Figure 4. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the seven serotypes (4, 6B, 9V, 14, 18C, 19F and 23F) in PCV7: individuals ≥5 years of age in South Africa, from 2012 to date. Viable isolates and those serotyped using molecular techniques included.

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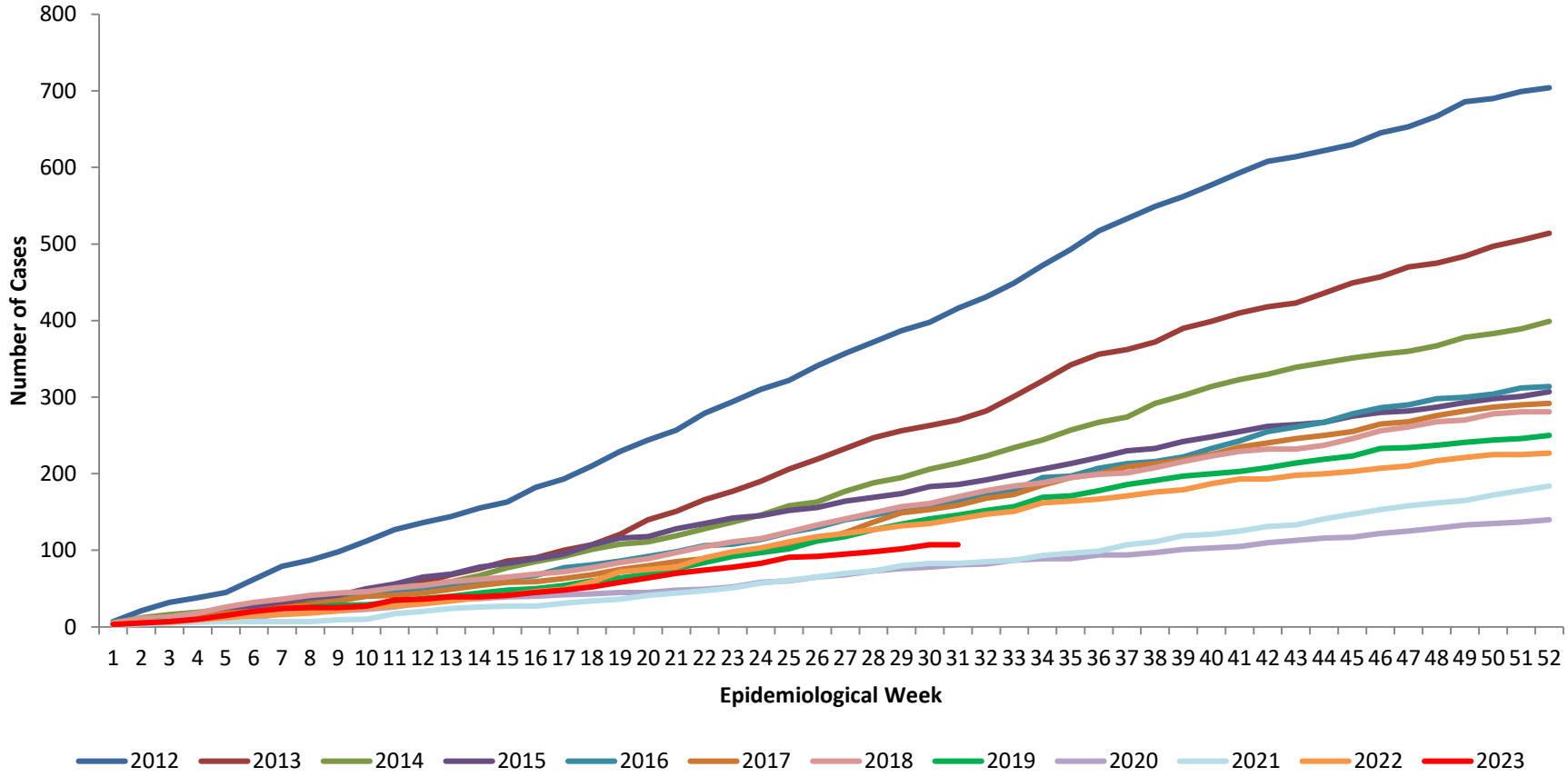

Figure 5: Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the six additional (1, 3, 5, 6A, 7F, 19A) serotypes in PCV13 but not in PCV7: individuals ≥5 years of age in South Africa, from 2012 to date. Viable isolates and those serotyped using molecular techniques included (Note: There is reported cross protection between 6A and 6B which is included in PCV7[7])

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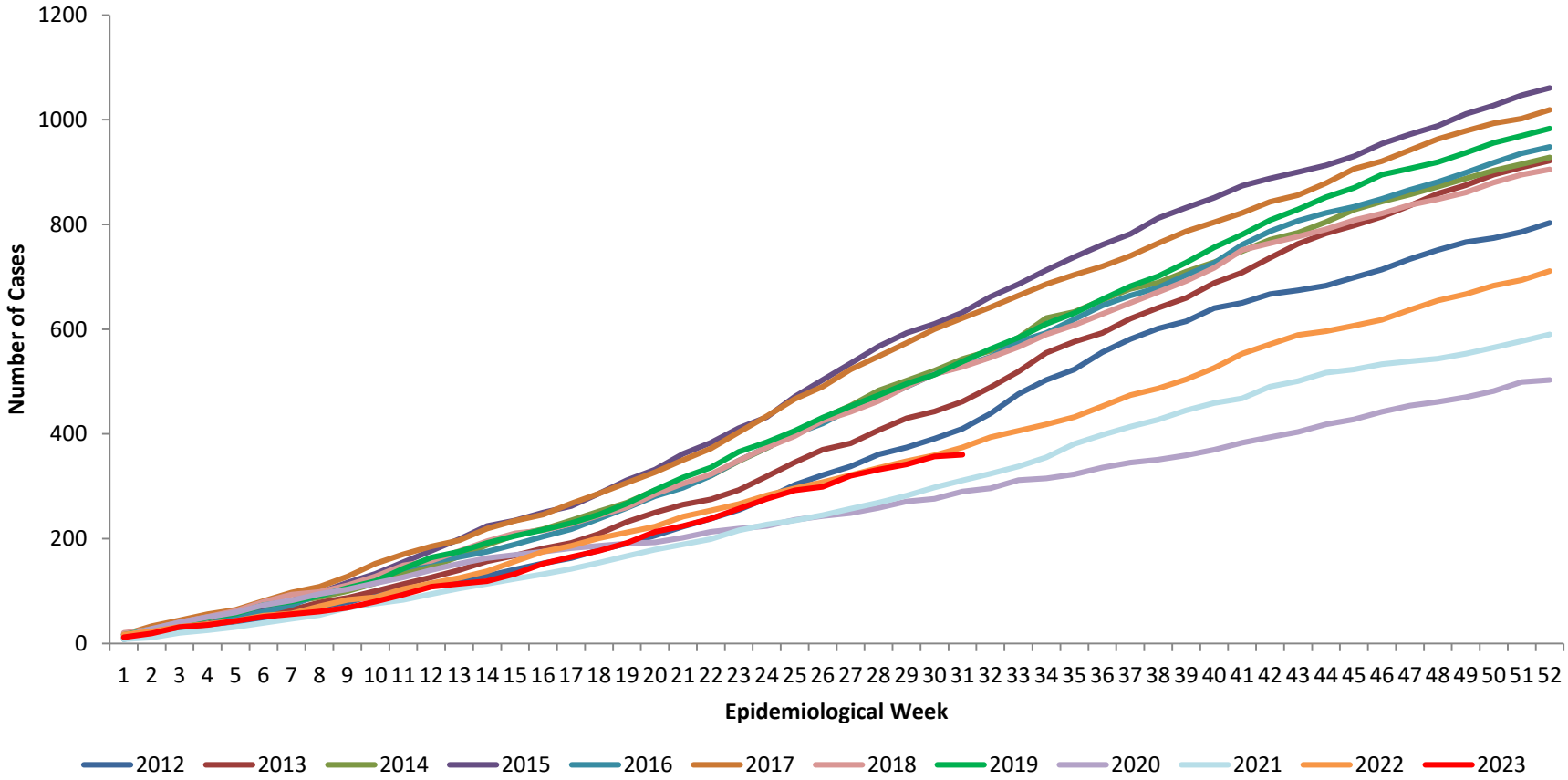

Figure 6. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the serotypes not in PCV13: individuals ≥5 years of age in South Africa, from 2012 to date. Viable isolates and those serotyped using molecular techniques included.

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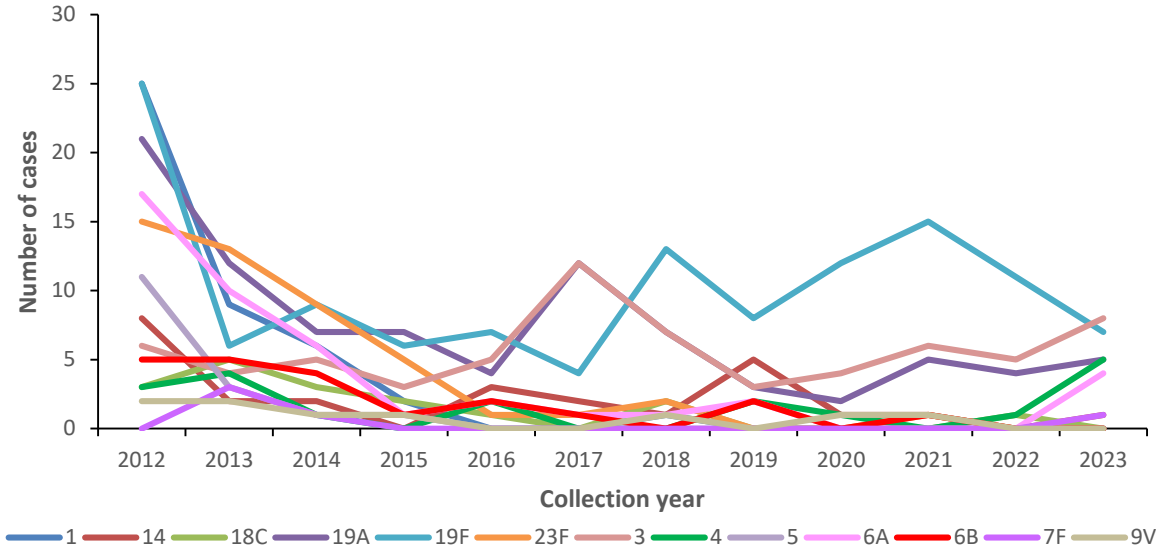

Figure 7. Number of disease episodes of invasive pneumococcal disease due to serotypes included in PCV13: individuals <5 years of age in South Africa, from January 2012 to July 2023. Viable isolates and those serotyped using molecular techniques included.

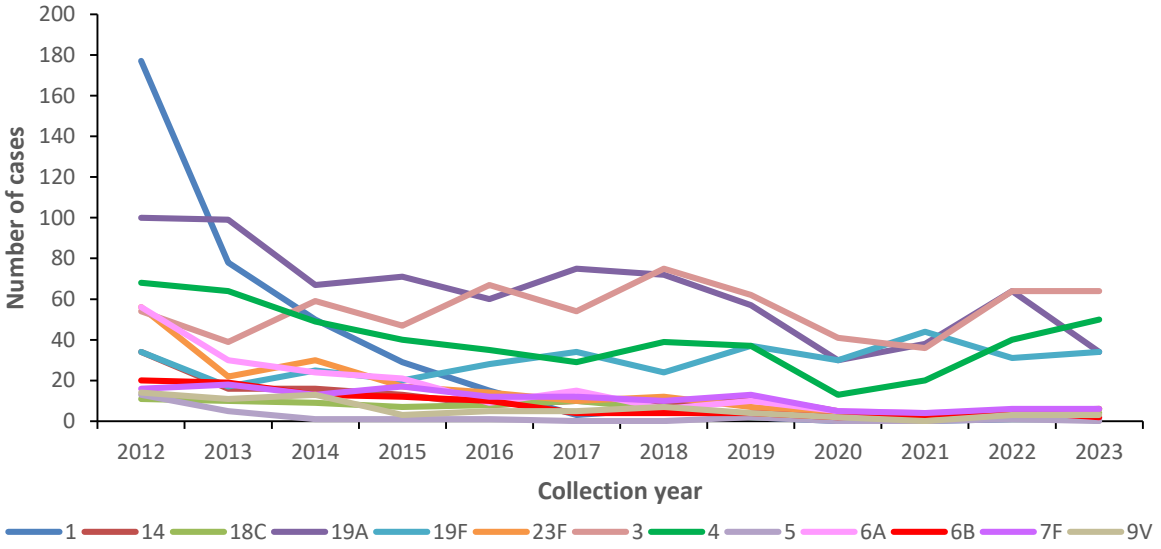

Figure 8. Number of disease episodes of invasive pneumococcal disease due to serotypes included in PCV13: individuals ≥5 years of age in South Africa, from January 2012 to July 2023. Viable isolates and those serotyped using molecular techniques included.

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Missing information

Age was unknown for 1,187 of the cases (Table 1). By the time that this report was produced there were no viable isolates with pending serotype results, but 55 isolates for which viability was yet to be captured (Table 2). For 572 isolates in the reporting period, serotype could not be identified due to high C_t value during *lytA* PCR, or PCR serotype target not distinguishing between vaccine and non-vaccine serotype.

Table 1. Isolates with missing age; number of viable, non-viable isolates and audit cases identified, January 2012 to date.

	Age missing, n(%)		Viable, n(%)		Non-viable, n(%)		Audit/missing isolates, n(%)		Capture delays*, n(%)		Total
2012	248	(8)	2,160	(67)	273	(8)	789	(24)	0	(0)	3,222
2013	138	(5)	1,932	(67)	268	(9)	665	(23)	0	(0)	2,865
2014	165	(6)	1,752	(64)	291	(11)	688	(25)	0	(0)	2,731
2015	157	(6)	1,700	(65)	208	(8)	727	(28)	0	(0)	2,635
2016	41	(2)	1,578	(65)	197	(8)	658	(27)	0	(0)	2,433
2017	34	(1)	1,535	(63)	280	(11)	625	(26)	0	(0)	2,440
2018	42	(2)	1,336	(58)	327	(14)	650	(28)	0	(0)	2,313
2019	38	(2)	1,385	(59)	345	(15)	621	(26)	0	(0)	2,351
2020	30	(2)	790	(64)	183	(15)	269	(22)	0	(0)	1,242
2021	96	(6)	981	(63)	245	(16)	323	(21)	0	(0)	1,549
2022	139	(8)	1,199	(65)	214	(12)	434	(23)	0	(0)	1,847
2023	59	(6)	658	(69)	62	(7)	172	(18)	55	(6)	947
All	1,187	(4)	17,006	(64)	2,893	(11)	6,621	(25)	55	(0)	26,575

*Cases reported to CRDM, but viability is unknown due to capturing delays.

Table 2. Cases where serotype was not available at the time this report was produced

	Not typed	Unknown serotype	Viable, serotype pending	Non-viable, serotype pending	Viability unknown*, serotype pending	Total serotypes pending
2012	38	9	0	0	0	0
2013	36	15	0	0	0	0
2014	0	38	0	0	0	0
2015	0	36	0	0	0	0
2016	2	28	0	0	0	0
2017	3	42	0	0	0	0
2018	0	28	0	0	0	0
2019	0	62	0	0	0	0
2020	0	58	0	0	0	0
2021	0	114	0	0	0	0
2022	0	106	0	0	0	0
2023	0	36	0	0	55	55
Total	79	572	0	0	55	55

* Viability unknown due to capturing delays

Discussion

Although the cumulative number of IPD episodes in children <5 years due to serotypes in PCV13 but not in PCV7 is higher in 2023 than for the same period in all the years since 2017 (Figure 2), the number of total cases in this age group (irrespective of serotype) was similar in 2023 (87) and 2022 (88). The proportion of all cases in this age group attributed to a PCV13 additional serotype was 21% (18/87) in 2023 and 10% (9/88) in 2022 (chi-square p value = 0.05). The increase was mostly driven by higher cases of serotype 3 and 6A detected in 2023 (Figure 7). While six percent of cases (5/88) in this age group in 2022 was due to serotype 3, 9% (8/87) was due to serotype 3 in 2023 (p=0.3), and while there were no cases of 6A detected in 2022, 5% (4/87) of cases in this age group were due to this serotype in 2023 (p=0.04). However, it important to note that overall case numbers in this age group are small and fluctuate over time. While these trends are not currently concerning, we will continue to monitor case numbers. We did not observe significant increases in specific serotype disease in individuals ≥5 years.

Serotypes 3, 19F, 19A and 4 are the most detected vaccine serotypes among young children <5 years of age (Figure 7) and serotypes 3, 4, 19A and 19F among individuals aged ≥5 years (Figure 8). Although IPD episode numbers reduced during 2020 and 2021 due to the coronavirus disease 2019 (COVID-19) pandemic, IPD episode numbers started returning to pre-pandemic levels since 2022. GERMS-SA is continuing to collaborate with laboratories to encourage the submission of specimens to improve the monitoring of trends.

Data Source
National Institute for Communicable Diseases | GERMS-SA

Last updated: 31 August 2023
Next update: 1 October 2023

References

1. Carvalho MdGS, Tondella ML, McCaustland K, et al. Evaluation and Improvement of Real-Time PCR Assays Targeting lytA, ply, and psaA Genes for Detection of Pneumococcal DNA. *J Clin Microbiol.* 2007;45(8):2460-2466.
2. Azzari C, Moriondo M, Indolfi G, et al. Realtime PCR Is More Sensitive than Multiplex PCR for Diagnosis and Serotyping in Children with Culture Negative Pneumococcal Invasive Disease. *PLoS One.* 2010;5(2):e9282.
3. Pholwat S, Sakai F, Turner P, Vidal JE, Houpt ER. Development of a TaqMan Array Card for Pneumococcal Serotyping on Isolates and Nasopharyngeal Samples. *J Clin Microbiol.* 2016;54(7):1842-1850.
4. WHO/UNICEF. South Africa: WHO and UNICEF estimates of immunization coverage. 2022; https://data.unicef.org/resources/dataset/immunization/.
5. von Gottberg A, de Gouveia L, Tempia S, et al. Effects of vaccination on invasive pneumococcal disease in South Africa. *N Engl J Med.* 2014;371(20):1889-1899.
6. Kleynhans J, Cohen C, McMorrow M, et al. Can pneumococcal meningitis surveillance be used to assess the impact of pneumococcal conjugate vaccine on total invasive pneumococcal disease? A case-study from South Africa, 2005-2016. *Vaccine.* 2019;37(38):5724-5730.
7. Whitney CG, Pilishvili T, Farley MM, et al. Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: a matched case-control study. *The Lancet.* 2006;368(9546):1495-1502.

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Appendix: Cumulative invasive pneumococcal disease case numbers reported by the GERMS-SA surveillance programme, January 2005 to December 2012

GERMS-SA surveillance programme

- GERMS-SA is a national, active, laboratory-based surveillance system initiated in 2003.
- Invasive pneumococcal disease (IPD) cases defined as hospitalised individuals with *Streptococcus pneumoniae* cultured from normally sterile site specimens (e.g. cerebrospinal fluid, blood or joint fluid).
- Repeat isolates from the same individual within 21 days were excluded.
- ~190 laboratories each year send reports and isolates.
- Age, sex, date of specimen collection, and source of specimen were captured.
- Pneumococci were serotyped by Quellung reaction using specific antisera (Statens Serum Institute, Copenhagen, Denmark).
- **Only viable isolates are included in cumulative graph case numbers as molecular diagnostic techniques were only introduced in 2007.**
- Figures 1 – 3 are for cases < 5 years, and Figures 4 – 6 for cases 5 years and older. Cases with unknown age were excluded from the figures.
- There are three graphs for each age group:
  - Disease caused by any of the seven serotypes in PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F)
  - Disease caused by any of the six additional serotypes in PCV13 but not in PCV7 (1, 3, 5, 6A, 7F, 19A)
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PCV vaccine introduction in South Africa

- The 7-valent pneumococcal conjugate vaccine (PCV-7) was introduced to the South African Expanded Programme on Immunization in April 2009, with no catch-up vaccination campaign.
- There was a graded replacement of PCV-7 by 13-valent pneumococcal conjugate (PCV-13) in 2011. By June 2011 all provinces were using PCV-13.
- There was a limited PCV-13 catch-up campaign in 2011 and 2012.

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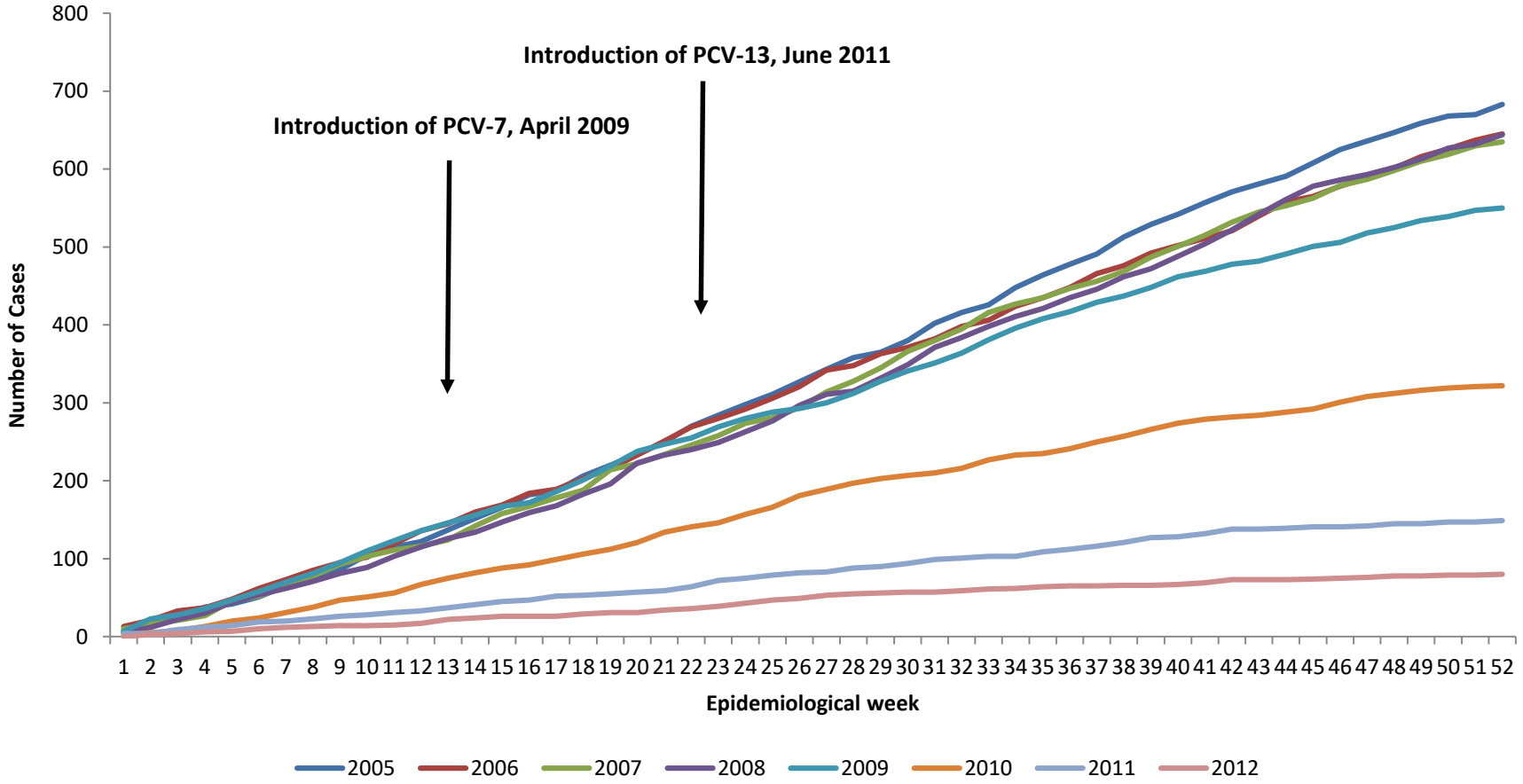

Figure 1. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the seven serotypes (4, 6B, 9V, 14, 18C, 19F and 23F) in PCV-7: children <5 years of age in South Africa, from 2005 to 2012. Only viable isolates serotyped using Quellung method included.

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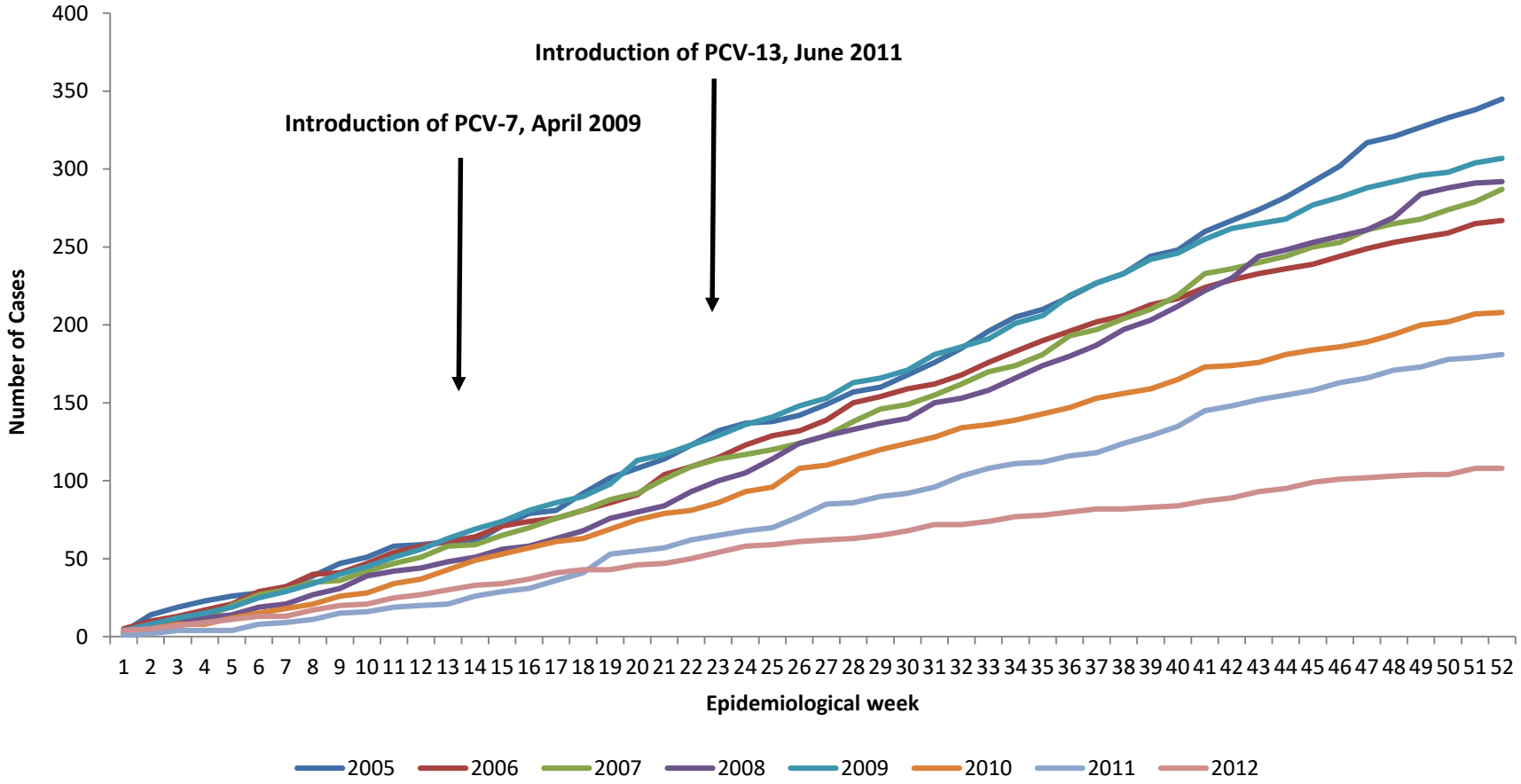

Figure 2. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the six additional (1, 3, 5, 6A, 7F, 19A) serotypes in PCV-13 but not in PCV7: children <5 years of age in South Africa, from 2005 to 2012. Only viable isolates serotyped using Quellung method included. (Note: There is reported cross protection between 6A and 6B which is included in PCV7[7])

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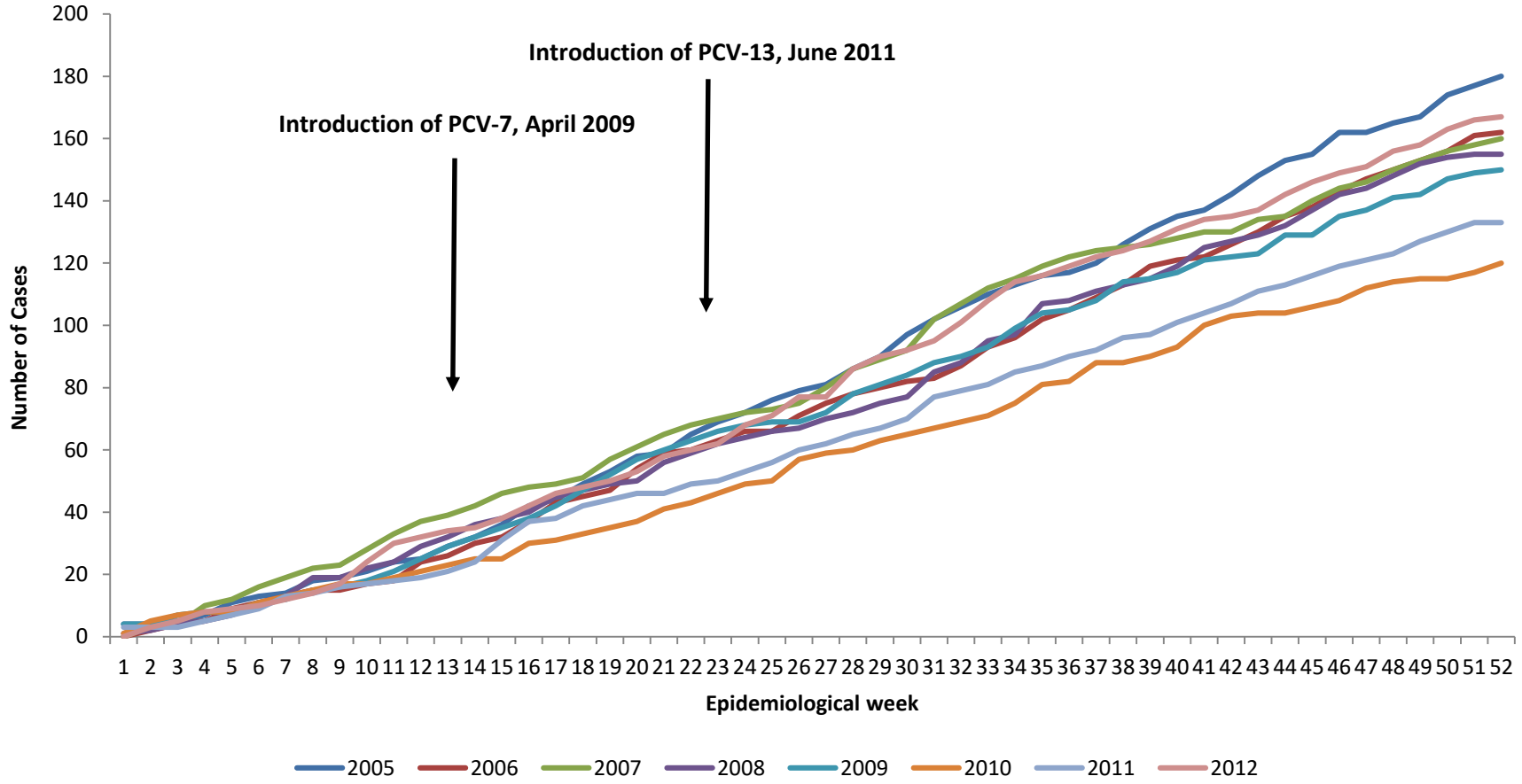

Figure 3. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the serotypes not in PCV13: Children <5 years of age in South Africa, from 2005 to 2012. Only viable isolates serotyped using Quellung method included.

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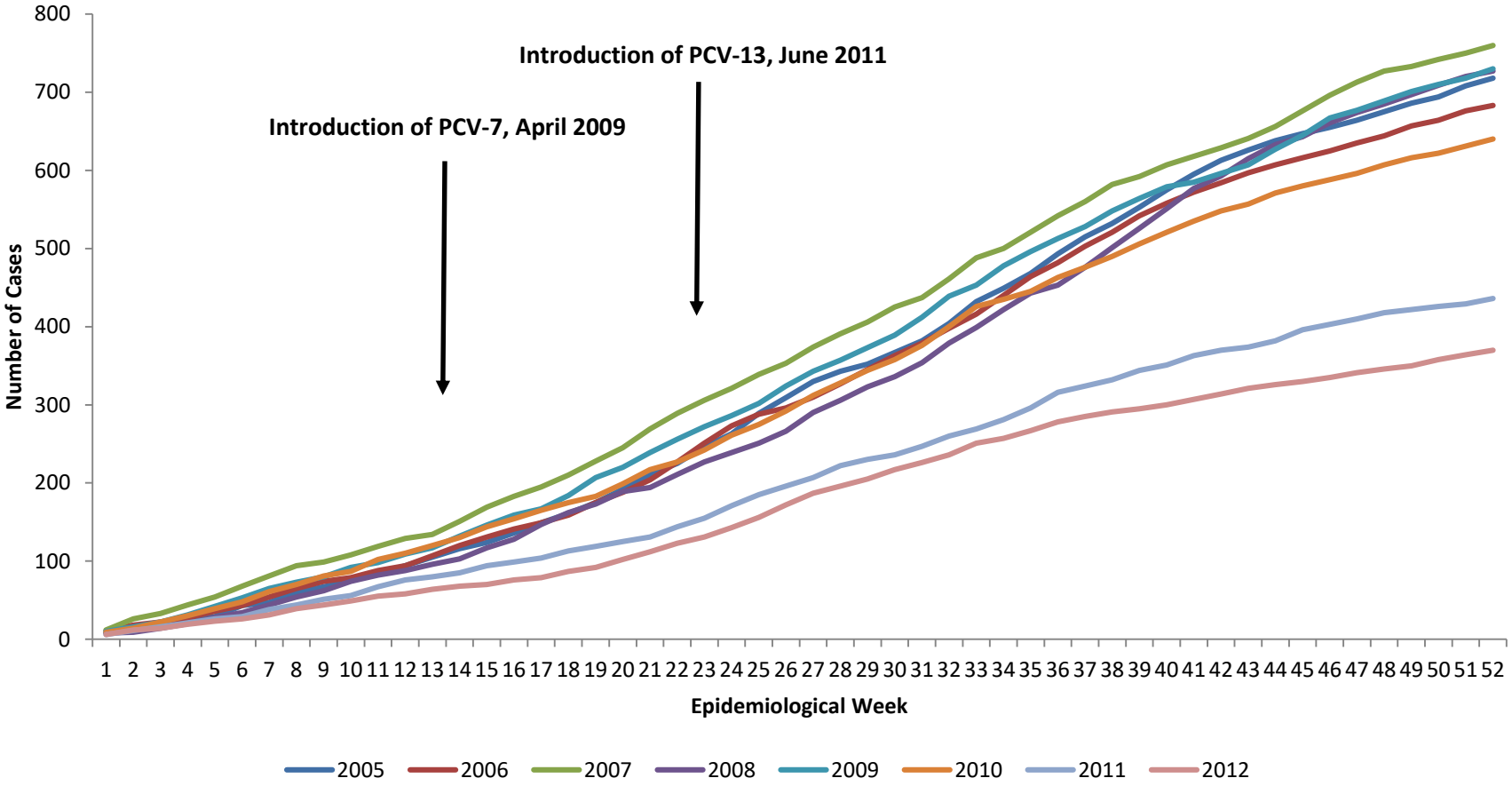

Figure 4. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the seven serotypes (4, 6B, 9V, 14, 18C, 19F and 23F) in PCV-7: Individuals ≥5 years of age in South Africa, from 2005 to 2012. Only viable isolates serotyped using Quellung method included.

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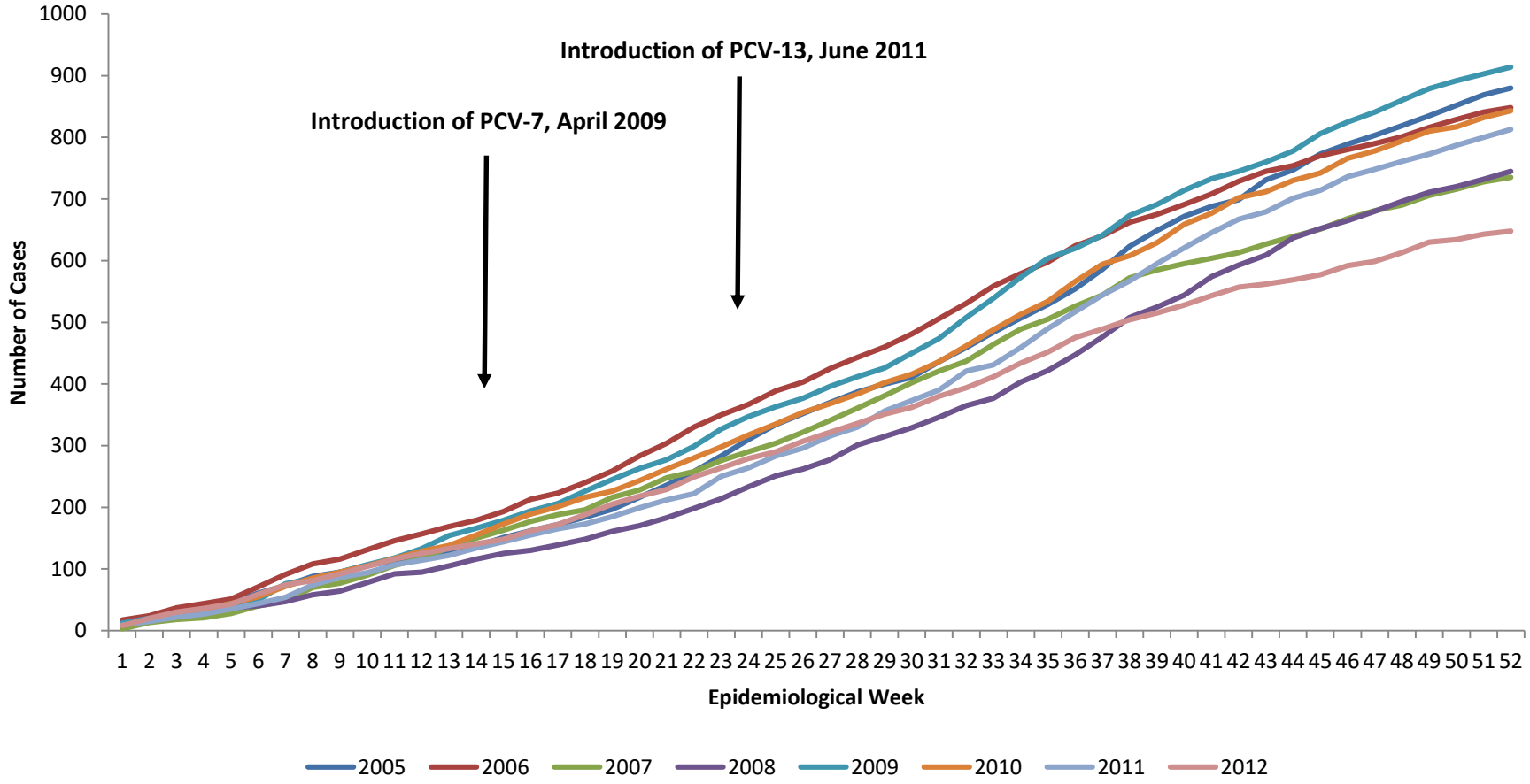

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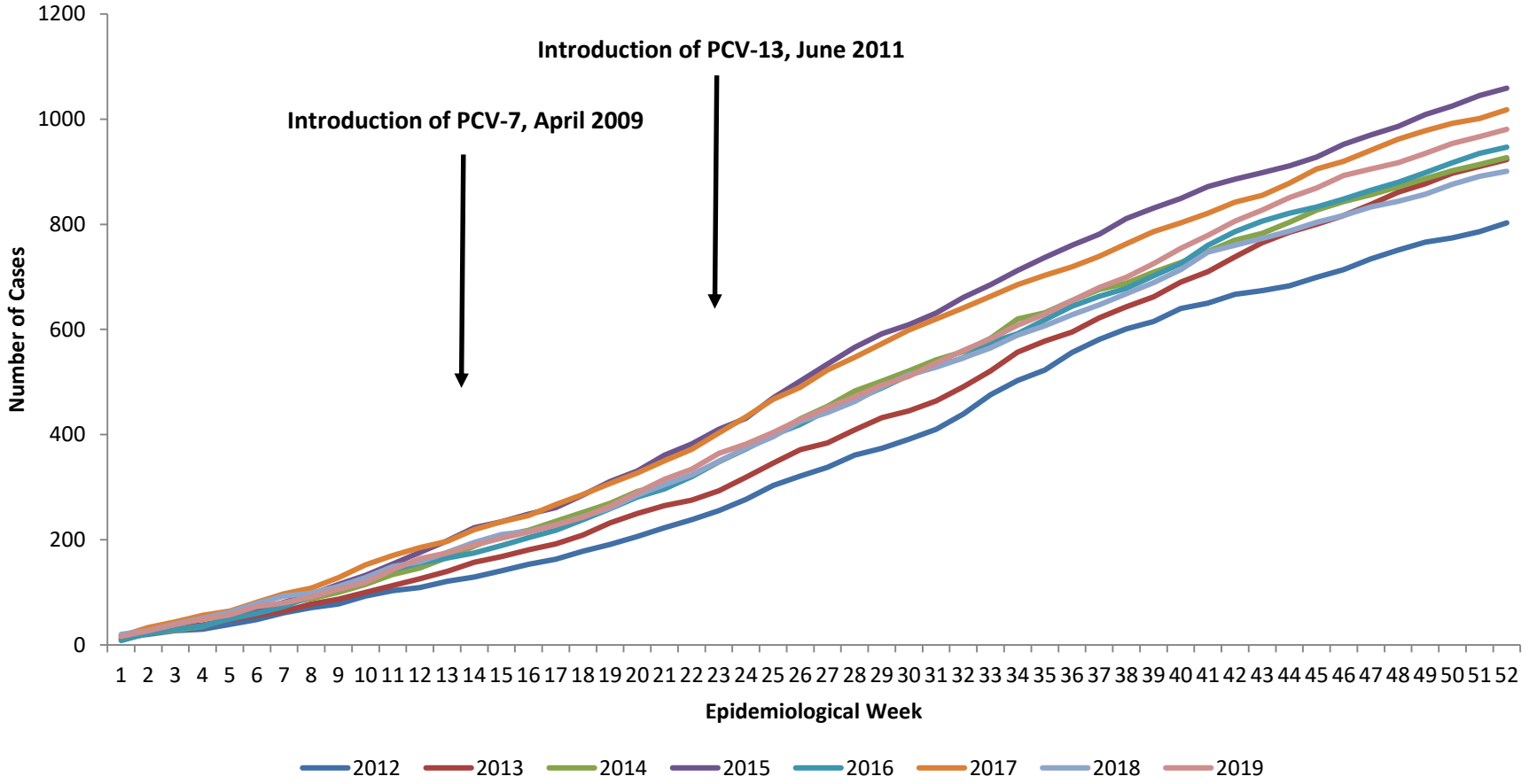

Figure 6. Cumulative weekly number of disease episodes of invasive pneumococcal disease due to any of the serotypes not in PCV-13: individuals ≥5 years of age in South Africa, from 2005 to 2012. Only viable isolates serotyped using Quellung method included.

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Appendix: Cumulative invasive pneumococcal disease case numbers reported by the GERMS-SA surveillance programme, 1 January 2005 to December 2012

Missing information

Table 1. Isolates with missing age; number of viable and non-viable isolates and audit cases identified, 2005-2012

	Age missing, n (%)		Viable, n (%)		Non-viable, n (%)		Audit, n (%)		Total
2005	236	(5)	3,650	(75)	380	(8)	856	(18)	4,886
2006	223	(5)	3,419	(72)	444	(9)	868	(18)	4,731
2007	217	(5)	3,329	(70)	597	(13)	816	(17)	4,742
2008	208	(4)	3,327	(69)	576	(12)	932	(19)	4,835
2009	161	(3)	3,387	(71)	532	(11)	841	(18)	4,760
2010	141	(3)	2,873	(68)	515	(12)	809	(19)	4,197
2011	218	(6)	2,409	(63)	451	(12)	944	(25)	3,804
2012	248	(8)	2,160	(67)	344	(11)	718	(22)	3,222
All	1,652	(5)	24,554	(67)	3,839	(12)	6,784	(20)	35,177