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Rotavirus Disease and Genotype Diversity in Older Children and Adults in Australia

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Background. Rotavirus is a major cause of gastroenteritis in children <5 years of age. The disease burden in older children, adults, and the elderly is underappreciated. This study describes rotavirus disease and genotypic diversity in the Australian population comprising children ≥5 years of age and adults.

Methods. Rotavirus positive fecal samples were collected from laboratories Australia-wide participating in the Australian Rotavirus Surveillance Program between 2010 and 2018. Rotavirus samples were genotyped using a heminested multiplex reverse-transcription polymerase chain reaction. Notification data from the National Notifiable Diseases Surveillance System were also analyzed.

Results. Rotavirus disease was highest in children aged 5–9 years and adults ≥85 years. G2P[4] was the dominant genotype in the population ≥5 years of age. Genotype distribution fluctuated annually and genotypic diversity varied among different age groups. Geographical differences in genotype distribution were observed based on the rotavirus vaccine administered to infants <1 year of age.

Conclusions. This study revealed a substantial burden of rotavirus disease in the population ≥5 years of age, particularly in children 5–9 years and the elderly. This study highlights the continued need for rotavirus surveillance across the population, despite the implementation of efficacious vaccines.

Keywords. Australia; gastroenteritis; genotype; rotavirus; surveillance.

Group A rotaviruses are a key etiological agent of acute gastroenteritis in infants and young children worldwide [1]. The burden of disease has decreased substantially over the last decade, largely due to the inclusion of rotavirus vaccines into the national immunization programs (NIP) of over 100 countries [2]. In Australia, the live-attenuated vaccines Rotarix (monovalent, human) and RotaTeq (pentavalent, human-bovine reassortant) were introduced into the NIP in mid-2007, with a state-based selection method in place until mid-2017, after which a national tender process was initiated with all states and territories now using Rotarix (Figure 1) [3, 4].

The burden of disease and genotypic diversity in young children has been well described [4, 5]. Rotavirus can also cause gastroenteritis in older children and adults in varied settings including outbreaks in hospitals and nursing homes, travel-related gastroenteritis, infections transmitted from children to adults, and endemic disease [6]. Severe symptoms are rare because healthy adults generally have protective immunity acquired from previous and regular asymptomatic infections. However, adolescents and adults may experience symptomatic infections, with symptoms including malaise, headache, abdominal cramping, diarrhea, and fever commonly reported [6–8].

The incidence of rotavirus diarrhea in adults has been reported ranging 2%–22% of gastroenteritis cases in numerous countries [6, 9]. Immediately before vaccine introduction in the United States, rotavirus was detected at a similar rate as bacterial pathogens from adults admitted to hospital with diarrhea, with rotavirus more common in older individuals and those with underlying immunosuppression [8]. Another study in the United States reported an estimated 24 000 rotavirus hospitalizations annually among individuals ≥5 years of age [10]. In the Netherlands, rotavirus was associated with an average of 1150 deaths each year in adults ≥65 years of age [11]. Despite these studies, the burden of rotavirus disease in adults has been largely underrecognized.

Group A rotavirus strains are classified into G and P genotypes based on the outer capsid proteins VP7 and VP4, respectively. To date, 36 G types and 51 P types have been described in humans

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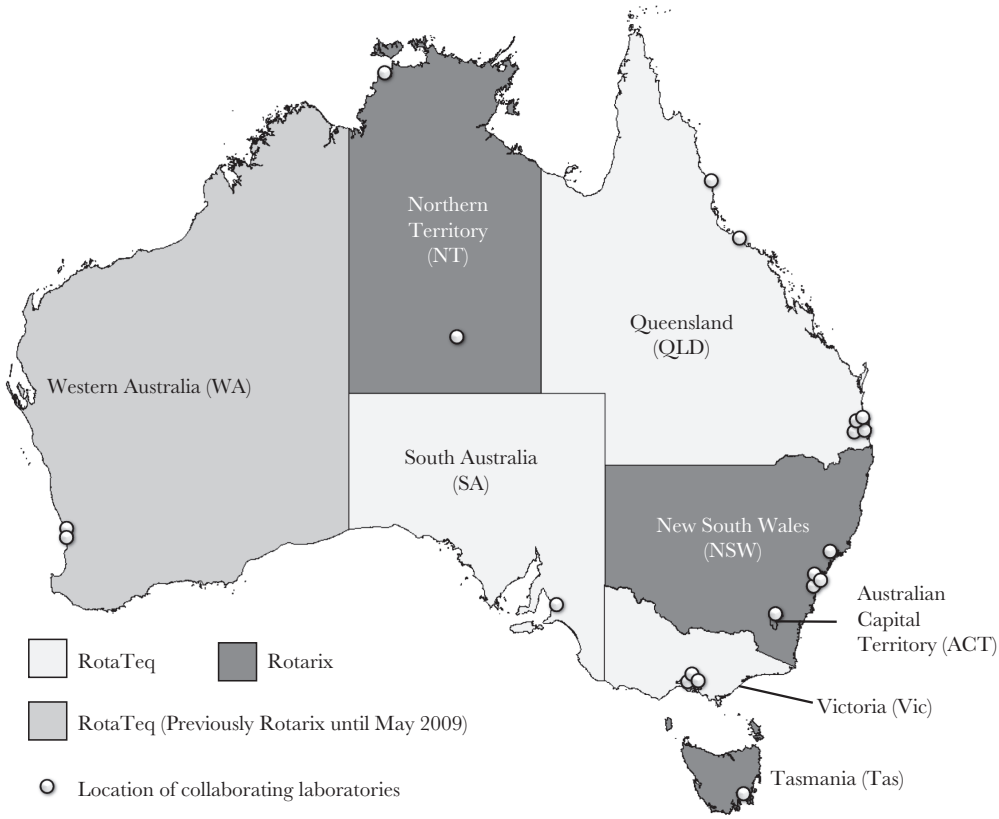

Figure 1. Pattern of state-based vaccine use within the national immunization program in Australia. Queensland, South Australia, and Victoria implemented RotaTeq (light gray); Australian Capital Territory, New South Wales, Northern Territory, and Tasmania implemented Rotarix (dark gray). Western Australia initially used Rotarix but switched to RotaTeq in 2009 (mid gray). All states and territories have implemented Rotarix since July 2017. Circles represent locations of collaborating laboratories and hospitals contributing samples to the Australian Rotavirus Surveillance Program.

and various animal species [12]. The most common genotypes in humans are G1, G2, G3, G4, G9, and G12, in combination with P[4], P[6], and P[8] [5]. Despite rotavirus surveillance programs in children <5 years of age, there are limited data describing the genotypic diversity in adults and the potential interplay of genotype diversity between adults and children.

The Australian Rotavirus Surveillance Program has characterized the G and P genotypes of rotavirus strains causing acute gastroenteritis in children <5 years of age since 1999, and in recent years it has extended surveillance to include children ≥5 years of age and adults [4]. In 2010, rotavirus caused an estimated 369 375 cases of gastroenteritis and 9864 hospitalizations in Australian individuals ≥5 years of age, revealing a considerable, previously unappreciated, burden of rotavirus disease in older children and adults [13]. In comparison, 10 000 hospitalizations in children <5 were reported annually in the prevaccine era [14]. The aim of this study was (1) to describe rotavirus disease in children ≥5 years of age and adults in Australia 2010–2018 and (2) to investigate temporal, geographic, or age-related variations in genotypic diversity.

METHODS

Study Design and Sample Collection

In this study spanning January 1, 2010 to December 31, 2018, fecal samples were collected from patients either hospitalized or presenting to a General Practice clinic with acute gastroenteritis. Fecal samples were tested for the presence of rotavirus using enzyme immunoassay (EIA), latex agglutination, or quantitative reverse-transcription polymerase chain reaction (RT-qPCR) by 32 laboratories and hospitals that collaborate with the ARSP (Supplementary Table 1). Deidentified rotavirus-positive specimens were sent to the National Rotavirus Reference Centre laboratory at the Murdoch Children's Research Institute. Where possible, metadata including date of collection, date of birth, gender, and postcode were collected. Samples were stored at –80°C until analyzed, allocated a unique laboratory code, and entered into a REDCap database. Samples were confirmed as rotavirus positive using the ProSpecT Rotavirus EIA (Thermo Fisher Scientific, Waltham, MA), as per manufacturer's instructions, and negative samples were not analyzed further.

Rotavirus Genotyping

Rotavirus G and P genotyping was performed using a heminested multiplex RT-PCR assay [15]. Viral ribonucleic acid (RNA) was extracted from 10% to 20% (w/v) fecal extracts using the QIAamp Viral RNA mini extraction kit (QIAGEN, Hilden, Germany) according to the manufacturer's instructions. First-round RT-PCR reactions were performed using the QIAGEN One Step RT-PCR kit, using the VP7 (VP7F/VP7R) or VP4 (VP4F/VP4R) primer pair [16, 17]. The second-round genotyping PCR were performed using the AmpliTaq DNA Polymerase with Buffer II (Applied Biosystems, Foster City, CA), together with specific oligonucleotide primers for G types (1, 2, 3, 4, 8, 9, and 12) or P types ([4], [6], [8], [9], [10] and [11]) as previously described [4]. Gel electrophoresis of second-round PCR products was performed to determine the G and P genotype of each sample.

The VP7 gene of G1P[8] samples from infants ≤8 months were sequenced to determine whether wild-type or Rotarix vaccine strain was detected. Sequencing of VP6 and VP7 genes was performed for suspect RotaTeq samples with mixed G types or were P nontypeable [18]. The current set of primers in the second-round G-typing protocol cannot assign genotypes to equine-like G3, G12, and unusual rotavirus strains so the first-round product of any G or P nontypeable samples were sequenced. Amplicons were purified using the QIAquick Gel Extraction Kit (QIAGEN) or the Wizard SV Gel and PCR Clean-Up System (Promega, Madison, WI) according to the manufacturer's instructions. Purified DNA and primers were sent to the Australian Genome Research Facility, Melbourne, and sequenced using an ABI PRISM BigDye Terminator Cycle Sequencing Reaction Kit (Applied Biosystems) using an Applied Biosystems 3730xl DNA Analyzer (Applied Biosystems). Electropherograms were visually analyzed using Sequencher v.4.10.1. Genotype assignment was determined using BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi) and confirmed using RotaC v2.0 http://rotac.regatools.be [19].

Data Analysis

Vaccine group was assigned according to where the sample was collected (RotaTeq states - Queensland, South Australia, Victoria; Rotarix states and territories - Australian Capital Territory, New South Wales, Northern Territory). Western Australia was analyzed separately due to the change in vaccine selection; with Rotarix used between July 2007 and May 2009, then RotaTeq until July 2017 (Figure 1). The data are presented as the proportion (percentage) of a specific genotype compared with the total number of rotavirus-positive samples in a given year or age group.

Rotavirus has been a notifiable disease in Australia since 2010, with all states and territories reporting through the National Notifiable Diseases Surveillance System (NNDSS) with exceptions noted in the figure legend. Notification data are available at http://www9.health.gov.au/cda/source/cda-index.cfm.

RESULTS

Samples Collected

During the period January 1, 2010 to December 31, 2018, the ARSP received a total of 11 555 rotavirus-positive fecal specimens. A total of 5163 samples did not meet the inclusion criteria: unknown age (n = 487), negative when processed at the Murdoch Children's Research Institute (n = 2552), insufficient sample for testing (n = 154), missing (n = 52), not processed due to high cycle threshold value determined by collaborating laboratory (n = 94), not processed due to insufficient funding (n = 668), or duplicate of sample already processed (n = 451) (Figure 2). Samples were also excluded if they were determined to be vaccine-like (n = 705), including 11 samples detected in patients ≥12 months of age. A total of 6392 samples were included in the final analysis, from children <5 years of age (n = 3742) and the population ≥5 years of age (n = 2650) (Supplementary Figure 1, Supplementary Table 2). Fewer samples were collected in 2011, 2016, and 2018 compared with other years, coinciding with lower notification rates in 2016 and 2018 (Supplementary Figure 1, Figure 3). Samples were collected from states that had implemented RotaTeq (n = 2645, 41.4%), Rotarix (n = 1901, 29.7%), and Western Australia (n = 1846, 28.9%) (Supplementary Table 2).

Burden of Disease Across Age Groups

The NNDSS notification rate data (per 100 000 population) was analyzed by calendar year to describe the age distribution of rotavirus disease (Figure 3). Within age categories, the overall notification rates displayed minor variations year-to-year, with the exception of 2017 when a higher-than-average burden of disease was observed across all age categories, and notifications were 2–3 times higher than the notification rates for other years (Figure 3). Consistently, the highest rates in the population ≥5 years of age was in the 5–9, 80–84, and ≥85 years of age categories, with the mean notification rate of 34.9, 23.6, and 45.5 per 100 000, respectively. The burden of disease in the population ≥5 years of age is substantially lower than in the population <5 years of age, which reported a mean notification rate of 177.1 per 100 000 (Figure 3).

When the ARSP data for the population ≥5 years of age were analyzed, the median age was 31.0 years (range, 5 to 103.8 years), and the majority of samples included in the study were from children 5–9 years of age (30.6%), followed by children 10–14 years (8.0%) and adults ≥85 years (9.3%) (Supplementary Figure 2).

The data cannot be fully reconciled between the NNDSS and ARSP; not all states and territories report data to the NNDSS, and the ARSP does not receive samples for all rotavirus cases.

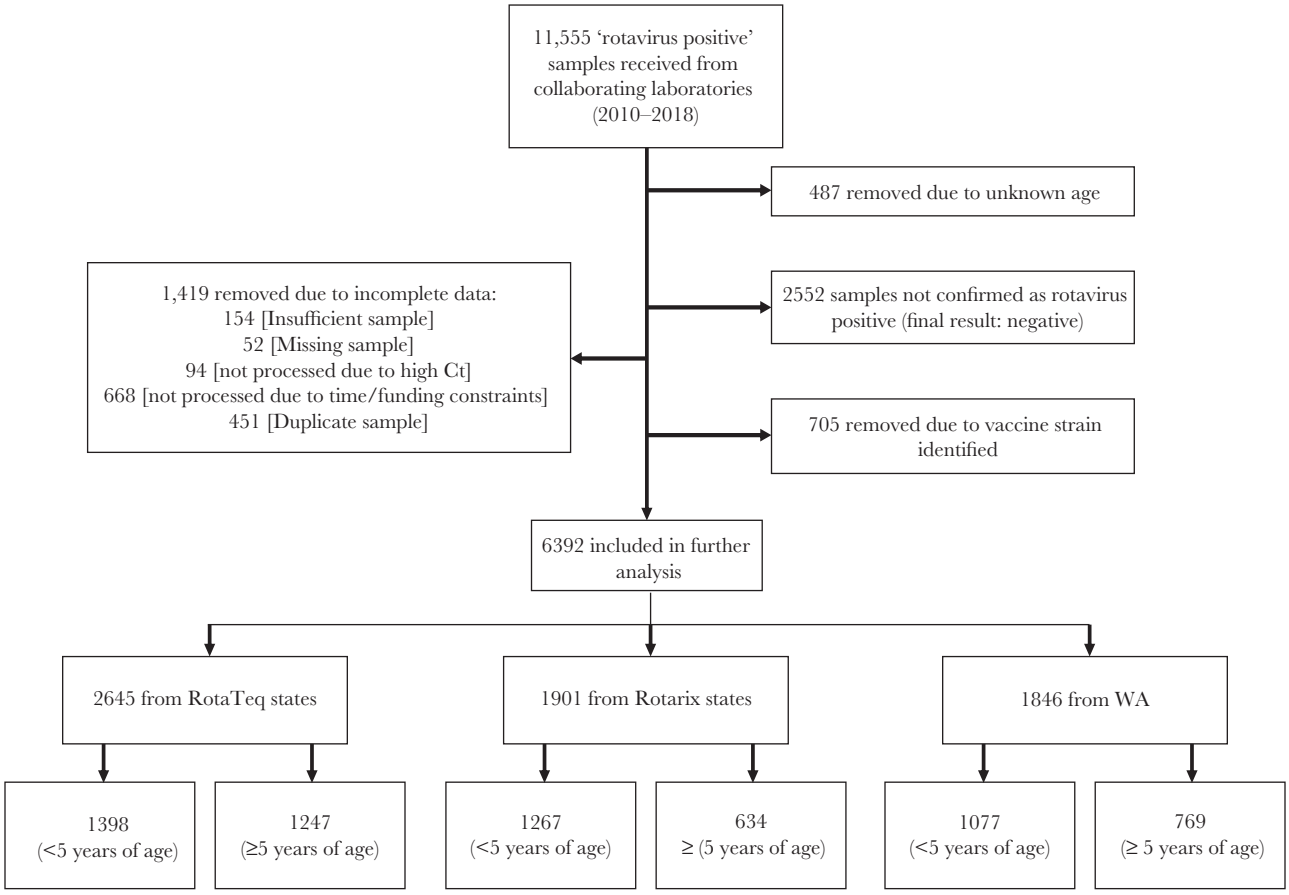

Figure 2. Flow chart of samples included in the study and exclusion criteria. Ct, cycle threshold; WA, Western Australia.

Hence both programs have the potential to underestimate the burden of rotavirus disease.

Genotype Distribution Annually in the Australian Population ≥5 Years of Age

Overall, G2P[4] was the most commonly detected genotype (n = 856, 32.3%) in individuals ≥5 years of age, followed by G12P[8] (n = 560, 21.1%), equine-like G3P[8] (n = 295, 11.1%), human G3P[8] (n = 276, 10.5%), and G1P[8] (n = 290, 10.9%) (Figure 4a). Genotype dominance and diversity varied over time; G2P[4] was dominant in 4 of 9 years, accounting for 29.0%–70.2% of samples genotyped annually (Figure 4b). G12P[8] was dominant for 3 consecutive years (2013–2015), accounting for 35.4%–59.7% of samples genotyped (Figure 4b). Equine-like G3P[8] emerged in 2013 accounting for 15.0% of samples genotyped, and detection ranged 5.8%–25.3%. G4P[8] accounted for 0%–4.8% of samples annually and 0.8% of samples overall. G8P[8] emerged as a rare genotype in 2015–2016 (0.7%–1.6%), increasing to represent 19.4% of samples in 2017. G9P[8] was a minor genotype accounting for <3.0% of samples annually except for sporadic years of increased detection in 2014 (9.6%), 2016 (11.3%), and 2018 (13.1%). Detection of unusual or mixed genotypes was low (<5.4%) in most years except 2016 (12.1%) and 2018 (9.6%), which was not attributable to any single genotype (Supplementary Table 3).

Genotype Distribution by Age

There were minor differences in genotype distribution among different age groups. G2P[4] was the dominant genotype in each age category ≥15 years, accounting for 26.9%–43.5% of samples genotyped (Figure 4c). G2P[4] and G12P[8] shared dominance in the 5–9 (25.5% and 25.7%, respectively) and 10–14 age groups (20.6% and 20.3%, respectively). The 70–74, 75–79, and ≥85 age groups reported the highest detection rate of G2P[4] (43.5%, 41.5% and 42.7%, respectively, compared with 20.8%–37.3% in the other age groups). The detection of other genotypes was similar across age groups; G4P[8], G8P[8], and G9P[8] were consistently minor genotypes. When genotype prevalence was compared between the <5 and ≥5 years of age categories, minor differences were observed for G1P[8] and G2P[4]. G1P[8] accounted for 19.9% of samples in the <5 age group compared with 9.4% in the ≥5 age group. In contrast, G2P[4] accounted for 30.6% of samples in the ≥5 age group compared with 21.6% in the <5 age group. The rates of all other genotypes were similar between the age groups (Figure 4a).

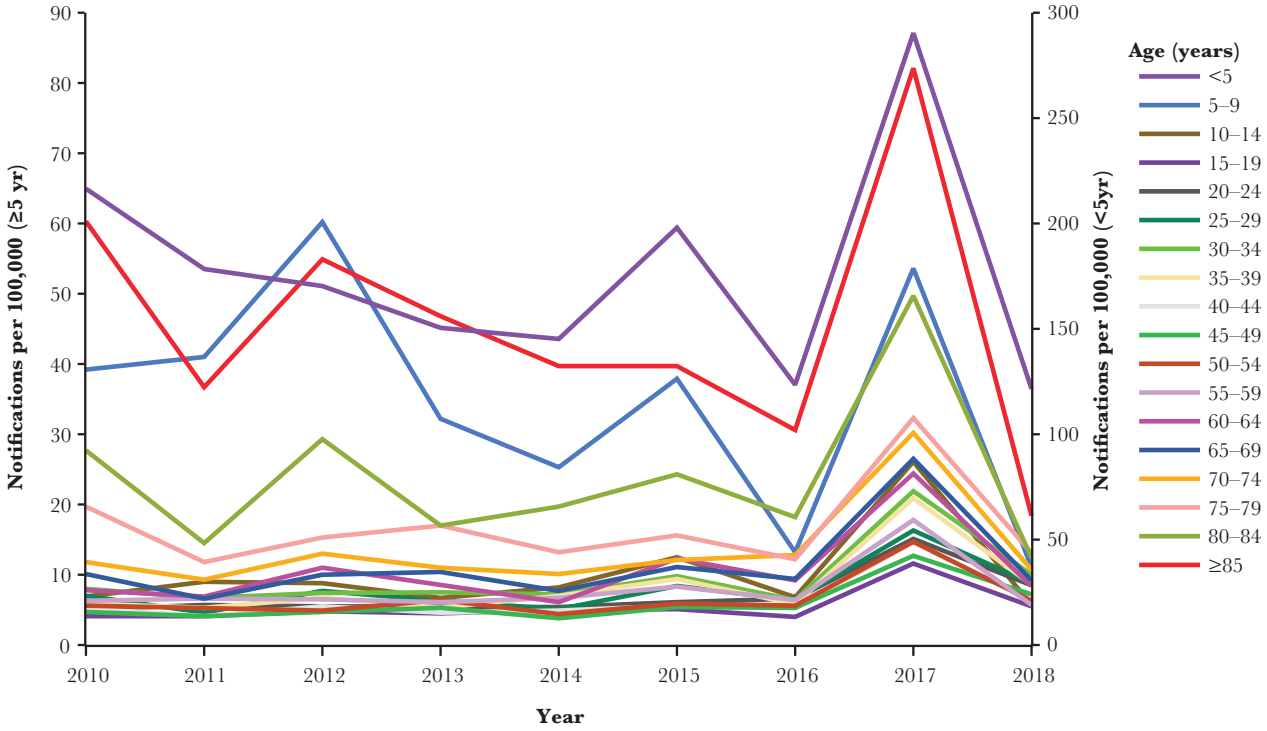

Figure 3. The age distribution of the burden of rotavirus disease in Australia based on the notification rates (per 100 000 population) reported to the Australian National Notifiable Diseases Surveillance System 2010–2018. All states and territories reported data, except Victoria, which did not report at all during this period, the Australian Capital Territory only reported in 2018 and the Northern Territory reported all years except 2010. Notification data are available at http://www9.health.gov.au/cda/source/cda-index.cfm.

When genotype distribution was compared between children <5 years of age (the majority of which would be vaccinated), 5–12 years of age (potentially previously vaccinated), and the population ≥13 to ≥85 years of age (unvaccinated), minor differences were observed (Supplementary Figure 3). G12P[8] accounted for 30.6% of samples in the 5–12 years category, compared with 19.1%–19.4% in the other age groups. G1P[8] accounted for 19.9% of samples in the <5 age group compared with 7.4%–9.8% in the other age groups. G2P[4] accounted for 33.1% of samples in the ≥13 to ≥85 years of age category compared with 16.9%–21.6% in the other age groups.

Identification of Vaccine Strains in Older Children and Adults

Eleven vaccine-like strains were identified in children ≥12 months of age and adults, confirmed by sequencing. Five RotaTeq strains were identified, from patients 13 months to 8 years of age. Six Rotarix strains were identified, from patients 16 months to 85 years of age (Supplementary Table 4).

Comparison of State-Wise Genotype Distribution of <5 and ≥5 Years of Age Groups

In RotaTeq states (Queensland, South Australia, and Victoria), the genotype distribution in the population ≥5 years of age was similar in diversity and proportion to that in the <5 population for most years (Figure 5a). Overall, G1P[8] were more frequent in the <5 age group (19.7%) compared with the ≥5 age group (10.8%), and conversely G2P[4] was more frequent in the ≥5 age group (24.2%) compared with the <5 age group (14.9%). Other genotypes were observed at a similar frequency between the <5 and ≥5 age groups, except G4P[8], which was detected at 2.1% and 0.1%, respectively. With the exception of 2012 and 2017, the same genotype was dominant in the <5 and ≥5 age groups (Figure 5a), with G1P[8] dominant in 2010, G2P[4] dominant in 2011, G12P[8] dominant 2013–2016, and human G3P[8] dominant in 2018.

In contrast to RotaTeq states, there were more differences in genotype distribution between the <5 and ≥5 age groups in Rotarix states (the Australian Capital Territory, New South Wales, the Northern Territory, and Tasmania). G1P[8] were more frequently detected in the <5 age group (20.4%) than the ≥5 age group (7.3%), and G2P[4] were more frequently detected in the ≥5 age group (35.5%) compared with the <5 age group (27.1%) (Figure 5b). G8P[8] were more frequently detected in the ≥5 age group (10.1%) compared with the <5 age group (2.7%). Human G3P[8], equine-like G3P[8], G4P[8], G9P[8], and G12P[8] were detected at similar rates in both age groups. For most years, genotype dominance varied between the <5 and ≥5 age groups. For the ≥5 age group, G2P[4] was dominant for all years excluding 2011 (G1P[8] and human

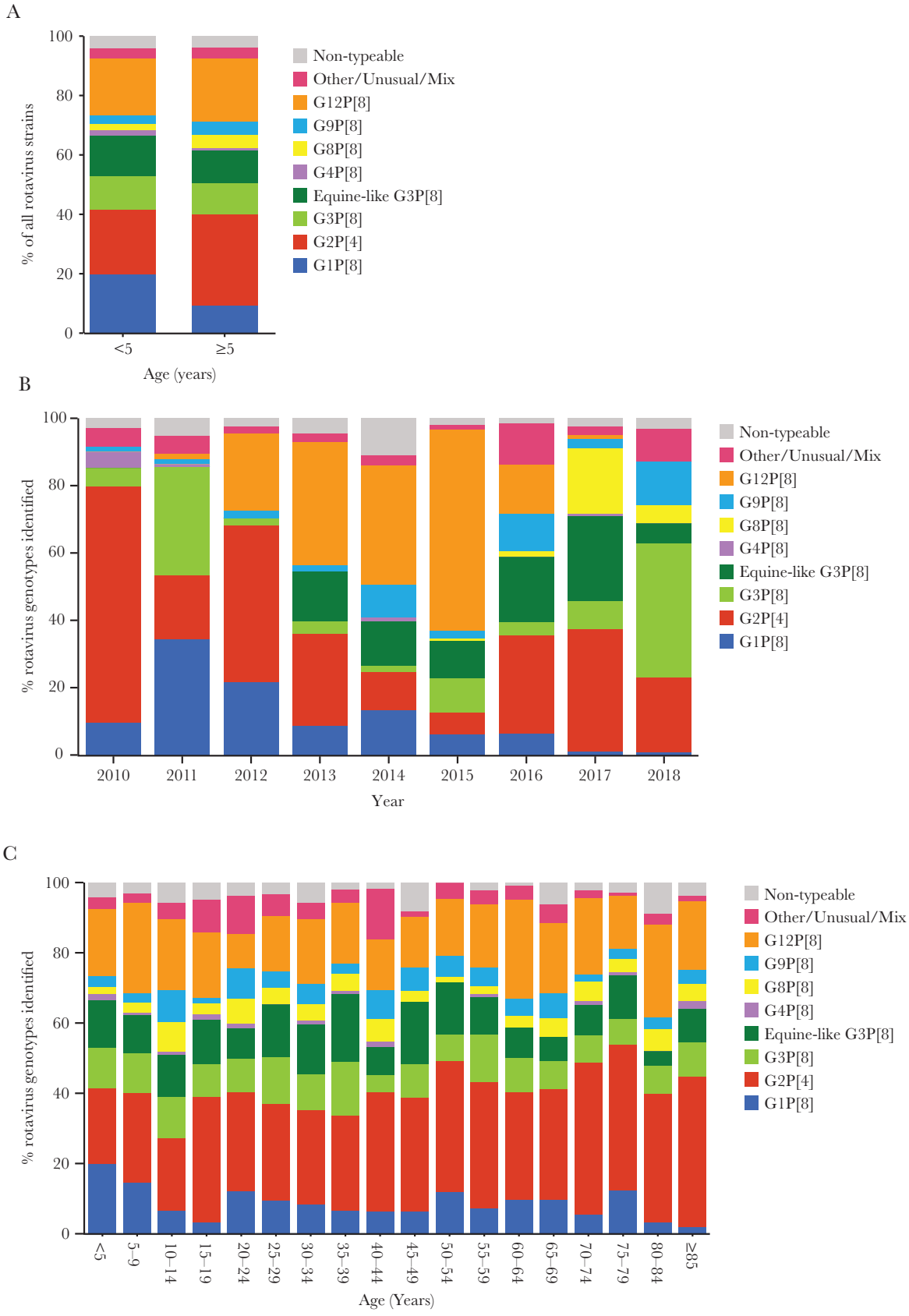

Figure 4. Comparison of the genotype distribution 2010–2018 (a) in children <5 years of age compared with the population ≥5 years of age, (b) annually in the Australian population ≥5 years of age, and (c) across the different age categories between <5 and ≥85 years of age. Data are presented as the proportion (%) of a specific genotype compared with the total samples collected within the age category.

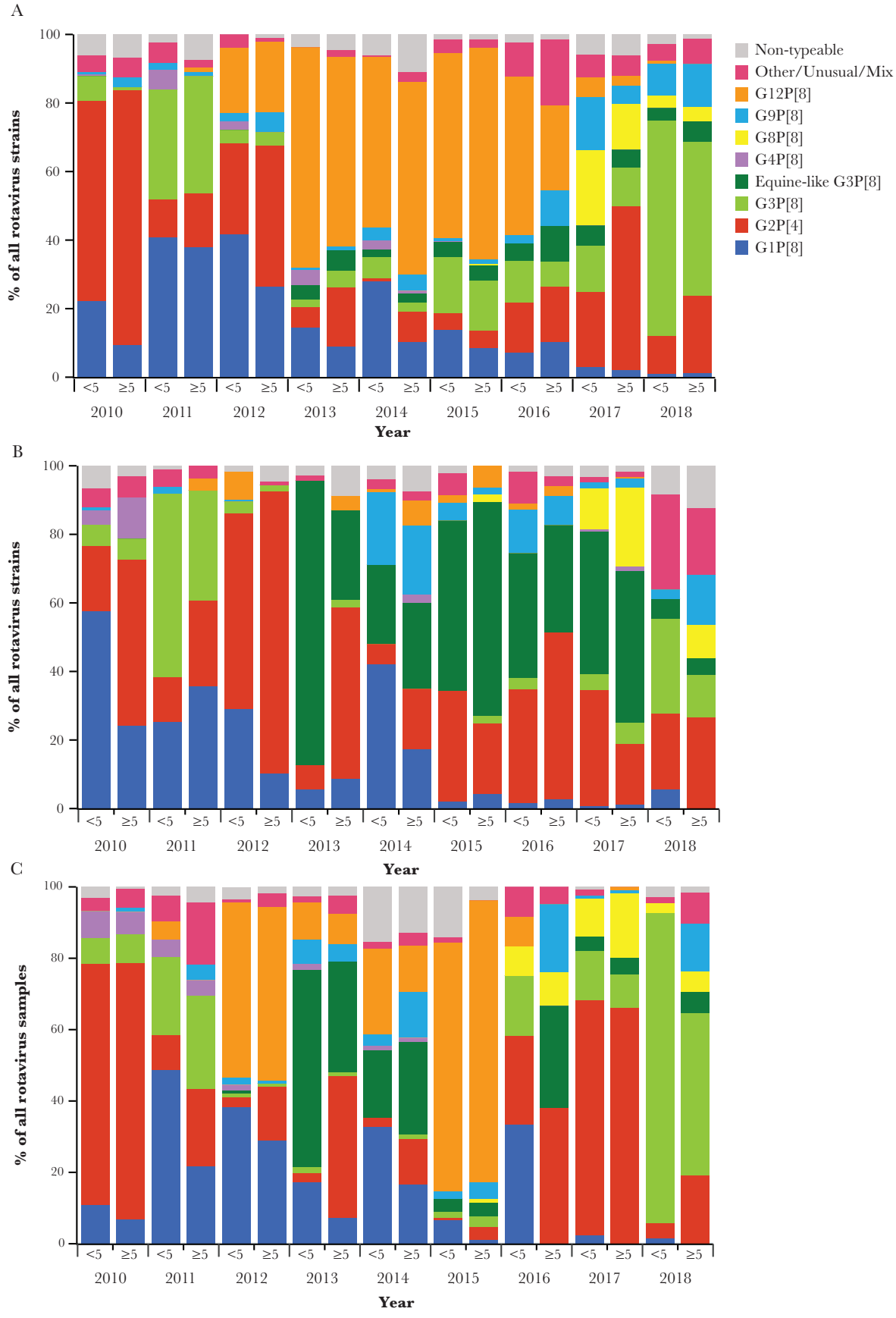

Figure 5. Comparison of the genotype distribution 2010–2018 in children <5 years of age compared with the population ≥5 years of age in (a) RotaTeq states, (b) Rotarix states and territories, and (c) Western Australia. Data are presented as the proportion (%) of a specific genotype compared with the total samples collected within the age category.

G3P[8] codominant) and 2014 (equine-like G3P[8] and G9P[8] codominant). Genotype dominance was more variable in the <5 population; changing annually to biannually (Figure 5b).

The genotype distribution in Western Australia was similar to what was observed in RotaTeq states, except for the increased circulation of equine-like G3P[8], a genotype more frequently detected in Rotarix states and territories (Figure 5c). G1P[8] were more commonly detected in the <5 age group (19.5%) compared to the ≥5 age group (9.0%), whereas G2P[4] were more common in the ≥5 age group (36.9%) compared to the <5 age group (23.8%). In 5 of 9 years, the same genotype was dominant in the <5 and ≥5 age groups, due to G2P[4] in 2010 and 2017, G12P[8] in 2012 and 2015, and human G3P[8] in 2018. G1P[8] was dominant in the <5 age group in 2011, 2014, and 2016, whereas equine-like G3P[8] was dominant in 2013. In contrast, in the ≥5 age group G1P[8], G2P[4] and human G3P[8] were detected at similar rates in 2011, G2P[4] was dominant in 2013 and 2016, whereas equine-like G3P[8] was dominant in 2016.

DISCUSSION

This study spanning 9 years of surveillance in Australia describes rotavirus disease and genotype distribution in children ≥5 years and adults, highlighting substantial rotavirus infection in the population ≥5 years of age; particularly impacting children 5–9 years of age and the elderly.

Rotavirus vaccine coverage is high in Australia (~89.5%) [20]. Rotavirus vaccines have had a major impact on rotavirus hospitalizations in Australia with a 71% decline observed in children <5 years of age and reductions also observed in patients <20 years of age [21]. Several studies in Australia, Europe, Latin America, and the United States have identified an indirect protective effect impacting populations ineligible to have been vaccinated [21–28]. This is likely due to the reduced amount of rotavirus circulating in the community, limiting exposure, and subsequent infectious episodes. Although this may be beneficial in some circumstances, the decreased circulation of rotavirus may reduce repeated exposure that is thought to boost immunity and ensure ongoing protection against severe disease. A modest increase in rotavirus-coded hospitalizations among adults over 20 years of age has been subsequently reported in Australia after vaccine introduction, particularly in those aged 65 years or older [21]. Our study revealed a notable burden of rotavirus disease remains in children 5–9 years of age who were vaccine-eligible during infancy, suggestive of a waning of vaccine or natural immunity. The median age of rotavirus cases in New South Wales increased from 3.9 years in 2010 to 7.1 years in 2017. This shift towards older, previously vaccinated children is suggestive of waning protection [29]. In recent years, there have also been reports of a shift in rotavirus disease to older, unvaccinated children in Belgium, Finland, and the United States [30–33].

Despite the clear protective benefit afforded by vaccination, rotavirus disease has not disappeared. Several outbreaks were reported during this study, impacting the spectrum of age groups. Outbreaks due to G2P[4] strains were reported in 2010 in South Australia and Western Australia [34]. An outbreak caused by G2P[4] occurred in New South Wales in 2012, predominantly impacting children aged 5–9 years [35]. In 2017, multiple outbreaks were recorded, including outbreaks due to G2P[4] in the Northern Territory, South Australia, and Western Australia, equine-like G3P[8] in New South Wales, and G8P[8] in New South Wales and Victoria [3]. Outbreaks due to G8P[8] strains have also been reported in adults in Singapore [36] as well as among vaccinated and unvaccinated children in Japan where rotavirus vaccination was effective against developing moderate and severe infections but did not protect against mild infections [37].

The Australian outbreaks in 2017 occurred in a variety of settings including childcare and elderly residential facilities, indicating that vaccine-eligible and -ineligible (due to age) groups are at risk of developing severe rotavirus infections, and that widespread outbreaks can still occur in the vaccine era. Rotavirus is a recognized cause of gastroenteritis outbreaks in aged-care facilities globally [38]. Expanding the rotavirus vaccination program to include the elderly has the potential to modify such outbreaks. A small phase I study demonstrated that RotaTeq was safe and immunogenic in the elderly, with an increase in serum anti-rotavirus immunoglobulin A levels observed after 1 dose. However, further evaluation of the potential of this vaccine in the elderly is required [39].

G2P[4] was a dominant genotype in all age groups investigated in this study, with the highest detection rate in the ≥85-year-old group. This age group also reported the lowest detection of G1P[8]. G2P[4] are also often reported as the dominant genotype in adults and the elderly in other locations [40–42]. In Finland, G2P[4] was dominant in the population >16 years of age in the vaccine era and G12P[8] also emerged as a dominant genotype [33, 43]. A prior study revealed differences in genotype distribution in Australia based on vaccine use in the population <5 year of age [4]. These differences were also observed in the population ≥5 years of age, with G12P[8] dominant in RotaTeq states, whereas G2P[4] and equine-like G3P[8] were dominant in Rotarix states and territories. This highlights that the diversity of rotavirus circulating in the population <5 years of age likely impacts the diversity observed in the older population. Changes in genotype distribution after vaccine introduction have been reported elsewhere, with G2P[4] emerging in Brazil after Rotarix introduction and G12P[8] emerging in the United States [44, 45]. Equine-like G3P[8] has also emerged in the vaccine era, detected in countries with and without rotavirus vaccines [3, 43, 46].

In this study, vaccine-like strains were detected in children too old to have recently received a rotavirus vaccine and in

individuals too old to have ever been vaccinated. It is not known whether these patients had recent contact with a vaccinated infant; however, it is consistent with transmission of the vaccine strain from a vaccinated infant to an older sibling or family contact. There are several reports of horizontal transmission of vaccine strains to both adult and child contacts resulting in gastrointestinal symptoms [47–49]. Community transmission resulting in symptomatic infection has been reported in children with no known contact with vaccinated individuals [48, 50].

CONCLUSIONS

In conclusion, this study highlights that rotavirus disease occurs in the Australian population ≥5 years of age. Conventionally, children are considered the reservoir for strains causing adult infections, but, equally, older children and adults could potentially serve as a reservoir maintaining strains in the population that may transmit to younger children. Despite the success of the vaccination program in decreasing the burden of rotavirus disease, the occurrence of outbreaks in the vaccine era in both vaccinated and vaccine-ineligible populations, including the elderly, highlights that continued surveillance is required to understand the emergence and epidemiology of rotavirus strains, to ensure the continued success of vaccination programs.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Supplementary Figure 1. Number of samples that met the study inclusion criteria for each year (2010–2018) from children <5 years of age and the population ≥5 years of age.

Supplementary Figure 2. Age breakdown of samples analyzed by the Australian Rotavirus Surveillance Program from children <5 years of age and the population ≥5 years of age with rotavirus gastroenteritis in Australia 2010–2018.

Supplementary Figure 3. Comparison of the genotype distribution between children <5 years of age (vaccinated), children 5–12 years of age (potentially previously vaccinated), and the population ≥13 years of age (unvaccinated).

Supplementary Table 1. List of collaborating centers in the Australian Rotavirus Surveillance Program by State and Territory.

Supplementary Table 2. Breakdown of samples analyzed in the study by state and vaccine in use.

Supplementary Table 3. List of rare and unusual genotypes detected in children <5 and in older children and adults across Australia 2010–2018.

Supplementary Table 4. Detection of vaccine-like strains in individuals ≥12 months of age.

Notes

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Author contributions. C. M. D. performed the literature search and data analysis and interpretation, contributed to study design, and wrote the first draft of the manuscript. S. R.-F. coordinated the Australian Rotavirus Surveillance Program 2010–2018, collecting samples and conducting experiments. S. R.-F. also contributed to study design. C. D. K., G. L. B., and J. E. B. designed and directed the study. These authors provided conceptual and technical guidance for all aspects of the project including data interpretation and revision of the manuscript.

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Australian Rotavirus Surveillance Group. Between 2010 and 2018, the Australian Rotavirus Surveillance Group included the following: P. Adamopolous, R. Alexander, R. Baird, C. Bletchly, S. Bradbury, J. Buttery, D. Coleman, H. Cook, N. Cooper, L. Dang, K. Delves, P. Derrington, R. Enbom, M. Finger,

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