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Invasive Pneumococcal Disease Due to Serotypes in Pneumococcal Vaccines in Older Adults of High-Income Countries

Lindsay R. Grant,[1] Mary P. E. Slack,[2] Christian Theilacker,[1] José Suaya,[1] Jelena Vojicic,[1] Stéphane Dion,[1] Ralf-Rene Reinert,[1] Bradford D. Gessner[1]

[1]Pfizer Vaccines, Medical Development and Scientific Affairs, Collegeville, PA, USA; [2]Medical School, Griffith University Gold Coast Campus, Southport, Queensland, Australia

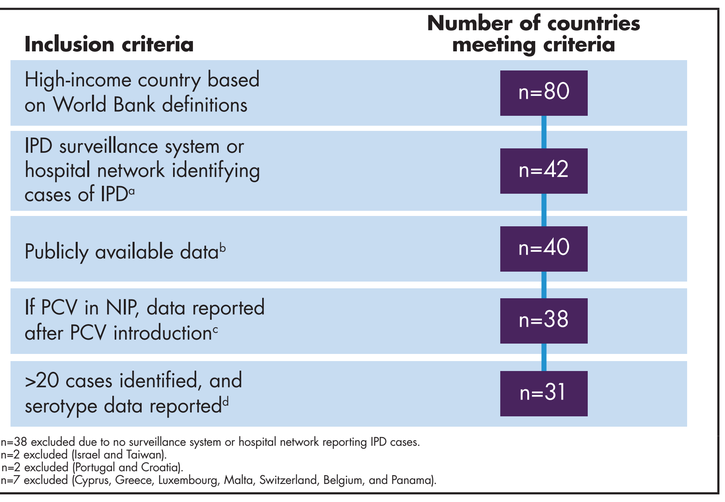
BACKGROUND

- Despite the indirect effects of routine pediatric pneumococcal conjugate vaccine (PCV) use, invasive pneumococcal disease (IPD) persists in older adults.
- The objective of this analysis is to estimate the percentage of IPD due to serotypes in the available 13-valent PCV (PCV13) and 23-valent plain polysaccharide pneumococcal vaccine (PPSV23), and the investigational 15-valent PCV (PCV15) and 20-valent PCV (PCV20).

METHODS

- We analyzed IPD cases by serotype from older adults ≥60 years old from high-income countries (except Singapore, adults >50 years). Country-specific IPD data were obtained from national, regional, or sentinel surveillance systems or from hospital networks. Up to the 3 most recent years of publicly reported data from peer-reviewed publications, online reports, and databases were included in the analysis. More than one source of data could be included for each country. Excluded countries reported <20 cases overall or only reported data prior to pediatric PCV introduction into the national immunization program (NIP) **(Figure 1)**.
- The percentage of IPD due to vaccine serotypes was calculated for PCV13 (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) plus 6C, which is structurally highly related to 6A; PCV15 (PCV13 serotypes and serotypes 22F and 33F) plus 6C; PCV20 (PCV15 serotypes and serotypes 8, 10A, 11A, 12F, and 15B) plus 6C and 15C, which is structurally highly related to 15B; and PPSV23 (serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F) plus 15C.
- Cases of IPD with missing serotype information or those non-typeable were excluded from the total count of IPD cases. If more than 1 year of data were reported, the percentage of IPD due to PCV serotypes was simply averaged over the total number of years reported. The percentage of IPD was reported for countries grouped by PCV use in the pediatric NIP.

Figure 1. Country inclusion flow diagram



[a] n=38 excluded due to no surveillance system or hospital network reporting IPD cases.
[b] n=2 excluded (Israel and Taiwan).
[c] n=2 excluded (Portugal and Croatia).
[d] n=7 excluded (Cyprus, Greece, Luxembourg, Malta, Switzerland, Belgium, and Panama).

RESULTS

Country and case inclusion

- The 31 high-income countries that met the criteria for inclusion reported approximately 65,900 cases of IPD with a serotype identified in older adults, the majority of which were ≥60 or ≥65 years old.
- The majority of countries introduced the 10-valent PCV (PCV10) or PCV13 into the country pediatric NIP >5 years prior to the beginning of the data reporting period included in this analysis. PCV10 was used in 9 (29.0%) countries, PCV13 in 18 (58.1%) countries, both PCV10 and PCV13 in 3 (9.7%) countries, and 1 country had not introduced a PCV into the pediatric NIP. Most countries (77.4%) used a 2+1 schedule **(Table 1)**.

Percentage of IPD due to vaccine serotypes by country pediatric NIP PCV use

- The percentage of IPD serotypes due to vaccine serotypes was similar in countries with pediatric NIP use of PCV10 or PCV13 regardless of the number of years between the start of PCV use and the beginning of the data reporting time period included in the analysis **(Table 2)**.
  - Countries with PCV10 only in the pediatric NIP: the percentage of IPD due to serotypes in PCV13, PCV15, PCV20, and PPSV23 ranged from 25.0% to 73.6%, 25.0% to 79.1%, 25.0% to 88.2%, and 25.0% to 86.6%, respectively.
  - Countries with PCV13 only in the pediatric NIP: the percentage of IPD due to serotypes in PCV13, PCV15, PCV20, and PPSV23 ranged from 16.2% to 66.5%, 27.7% to 71.3%, 51.1% to 83.1%, and 48.8% to 84.0%, respectively.
  - Countries with PCV10 and PCV13 in the pediatric NIP: the percentage of IPD due to serotypes in PCV13, PCV15, PCV20, and PPSV23 ranged from 41.1% to 61.5%, 48.3% to 61.5%, 62.7% to 75.8%, and 62.3% to 77.0%, respectively.

Prevalent vaccine serotypes

- Serotype 3 ranked among the top 3 pneumococcal vaccine serotypes in most countries regardless of region, type of pediatric NIP PCV use, duration of pediatric NIP PCV use, and schedule.
- Serotype 19A ranked among the top 3 pneumococcal vaccine serotypes in countries with pediatric NIP use of only PCV10 or using both PCV10 and PCV13 but not in countries with pediatric NIP use of only PCV13.
- Serotypes 8, 12F, and 22F ranked among the top 3 serotypes in most countries with pediatric NIP use of only PCV13 but not PCV10 regardless of region, duration of pediatric NIP PCV use, and schedule.

RESULTS (continued)

Table 1. Country characteristics and pneumococcal vaccine use

Country	WHO region	Surveillance system (type) or hospital network (n hospitals)	NIP pediatric schedule[a]	Year PCV introduced into pediatric NIP	PCV used during years of data reported in the analysis	Year PCV use began relevant to years of data reported in the analysis
Australia	WPRO	National, passive, mandatory	3+0[b]	2005	PCV13	2011
Austria	EURO	National, passive, mandatory	2+1	2002	PCV10	2012[c]
Canada	AMRO	Multi-provincial, passive, voluntary	2+1	2002–2006 depending upon province	PCV13	2010[d]
Chile	AMRO	Laboratory based	2+1	2011	PCV10	2011[e]
Czech Republic	EURO	National, active, mandatory	3+1[f]	2005	PCV10, PCV13	2009 (PCV10), 2010 (PCV13)
Denmark	EURO	National, passive, mandatory	2+1	2007	PCV13	2010
England & Wales	EURO	National, passive, mandatory	2+1[g]	2006	PCV13	2010
Estonia	EURO	National, passive, mandatory	2+1	NA (private market only)	PCV10, PCV13	2014
Finland	EURO	National, passive, mandatory	2+1	2010	PCV10	2010
France	EURO	National, active, voluntary	2+1	2006	PCV13	2010
Germany	EURO	National, active, mandatory	2+1[h]	2006	PCV10, PCV13	2009, 2010
Hong Kong	WPRO	National, passive, mandatory	3+1[i]	2010	PCV13	2011
Hungary	EURO	National, passive, voluntary	2+1	2009	PCV13	2010
Iceland	EURO	National, passive, voluntary	2+1	2011	PCV10	2011
Ireland	EURO	National, passive, mandatory	2+1	2008	PCV13	2010
Italy	EURO	National, passive, voluntary	2+1	2005	PCV13[j]	2010
Japan	WPRO	Hospital network (n=341)	3+1	2011	PCV13	2013
Latvia	EURO	National, passive, mandatory	2+1	2010	PCV10	2010
Lithuania	EURO	National, passive, mandatory	2+1	2014	PCV10	2014
Netherlands	EURO	Sentinel, passive, voluntary	2+1	2006	PCV10	2011
New Zealand	WPRO	National, passive, mandatory	3+1	2008	PCV13	2014[k]
Norway	EURO	National, passive, mandatory	2+1	2006	PCV13	2011
Poland	EURO	National, passive, mandatory	2+1	2017	PCV10	2017[l]
Singapore	WPRO	National, passive, mandatory	2+1	2009	PCV13	2011
Slovakia	EURO	National, active, mandatory	2+1	2009	PCV10, PCV13	2010
Slovenia	EURO	National, passive, mandatory	2+1	2005	PCV10[m]	2015
South Korea	WPRO	Hospital network (n=44)	3+1	2014	PCV10, PCV13	2014
Spain	EURO	Regional, passive, mandatory	2+1	2001	PCV13	2015
Sweden	EURO	National, passive, mandatory	2+1	2009	PCV10, PCV13[n]	2010
United States	AMRO	Sentinel, passive, mandatory	3+1	2001	PCV13	2010
Uruguay	AMRO	Laboratory based	2+1	2008	PCV13	2010

AMRO: Americas Region; EURO: European Region; NIP: national immunization program; PCV: pneumococcal conjugate vaccine; PCV10: 10-valent pneumococcal conjugate vaccine; PCV13: 13-valent pneumococcal conjugate vaccine; WHO: World Health Organization; WPRO: Western Pacific Region.
[a] PCV schedule information accessed on International Vaccine Access Center ViewHub (https://view-hub.org/).
[b] In Australia, a 3+0 schedule was used during the years of data included in this analysis (2016–2018). In 2018, Australia switched from a 3+0 to a 2+1 schedule.
[c] In Austria, PCV10 was used during the years of data included in this analysis (2016–2018). Austria switched to PCV13 in 2020.
[d] In Canada, PCV10 was used from 2009 to 2010 in 2 provinces.
[e] In Chile, PCV10 was used during the years of data included in this analysis (2014–2015). Chile switched from PCV10 to PCV13 in 2017.
[f] In the Czech Republic, a 3+1 schedule was used during the years of data included in this analysis (2016–2018). In 2018, they switched to a 2+1 schedule. Both PCV10 and PCV13 are recommended and estimates of PCV coverage do not differentiate between use of PCV10 and PCV13.
[g] England and Wales switched to a 1+1 schedule in 2020.
[h] In Germany, PCV13 is used primarily. In 2015, Germany switched from a 3+1 to a 2+1 schedule.
[i] In Hong Kong, a 3+1 schedule was used during the year of data included in this analysis (2018). They switched from a 3+1 to a 2+1 schedule in July 2019.
[j] The Piemonte region of Italy switched from PCV13 to PCV10 in 2018. The other regions continue to use PCV13.
[k] New Zealand switched from PCV7 to PCV10 in 2011, to PCV13 in 2014 (the year marking the beginning of data included in this analysis), and to PCV10 in 2017.
[l] In Poland, serotype data were available from 2016–2017; however, these years of data were excluded from the analysis because they were prior to introduction of PCV10 in the NIP.
[m] Slovenia switched from PCV10 to PCV13 in 2019.
[n] In Sweden, both PCV10 and PCV13 are recommended; however, PCV10 is primarily used.

Table 2. Percentage of IPD due to vaccine serotypes older adults

Country	Age group	Data reporting period[a]	Years between start of PCV use and beginning of data reporting period	Total IPD cases with a serotype identified[b]	Percentage of IPD serotypes due to vaccine serotypes				Top 3 vaccine serotypes	Data source
					PCV13	PCV15	PCV20	PPSV23		
Countries without a NIP										
Estonia	≥65 y	2016–2018	2	49	48.5%	48.5%	48.5%	48.5%	3; 14; 7F	3
Countries with pediatric NIP use of PCV10										
Austria	≥65 y	2016–2018	4	890	54.7%	63.9%	77.7%	75.2%	3; 19A; 22F	3
Austria	≥65 y	2016–2018	4	820	54.3%	63.4%	77.2%	74.4%	3; 19A; 22F	17
Chile	≥60 y	2014–2015	3	492	63.8%	68.5%	80.5%	76.4%	3; 19A; 14	2
Finland	≥65 y	2016–2018	6	1246	61.1%	72.2%	81.3%	72.6%	19A; 3; 22F	3
Finland	≥65 y	2017–2019	7	1941	62.5%	70.2%	79.9%	74.0%	19A; 3; 6C	4
Iceland	≥65 y	2016–2018	5	37	37.4%	37.4%	42.6%	39.6%	19A; 6C; 3	3
Latvia	≥65 y	2016–2018	6	89	52.8%	58.8%	79.6%	83.0%	19A; 3; 8	3
Lithuania	≥65 y	2016–2018	2	107	25.0%	25.0%	25.0%	25.0%	3; 19A; 7F	3
Netherlands	≥65 y	2016–2018	5	1188	36.0%	45.7%	77.5%	82.4%	8; 19A; 3	3
Slovenia	≥65 y	2016–2018	1	474	73.6%	79.1%	88.2%	86.9%	3; 19A; 14	3
Sweden	≥65 y	2016–2018	6	2577	36.4%	49.3%	66.8%	66.8%	3; 22F; 19A	3
Countries with pediatric NIP use of PCV13										
Australia	≥65 y	2016–2018	5	1315	34.3%	45.9%	56.8%	56.0%	3; 22F; 6C	5
Canada	≥65 y	2015–2017	5	3270	28.8%	41.9%	58.4%	62.2%	22F; 3; 19A	6
Denmark	≥65 y	2016–2018	6	1459	16.2%	27.7%	64.5%	75.6%	8; 3, 22F; 12F	3
England and Wales	≥65 y	2016–2018	6	10,055	23.1%	34.6%	65.9%	74.0%	8; 3; 22F, 12F	3
England and Wales	≥65 y	July 2016–June 2017	6	5228	24.6%	36.1%	70.9%	79.0%	8; 3; 12F	8
France	≥65 y	2016–2018	6	6297	30.6%	39.6%	61.3%	68.8%	3; 22F; 8	3
France	≥65 y	2013, 2015, 2017	3	1310	36.3%	46.1%	65.6%	70.9%	3; 19A; 22F	9
Germany	≥60 y	July 2015–June 2018	5	10,475	32.0%	42.5%	64.4%	71.7%	3; 22F; 8	19
Hong Kong	≥65 y	2018	7	72	65.3%	65.3%	72.2%	79.2%	3; 14; 20; 4; 19F; 23F; 8; 15B	10
Hungary	≥65 y	2016–2018	6	369	34.6%	39.9%	51.1%	55.5%	3; 8; 22F	3
Ireland	≥65 y	2013/2014–2015/2016	3	82	51.2%	51.2%	51.2%	48.8%	19A; 6B; 14	20
Ireland	≥65 y	2016–2018	6	660	27.8%	40.0%	65.8%	73.9%	19A; 8; 3	3
Italy	≥65 y	2016–2018	6	2790	31.0%	39.2%	71.1%	74.6%	8; 3; 22F	3
Italy	≥65 y	2015–2017	5	1593	31.9%	40.8%	73.4%	76.6%	8; 3; 12F	11
Japan	≥65 y	April 2014–March 2016	1	880	47.2%	55.1%	74.2%	68.9%	3; 19A; 12F	12
New Zealand	≥65 y	2014–2016	0	594	49.0%	63.1%	73.6%	73.6%	19A; 22F; 3	13
Norway	≥65 y	2016–2018	5	1053	23.3%	46.2%	63.4%	68.3%	22F; 3; 9N	3
Poland	≥65 y	2018	1	1138	65.3%	71.3%	83.1%	84.0%	3; 14; 22F	14
Singapore	>50 y	2015–2017	4	272	66.5%	68.0%	74.6%	73.9%	3; 14; 19A; 23F	15
Spain	≥65 y	2016–2018	1	3398	36.1%	43.7%	69.6%	71.0%	3; 8; 22F	3
United States	≥65 y	2015–2016	5	1989	26.7%	43.1%	57.0%	59.8%	3; 22F; 6C; 33F	16
Uruguay	≥60 y	2014	4	43	27.9%	32.6%	72.1%	83.7%	3; 12F; 11A	2
Countries with pediatric NIP use of PCV10 and PCV13										
Czech Republic	≥65 y	2016–2018	7 (PCV10), 8 (PCV13)	649	50.2%	58.2%	75.8%	77.0%	3; 19A; 8	3
Czech Republic	≥65 y	2016–2018	7 (PCV10), 8 (PCV13)	751	41.1%	48.3%	62.7%	63.2%	3; 19A; 22F	7
Slovakia	≥65 y	2016–2018	6	78	61.5%	61.5%	75.5%	76.8%	3; 19A; 8	3
South Korea	≥65 y	May 2014–May 2016	0	199	46.7%	51.3%	66.3%	64.3%	3; 19A; 11A	19

IPD: invasive pneumococcal disease; PCV: pneumococcal conjugate vaccine; PCV10: 10-valent pneumococcal conjugate vaccine; PCV13: 13-valent pneumococcal conjugate vaccine; PCV15: 15-valent pneumococcal conjugate vaccine; PCV20: 20-valent pneumococcal conjugate vaccine; PPSV23: 23-valent plain polysaccharide pneumococcal vaccine.
[a] Reported as calendar years unless otherwise specified.
[b] Excludes cases with a missing or non-typeable isolate serotype result.

CONCLUSIONS

- **Among the PCVs, the percentage of IPD due to PCV15 and PCV20 serotypes was higher compared to PCV13, with PCV20 serotypes accounting for the highest percentage of IPD among older adults in high-income countries. The percentage of IPD due to serotypes in PCV20 and PPSV23 was highest; however, to accurately account for the potential impact of adult pneumococcal vaccination, not only the percentage of IPD due to vaccine serotypes, but also expected vaccine effectiveness, duration of protection, and protection against mucosal disease needs to be considered, emphasizing the utility of conjugate vaccines.**

ACKNOWLEDGEMENTS

The authors would like to acknowledge any individuals involved in the surveillance systems or hospital networks who identified and reported IPD cases and Cody Bender who compiled all of the data included in this analysis.

DATA SOURCE

#	Description
1	National Reference Centre *Streptococcus pneumoniae*. Report National Reference Centre *Streptococcus pneumoniae*. https://nrchm.wiv-isp.be/nl/nl/ref_centra_labo/streptococcus_pneumoniae_invasive/Rapporten/Streptococcus%20pneumoniae%202018.pdf https://nrchm.wiv-isp.be/nl/nl/ref_centra_labo/streptococcus_pneumoniae_invasive/Rapporten/Streptococcus%20pneumoniae%202017.pdf https://nrchm.wiv-isp.be/nl/ref_centra_labo/streptococcus_pneumoniae_invasive/Rapporten/Streptococcus%20pneumoniae%202016.pdf
2	Pan American Health Organization. Institutional Repository for Information Sharing. Informe regional de SIREVA II, 2015. https://iris.paho.org/handle/10665.2/49091 Informe regional de SIREVA II, 2014. https://iris.paho.org/handle/10665.2/33875
3	European Centre for Disease Prevention and Control. Surveillance Atlas for infectious diseases. https://www.ecdc.europa.eu/en/data-tools
4	Finnish Institute for Health and Welfare (THL). Incidence of invasive pneumococcal disease in Finland, serotype-specific appendix tables. https://thl.fi/en/web/thlfi-en/research-and-expertwork/projects-and-programmes/monitoring-the-population-effectiveness-of-pneumococcal-conjugate-vaccination-in-the-finnish-national-vaccination-programme/incidence-of-invasive-pneumococcal-disease-in-finland
5	Australian Government Department of Health. National Notifiable Diseases Surveillance System. Pneumococcal Disease Public Dataset. http://www9.health.gov.au/cda/source/pub_pneum.cfm Communicable Diseases Intelligence. Invasive Pneumococcal Disease Surveillance, 1 January to 31 March 2018. https://doi.org/10.33321/cdi.2019.43.50 Communicable Diseases Intelligence. Invasive Pneumococcal Disease Surveillance, 1 April to 30 June 2018. https://doi.org/10.33321/cdi.2019.43.51 Communicable Diseases Intelligence. Invasive Pneumococcal Disease Surveillance, 1 July to 30 September 2018. https://doi.org/10.33321/cdi.2019.43.57 Communicable Diseases Intelligence. Invasive Pneumococcal Disease Surveillance, 1 October to 31 December 2018. https://doi.org/10.33321/cdi.2019.43.55
6	Public Health Agency of Canada. National Laboratory Surveillance of Invasive Streptococcal Disease in Canada. Annual Summary 2017. https://canada.ca/en/public-health/services/publications/drugs-health-products/national-laboratory-surveillance-invasive-streptococcal-disease-canada-annual-summary-2016.html
7	INFORMACE Z NRL A ODBORNÝCH PRACOVIŠŤ SZÚ. Invazivní pneumokokové onemocnění v České republice. http://www.szu.cz/uploads/IPO/IPO_v_CR_2016.pdf http://www.szu.cz/uploads/IPO/Zaverecna_zprava_IPO/Zpravy_CEM_IPO_2017.pdf http://www.szu.cz/uploads/IPO/Zaverecna_zprava_IPO/IPO_v_CR_za_rok_2018.pdf
8	Ladhani SN, et al., *Lancet Infect Dis.* 2018;18: 441–51. https://doi.org/10.1016/S1473-3099(18)30052-5
9	Centre National de Reference des Pneumocoques. Rapport d'activite 2018. Epidemiologie 2019. Centre National de Reference des Pneumocoques. Available at http://cnr-pneumo.com/docs/rapports/CNRP2018.pdf Rapport d'activite 2017, Epidemiologie 2018. Centre National de Reference des Pneumocoques. Available at http://cnr-pneumo.com/docs/rapports/CNRP2017.pdf Rapport d'activite 2016, Epidemiologie 2017. Centre National de Reference des Pneumocoques. Available at http://cnr-pneumo.com/docs/rapports/CNRP2016.pdf
10	Hong Kong Center for Health Protection. https://www.chp.gov.hk/en/resources/29/636.html
11	Dipartimento Malattie Infettive, Istituto Superiore di Sanità. Sorveglianza delle malattie batteriche invasive in Italia, Rapporto Consolidato 2017. Available at http://old.iss.it/binary/mabi/cont/Report2017.pdf
12	Ubukata K, et al., *Emerg Infect Dis.* 2018; 24(11): 2010–2010. https://doi.org/10.3201/eid2411.180326
13	Institute of Environmental Science and Research Ltd (ESR). Invasive pneumococcal disease in New Zealand, 2014. Porirua: ESR; 2016. Available at: https://surv.esr.cri.nz/PDF_surveillance/IPD/2014/2014IPDAnnualReport.pdf Institute of Environmental Science and Research Ltd (ESR). Invasive pneumococcal disease in New Zealand, 2015. Porirua: ESR; 2017. Available at: https://surv.esr.cri.nz/PDF_surveillance/IPD/2015/2015IPDAnnualReport.pdf Institute of Environmental Science and Research Ltd (ESR). Invasive pneumococcal disease in New Zealand, 2016. Porirua: ESR; 2019. Available at: https://surv.esr.cri.nz/PDF_surveillance/IPD/2016/2016IPDAnnualReport.pdf
14	Krajowy Ośrodek Referencyjny. http://korour.nil.gov.pl/wp-content/uploads/2019/07/Inwazyjna-choroba-pneumokokowa-IChP-w-Polsce-w-2018-roku-22.07.2019.pdf
15	Ministry of Health Singapore. Communicable Diseases Surveillance in Singapore. https://www.moh.gov.sg/resources-statistics/reports/communicable-diseases-surveillance-in-singapore-2017 https://www.moh.gov.sg/resources-statistics/reports/communicable-diseases-surveillance-in-singapore-2016 https://www.moh.gov.sg/resources-statistics/reports/communicable-diseases-surveillance-in-singapore-2015
16	Beall B, et al., *Front Microbiol.* 2018 Nov 19:9:2670. https://doi.org/10.3389/fmicb.2018.02670
17	Nationale Referenzzentrale für Pneumokokken https://www.ages.at/service/service-oeffentliche-gesundheit/referenzzentralen/rz-pneumokokken/#downloads
18	van der Linden M, et al., *PLoS One.* 2020 Jan 16;15(1):e0228126. https://doi.org/10.1371/journal.pone.0228126
19	Park DC, et al., *Ann Lab Med.* 2019;39:537–544. https://doi.org/10.3343/alm.2019.39.6.537
20	Corcoran M, et al., *Epidemiol. Infect.* (2017), 145, 2390–2399. https://doi.org/10.1017/S0950268817001194

Presented at ISPPD-12