Concomitant marked decline in prevalence of SARS-CoV-2 and other respiratory viruses among symptomatic patients following public health interventions in Australia: data from St Vincent's Hospital and associated screening clinics, Sydney, NSW.

Deborah Marriott[1], Rohan Beresford[2] Feras Mirdad[1], Damien Stark[1], Allan Glanville[1], Scott Chapman[1], Jock Harkness[1] Gregory J. Dore[1,3,] David Andresen[1*], Gail V. Matthews[1,3*]

[1]*St Vincent's Hospital, Sydney, Australia,* [2]*Concord Hospital, Sydney, Australia,* [3]*Kirby Institute, University of New South Wales Sydney, Sydney, Australia*

*joint senior author

Corresponding Author:

Gail V Matthews

The Kirby Institute, UNSW Sydney NSW 2052 Australia

E-mail: gmatthews@kirby.unsw.edu.au

Abstract:

Our Australian hospital tested almost 22,000 symptomatic people over 11 weeks for SARS-CoV-2 in a multiplex PCR assay. Following travel bans and physical distancing, SARS-CoV-2 and other respiratory viruses diagnoses fell dramatically. Increasing rhinovirus diagnoses as social control measures were relaxed may indirectly indicate an elevated risk of COVID-19 resurgence

Key words: COVID-19, SARS CoV-2, influenza, screening, public health

Introduction:

The severe acute respiratory syndrome novel coronavirus (SARS-CoV-2) pandemic and resulting coronavirus disease (COVID-19) burden has been the major global health issue of this century. Enhanced understanding of transmission patterns and the potential impact of respiratory viral co-infection are critical for prevention and management of this disease.

The first Australian case of SARS-CoV-2 infection was diagnosed on 25th January 2020, in a traveller returning from Wuhan, China with the first locally acquired case reported on 2nd March. Contact tracing with isolation, and a ban on nationals entering Australia from high risk countries (China, South Korea, Italy), were implemented between 1st February and 11th March. Subsequent measures included 14-day self-quarantine for all returning travellers (15th March), closure of borders to non-residents (19th March), physical distancing recommendations (21st March), closure of gathering places (23rd March), and stage 3 "stay at home" isolation requirements (29th March). The number of Australian SARS-CoV-2 diagnoses increased rapidly to a peak of 460 daily cases on 28th March, before declining to fewer than less than ten per day by mid-April. Stage 3 requirements were relaxed by the end of April and by mid-May restaurants and businesses had largely re-opened. By 14th May a total of 6,989 COVID-19 cases had been diagnosed, with almost half in New South Wales (NSW).[6]

A screening service for SARS-CoV-2, using a multiplex PCR assay was established on 9th March at St. Vincent's Hospital, a University-affiliated hospital in inner-Sydney, NSW. Two community satellite testing services were opened in April. We report the prevalence of SARS-CoV-2 and other respiratory pathogens including co-infection, and evaluate the

temporal pattern of respiratory infections alongside the introduction, and subsequent relaxation, of physical distancing measures.

Methods:

Nasopharyngeal (NP) swabs were collected by trained nurses using appropriate infection control measures at the dedicated COVID-19 clinic at St Vincent's Hospital and satellite clinics at Bondi Beach and East Sydney. Testing was performed in the hospital Emergency Department (ED) when clinically indicated. A small proportion of specimens were referred from other sites such as rural laboratories, correctional facilities and general practitioners.

Testing was carried out in accordance with NSW Health policy during the study period. Initially, testing was offered to individuals with respiratory symptoms who had returned from overseas, had severe respiratory illness, had been in contact with a known COVID-19 case, or had healthcare employment. These criteria were subsequently expanded to include anyone with fever or respiratory symptoms in local 'hot spots' (30th March 2020), defined geographical areas of Sydney (14th April 2020), and subsequently in all areas of NSW (from 23rd April 2020).

Laboratory testing was performed using the EasyScreen ™ Respiratory Detection kit[7] (Genetic Signatures , Sydney, Australia), and the EasyScreen™ SARS-CoV-2 Detection kit. This included targets for SARS-CoV-2, influenza A and B, parainfluenza 1 - 4, respiratory syncytial virus (RSV) A and B, rhinovirus, enterovirus, coronaviruses HKU-1, 229E, NL63, and OC43, human metapneumovirus (hMPV), adenovirus, *Mycoplasma pneumoniae*, *Bordetella pertussis* and *Pneumocystis jirovecii*. Nucleic acid extraction utilised EasyScreen

™ Sample processing kits on an automated GS1 platform. Duplicate and subsequent samples were excluded.

Results:

Over the eleven-week period from 12th March to 27th May 2020, 21,808 people were tested. 52% were female and the median age was 42 years (interquartile range 30-57 years). The weekly number of tests varied from 1025 to 2586. Increased testing followed the opening of community clinics and broadening of NSW testing criteria (Figure). Overall, 175 (0.8%) people were positive for SARS-CoV-2. The proportion of patients with SARS-CoV-2 reached a peak of 3.7% in the third week of testing (26th March – 1st April). There was only one positive test in each of the last three testing weeks.

Of 2,293 (10.5%) people who tested positive for any respiratory pathogen, the most common endemic viruses detected included rhinovirus (n=1449, 63.2%), parainfluenza viruses (n=171, 7.5%), RSV (n=145, 6.3%), other coronaviruses (n=91, 4.0%), and influenza A/B (n=71, 3.1%). Eight (5%) of SARS-CoV-2 positive swabs were also positive for another respiratory pathogen including one parainfluenza virus type 4, five rhinovirus, and two with RSV. There were no cases of co-detection of SARS-CoV-2 and other coronaviruses or influenza viruses.

The proportion of people in whom any respiratory pathogen was detected declined markedly during the study period, from 32.5% in week one to 3.1% in week eight before rising again to 12.9% in week 11 (Figure) ($p<0.001$ for each subsequent week, compared to baseline, in a two-sample test of proportions). In most cases a greater than 10-fold reduction was observed: rhinovirus, 19.9% to 1.7% (before increasing again to 11.8% by late-May); parainfluenza,

3.0% to 0.1%; and non-SARS-COV-2 coronaviruses, 2.3% to less than 0.1%. Of note, non-viral respiratory pathogens such as *Bordetella pertussis, Mycoplasma pneumoniae* and *Pneumocystis jiroveci* did not demonstrate marked reduction. (Supplementary Table).

Discussion:

At a major hospital serving the initial geographical epicentre of Australian SARS-CoV-2 diagnoses, 175 cases were identified over an 11-week period. Despite the broadening of testing criteria, an increase in total testing numbers, and a move into cooler months, SARS-CoV-2 positive cases fell from a peak of 55 in week two (3.6% of tests positive), to one case in each of weeks nine to eleven. The decline in SARS-CoV-2 positive cases was consistent with Australian national trends, and probably reflected the success of the enhanced public health COVID-19 prevention measures. The prevalence of other respiratory viral pathogens also declined significantly, indicating that public health measures for SARS-CoV-2 had wider infection transmission consequences. The rise of rhinovirus in latter weeks of testing probably reflects loosening of physical distancing measures at that time. Failure of SARS CoV-2 cases to similarly rise supports the absence of circulating SARS CoV-2 in the NSW community during that period, but the increased rhinovirus transmission does raise concern that SARS CoV-2 may also spread readily if reintroduced.

SARS-CoV-2 detection by multiplexed PCR including other major respiratory pathogens is unusual in Australian laboratories. As such, our data provide unique insights into the spectrum and effect of public health measures on other respiratory illnesses. The dramatic decline in prevalence of any respiratory pathogen, from over 32% of samples positive in week one to 3-4% two months later demonstrates the impact of these COVID-19 measures on

infection transmission more broadly. A reduction in the absolute weekly numbers of most infections, as well as the proportion of tests positive, indicates that this reduction was not simply due to an inflated denominator related to increased testing. Influenza surveillance data from our Local Health District for March-April 2019[8] also suggest that influenza rates are about 10-fold lower than historically observed. Data from Taiwan have shown near-elimination of influenza circulation during COVID-19 control measures,[9] whereas a Singaporean report[10] showed a 76% reduction over historical rates. To our knowledge, ours is the first report from the Southern hemisphere demonstrating a reduction during a move into the cooler months, and also the first to document simultaneous trends in other infectious respiratory pathogens.

Among individuals with SARS-CoV-2, 5% had co-infection with other respiratory pathogens, with rhinovirus most common. Limited data have been reported on co-infection between SARS-CoV-2 and other respiratory viruses. In a Seattle surveillance study,[11] 4 of 25 people (16%) with SARS-CoV-2 had rhinovirus coinfections. Interestingly, in that study (as in ours) no coinfections between SARS-CoV-2 and non-pandemic coronaviruses were found. This raises the hypothesis that co-exposure to different human coronaviruses may lead to only one establishing infection, or that shared viral epitopes lead to some degree of cross-immunity within the coronavirus group. A Californian report,[12] however, has shown occasional coinfections between SARS-CoV-2 and non-pandemic coronaviruses.

There are some key limitations of our study. Firstly, during the eleven-week period the SARS-CoV-2 testing criteria changed, with broadened testing initially in local geographical "hotspots" then our entire catchment area. However, guidance was consistent that only people with fever or other respiratory tract symptoms should be tested. Secondly, detailed data on

the timing of testing in relation to symptom onset were not available. In general, however, most people were tested within a few days of symptom onset, when SARS-CoV-2 should have remained detectable. Thirdly, we are unable to determine which SARS-CoV-2 prevention measures had the greatest impact on respiratory virus prevalence, as they were introduced in rapid succession. It is also unclear how much impact a shift in SARS-CoV-2 cases from largely returned overseas travellers (predominantly from North America and Europe) to locally acquired cases had on temporal trends in respiratory viral pathogen prevalence. Higher prevalence of all respiratory viral pathogens would have been expected among returned travellers from the Northern Hemisphere late in the Northern winter, and these may have reduced naturally over time even without local COVID-19 prevention measures. Our study period is too short however to assess any seasonal trends.

In conclusion, the introduction of multiple public health measures to minimise SARS-CoV-2 transmission in Australia from mid to late-March 2020 had a major impact on the prevalence of all respiratory viral infections highlighting the effectiveness of this approach. Changes in the prevalence of circulating respiratory viruses may provide a useful reflection of the success of ongoing measures including physical distancing restrictions.

Potential Conflicts of Interest

GM reports grants from Abbvie and Gilead Sciences, outside the submitted work. GD reports grants, advisory board fees, and travel support from Gilead, Abbvie, and Merck; and consulting and speaker fees from Gilead and Merck, outside the submitted work.

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Figure Legend:

Title: Changes in social restrictions, testing policy, and respiratory pathogen detection 12th March-27th May 2020

X axis: Calendar time period

Primary y axis: Number of nasopharyngeal swabs positive for respiratory pathogen

Secondary y axis: Number of nasopharyngeal swabs performed on unique patients

"Nonviral" includes *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Pneumocystis jirovecii*

"Other viral" includes adenoviruses, enteroviruses, respiratory syncytial virus, and human metapneumovirus

Figure 1