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REVIEW

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Maintaining mask momentum in transplant recipients

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The widespread use of facemasks has been a crucial element in the control of the SARS-CoV-2 pandemic. With mounting evidence for mask efficacy against respiratory infectious diseases and greater acceptability of this intervention, it is proposed that masking should continue after the pandemic has abated to protect some of our most vulnerable patients, recipients of stem cell and solid organ transplants. This may involve not only masking these high-risk patients, but possibly their close contacts and the healthcare workers involved in their care. We review the evidence for mask efficacy in prevention of respiratory viruses other than SARS-CoV-2 and address the burden of disease in transplant recipients. Although we acknowledge that there are limited data on masking to prevent infection in transplant recipients, we propose a framework for the study and implementation of routine masking as a part of infection prevention interventions after transplantation.

KEYWORDS
bone marrow transplant, COVID-19, masks, respiratory virus, SARS-CoV-2, solid organ transplant, stem cell transplant

1 | INTRODUCTION

The use of facemasks is a simple and inexpensive intervention that decreases spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1–3] and other respiratory virus infections (RVIs). Hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) recipients experience a significant burden of disease due to these pathogens, constituting a major risk to their health. Prior studies have been either favorable or inconclusive regarding the efficacy of masking to prevent RVIs, but the recent experience with COVID-19 has dramatically changed both the evidence base for and the acceptability of the intervention. Further, prior lack of acceptance of masking may have contributed to inadequate adherence and therefore, an inability to demonstrate efficacy in past studies. We address studies and recommendations regarding masking of these populations and of healthcare workers (HCWs) who care for them.

Given the renewed appreciation of the efficacy of masking and its increased acceptability, we believe it is prudent now to incorporate masking into care protocols during high-risk periods after HSCT and SOT. We propose that this should be done going forward regardless of COVID-19 incidence, although of course if there continues to be COVID-19 infection in communities that would be extra impetus to continue masking in such high-risk individuals. We urge the development of careful studies to evaluate the optimal approach to masking for prevention of RVIs after transplantation, but we suggest that care protocols should be adjusted now and need not await the results of future studies.

2 | MASKING EFFICACY AGAINST RESPIRATORY VIRUSES OTHER THAN SARS-COV-2

Most RVIs in transplant recipients are transmitted by droplets or aerosols, including respiratory syncytial virus (RSV), adenovirus, influenza, parainfluenza, human metapneumovirus (hMPV), and rhinovirus.[4,5] As per the Centers for Disease Control and Prevention guideline[6] (sections I.B.3.b, III.B.2., and Appendix A), HCWs caring for inpatients with these RVIs are recommended to wear surgical masks (as defined by the United States Food and Drug Administration[7]) as part of droplet precautions, with the exception of hMPV. Masking of infected patients is also important for source control, as studies have shown that surgical masks decrease droplet and aerosol spread

TABLE 1 Selected results on the impact of community interventions (which included masking in addition to various distancing or isolation practices) for COVID-19 on other infections

Organism	Country/Countries	Intervention period	Comparison period	Result	Reference
Adenovirus	New Zealand	May 2020-Sep 2020	2015–2019	81.4% reduction	30
Adenovirus	USA (Northern California)	Mar 25, 2020-Jul 31, 2020	Aug 1, 2019-Mar 24, 2020	77% reduction	31
hMPV	New Zealand	May 2020-Sep 2020	2015–2019	92.2% reduction	30
Influenza	New Zealand	May 2020-Sep 2020	2015-2019	99.9% reduction	30
Influenza	USA (Northern California)	Mar 25, 2020-Jul 31, 2020	Aug 1 2019-Mar 24, 2020	93% reduction	31
Influenza	Taiwan	Jan 2020-Sep 2020	Jan 2019-Sep 2019	85.4% reduction	32
Influenza	Australia, Chile, South Africa	April 2020-Jul 2020	Apr-Jul 2017–2019	99.8% reduction	33
Influenza	37 countries	week 40 2020–week 8 2021	2014/15–2019/20	99.4% reduction	34
Parainfluenza	USA (Northern California)	Mar 25, 2020-Jul 31, 2020	Aug 1 2019-Mar 24, 2020	91% reduction	31
Parainfluenza	New Zealand	May 2020-Sep 2020	2015–2019	80.1% reduction	30
RSV	New Zealand	May 2020-Sep 2020	2015–2019	98.0% reduction	30
RSV	USA (Northern California)	Mar 25, 2020-Jul 31, 2020	Aug 1 2019-Mar 24, 2020	67% reduction	31
S. pneumoniae	26 countries	Jan 1 2020-May 31,2020	2018–2019	82% reduction	35
S. pneumoniae	Taiwan	Jan 2020-Sep 2020	Jan 2019-Sep 2019	44.4% reduction	32

Abbreviations: hMPV, human metapneumovirus; RSV, respiratory syncytial virus; *S. pneumoniae*, *Streptococcus pneumoniae*.

and can reduce shedding of detectable virus,[1,8] even when there is expiratory airflow leakage around the edges of the mask.[9]

The preponderance of evidence before the SARS-CoV-2 pandemic suggests that masks decrease spread of RVIs, including a recent meta-analysis of 21 studies which estimated that mask use by HCWs may reduce transmission by 80%, and mask use in the community may reduce transmission by 47%.[10] However, other meta-analyses have noted that data quality is limited by potential bias, variable outcomes, and poor compliance with studied interventions.[11]

Community mitigation measures during the COVID-19 pandemic have generally included masking, which has essentially created large-scale experiments on the efficacy of this intervention in preventing droplet-borne infections. Institution of these measures has been shown to be effective in many countries and for many organisms (Table 1). Although the impact of masking alone cannot be determined from these results, it has been a consistent component in all interventions which have had a major impact on RVI transmission.

3 | BURDEN OF DISEASE OF MASK-PREVENTABLE VIRUSES IN TRANSPLANT RECIPIENTS

HSCT and SOT patients are at high risk for RVIs, particularly during the first 6 months after transplantation. In the immunocompetent population, RVIs are typically self-limited, although not without morbidity (e.g., RSV in neonates and infants) or mortality (e.g., influenza). Treatment is generally supportive, with the exception of neuraminidase inhibitors for influenza. However, RVIs result in greater morbidity and mortality in the immunocompromised host (Table 2).

Due to this significant burden of disease, a number of treatment modalities have been explored in HSCT or SOT recipients but are often not recommended due to low efficacy, toxicity, or cost. For example, cidofovir may be given for treatment of adenovirus but supportive data are lacking.[12,13] Ribavirin and intravenous immunoglobulin have unclear benefit in treating other respiratory viruses, and palivizumab has demonstrated benefit only as prophylaxis against RSV in high-risk neonates.[4,5,14]

Another approach to the burden of RVIs in HSCT and SOT recipients is vaccination. Studies have shown that HSCT and SOT recipients typically respond poorly to vaccination[15,16] and often shed RVIs for prolonged periods if infected. These make masking of the uninfected transplant patient attractive to prevent acquisition in the setting of impaired immunity, and also favor masking of the infected transplant recipient to control community transmission and nosocomial spread.

4 | CURRENT GUIDELINES AND PRACTICE OF MASKING AMONG HSCT RECIPIENTS

The 2009 guideline for safe living after HSCT[17] recommends that others with upper respiratory infections (URIs) who are in close contact

TABLE 2 Seasonality, clinical syndromes, incidence, and mortality of selected respiratory viral infections. Ranges from the sources cites are approximate and/or inferred

		HSCT and hematologic malignancies			SOT		
Virus	Seasonality	Clinical syndrome(s)	Incidence[4]	Mortality[4]	Clinical syndrome(s)	Incidence	Mortality
Influenza	Winter to spring	LRTI	1.3%–40%	8%–28%	LRTI, allograft dysfunction	0%–13%[14]	3%–8%[5]
Parainfluenza	Year-round, some strains summer	URTI, LRTI	3%–27%	10%–50%	URTI, LRTI, lung allograft rejection, BOS	5%–16%[14]	<15%[36]
Respiratory syncytial virus	Autumn to spring	Pneumonitis	1%–50%	11%–47%	Pneumonitis, lung allograft rejection, BOS	6%–12% (lung)[36]	10%–20%[14]
Human metapneumovirus	Winter to spring	URTI, LRTI	2%–11%	6%–40%	URTI, LRTI, lung allograft dysfunction	4%–7%[14]	17%–32% (inferred)[14]
Adenovirus	Year-round	URTI, LRTI, enterocolitis, hepatitis, nephritis, hemorrhagic cystitis, meningoencephalitis	1%–30%	14%–73%	URTI, LRTI, enteritis, hepatitis, nephritis, hemorrhagic cystitis, orchitis, diffuse alveolar hemorrhage, BOS	3.5%–57%[12]	Case reports

Abbreviations: BOS, bronchiolitis obliterans syndrome.; HSCT, hematopoietic stem cell transplant; LRTI, lower respiratory tract infection; SOT, solid organ transplant; URTI, upper respiratory tract infection.

with HSCT recipients "consider wearing surgical masks," but that for masking of the HSCT recipients "the degree of protection…has not been determined." In the inpatient setting, HSCT infection control guidelines[18] make strong evidence-based recommendations for masking of HCWs in contact with HSCT recipients with URIs. The guidelines mention only in passing the possibility of universal masking, either during seasons of high RVI prevalence (Table 2) or year-round. More recent studies have shown that enhanced masking of HCWs and visitors in HSCT wards can decrease RVIs.[19,20]

In addition to RVI prevention, the 2009 guidelines also suggest without evidence that HSCT recipients wear masks to prevent fungal infections during contact with soil, plants, or construction,[17] or in the hospital during periods of construction.[18] However, to our knowledge, there is only one small randomized trial regarding the use of FFP2 masks (similar to N95) in allogeneic HSCT recipients to prevent aspergillosis,[21] which showed no benefit.

5 | CURRENT GUIDELINES AND PRACTICE OF MASKING AMONG SOT RECIPIENTS

Similar to the HSCT guideline, a 2019 SOT guideline suggests that during contact with individuals with URIs, "both the infected person and the transplant recipient should wear a standard surgical mask.[22]" Masking of SOT recipients was also suggested during exposure to fungal spores or animal waste.[22] However, outside of these situations, routine masking was not recommended.

To our knowledge, there are no studies evaluating benefits of masking in SOT populations or their HCWs, but some sites still recommend masking. A transplant center survey[23] found that some programs recommended masks for inpatients outside of hospital rooms and for outpatients outside of the hospital. However, practices varied by organ and time from transplantation, and most centers had no such policies. Not unexpectedly, given the information available and poor acceptability of masking at the time, one survey of lung transplant recipients showed poor mask uptake.[24]

6 | ACCEPTABILITY OF MASKING

It has been hypothesized that mask wearing may result in significant health and safety issues, such as hypoxemia, hypercapnia, acidemia, "self-contamination," tachycardia, and mood disorders,[25] although supporting data are scant. On the contrary, a meta-analysis suggests that the adverse effects of masking, including skin irritation, discomfort, inconvenience, and cost, are generally minor.[26] The COVID-19 pandemic has led to increased mask acceptance and has resulted in substantial self-reported[27] and observed[28] uptake. As COVID-19 will likely persist for years, mask-wearing is likely to gain further acceptance moving forward and may prove to be even more efficacious in transplant patients than previously demonstrated.

7 | MASK TYPE

It should be noted that most studies have primarily tested the use of a single surgical mask, which may have limited the ability to demonstrate efficacy. Emerging data suggest that other interventions (double

surgical masks, N95, KN95, or even surgical plus cloth masks[29]) may have higher efficacy. If tolerated and available, more protective masks would be preferable in the highest-risk periods after transplantation.

8 | CONCLUSIONS

Data from before the SARS-CoV-2 pandemic regarding efficacy of masking HSCT and SOT recipients are limited, and compliance with the intervention was low. As such, guidelines and care protocols often did not recommend routine masking. However, emerging data from the COVID-19 pandemic have provided strong evidence that routine masking protects against the spread of RVIs, which cause significant morbidity and mortality among HSCT and SOT recipients. In addition, the acceptability of masking has greatly increased during the pandemic and likely will remain high for years to come. Given the relatively low-cost, low-risk nature of masking and its many potential benefits, we propose the following:

1. Universal surgical masking (or more protective mask types) should be incorporated into HSCT and SOT protocols for at least 6 months after transplantation and after intensified immunosuppression. This should apply outside of the home, when in close contact with others, and during hospitalizations.
2. Universal masking by HCWs and visitors to inpatient wards which care for HSCT and SOT patients. This may be during seasons of highest RVI prevalence or year-round given the variable seasonality of different RVIs.
3. Randomized controlled trials to determine the benefit of universal masking of transplant recipients, including optimal timing and duration after transplantation (e.g., 6 vs. 12 months). Initial studies might focus on the highest-risk populations, for example, lung transplant recipients, allogeneic HSCT recipients, patients undergoing intensified immunosuppression for rejection or graft-versus-host disease.
4. Formal studies to address the comparative effectiveness of different mask interventions such as a single surgical mask versus other mask types (double-masking, N95, KN95, etc.)

CONFLICT OF INTEREST

The authors declare no conflict of interest

AUTHOR CONTRIBUTIONS

All authors contributed to the drafting, review, and final approval of this manuscript.

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