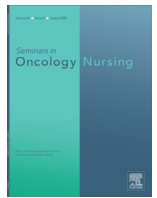




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## Perceptions and Experiences of Hematopoietic Cell Transplantation Patients During the COVID-19 Pandemic

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### ABSTRACT

**Objectives:** Since March 2020, the severe acute respiratory syndrome coronavirus-2 pandemic has affected the global community, but poses unique challenges for individuals with cancer. Patients diagnosed with hematologic malignancies undergo aggressive therapies followed by hematopoietic cell transplantation (HCT) as a potential curative treatment. HCT recipients can be immunocompromised for extended periods of time, and even pre-pandemic, transplant patients reported depression and anxiety due to restrictions and infection prevention measures they had to adhere to as part of transplant precautions. This study aimed to understand psychological distress and capture perspectives on coping strategies and access to healthcare in the HCT population during the COVID-19 pandemic.

**Data Sources:** Adult patients who received a transplant or were awaiting transplant and had a scheduled appointment at the transplant clinic were eligible to participate in this cross-sectional study. Participants completed an online survey that included questionnaires, clinical data and demographic information.

**Conclusion:** Fifty-four participants completed the survey. HCT participants reported relatively high psychological distress during the initial phase of the COVID-19 pandemic, but indicated use of healthy coping mechanisms to deal with stress.

**Implication for Nursing Practice:** Study data informs healthcare providers that psychological distress and mental health warrants increased attention during periods of heightened stress. Education and resources on healthy, beneficial coping strategies should be provided to support HCT patients. Nurses and advanced nurse practitioners are well poised to interact with HCT patients and provide necessary support or appropriate referral during routine clinical interactions, preparing patients for prolonged effects of the pandemic and similar future events.

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### Background

In the midst of March 2020, the World Health Organization (WHO) declared the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) a public health emergency.<sup>1</sup> As of October 2021, there were over 240 million coronavirus cases and close to 5 million deaths globally, with over 92 million cases and nearly 2 million deaths within the United States alone.<sup>2</sup> SARS-CoV-2 belongs to the coronavirus

family of viruses and varies in its severity from mild symptoms to severe complications such as severe acute respiratory distress syndrome, acute renal failure, septic shock and severe pneumonia.<sup>1,3</sup>

The pandemic has affected the livelihood and well-being of the global community; however, it is vital to acknowledge that certain populations such as the elderly, individuals with comorbidities, and immunocompromised individuals are at increased risk of and more susceptible to the disease.<sup>4</sup> Patients with cancer are usually immunocompromised either due to their diagnosis or corresponding treatment and are at an increased risk of infection compared to the general population. A position statement from the American Society of Clinical Oncology (ASCO) on the pandemic states that cancer patients are at a risk of increased mortality if infected with

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coronavirus disease-2019 (COVID-19) when compared to those without cancer.<sup>5</sup> When compared to those without blood cancers, patients diagnosed with hematologic malignancies report increased severity of COVID-19 and a higher mortality rate.<sup>6,7</sup>

For patients with a hematologic malignancy (e.g. multiple myeloma, leukemia, lymphoma), hematopoietic cell transplantation (HCT) is a potentially curative treatment. Approximately 22,000 HCTs are performed annually in the US,<sup>8</sup> with its use and indications continuing to increase. During the process of HCT, these patients receive aggressive therapies, whereby following transplant they can be immunocompromised for extended periods of time, increasing their risk for contracting infections due to immunosuppressive regimens and transplant related complications.<sup>9</sup> In addition to this, psychological distress can have a significant negative impact on health outcomes, recovery, and function in HCT patients, leading to mortality and other severe transplant related effects.<sup>10</sup> HCT patients experience depression, anxiety and stress throughout the HCT process. Even prior to COVID-19, transplant patients reported experiencing depression and anxiety due to restrictions and infection prevention measures that they had to adhere to in preventing opportunistic infections and post-transplant complications.<sup>11</sup> Ongoing distress during the transplant process increases their risk for mortality.<sup>12</sup> Patients use various strategies to deal with stress and certain coping strategies (e.g., resignation), are associated with depression and anxiety pre-HCT.<sup>12</sup>

In general, the pandemic led to changes in access to healthcare and a rapid uptake of telemedicine in various clinical settings and populations including cancer patients.<sup>13</sup> The American Society for Transplantation and Cellular Therapy also provided guidelines stating that visits that are not critical should be either deferred or substituted with telemedicine as appropriate.<sup>14</sup> It is important to understand HCT patient's experience with access to healthcare, especially since these patients are seen frequently in the transplant clinic for their routine, scheduled visits in the acute phase of transplant (first 100 days of transplant), periodically for long-term follow up appointments, and as needed for transplant related complications.

Due to the extended nature of the recovery process, caregivers play a significant role through the transplant process. Since the pandemic led to public and health system restrictions, it is important to determine if HCT recipients have experienced barriers with caregiver support and challenges with following preventative recommendations such as social distancing and wearing masks.

Recent studies have reported on the clinical consequences and outcomes of COVID-19 on HCT patients<sup>15,16</sup> and the impact of COVID-19 on HCT centers; however, to our knowledge, there are no studies that have reported on patient reported experiences during the pandemic. Given the unique challenges faced by the HCT population during the COVID-19 pandemic, it is important to understand experiences and perspectives of this patient population. This descriptive study in HCT patients was designed to determine levels of distress, anxiety, and depression; capture perspectives on coping strategies; and understand patient experiences with access to healthcare and resources during the COVID-19 pandemic.

## Methods

### Study Design

This pilot study employed a descriptive, cross-sectional study design using a convenience sample of HCT eligible patients or HCT recipients. This study was conducted using online surveys on the Qualtrics platform.

### Setting and Participants

HCT patients were recruited from the Cellular Immunotherapies and Transplant (CIT) program at a large mid-Atlantic research

university. Adult patients  $\geq 18$  years of age and who have received a transplant or are awaiting transplant and were scheduled to be seen in the clinic (in person or via telehealth) were eligible to participate in the study.

### Recruitment Procedures

The study was approved by the university's Institutional Review Board. Participants were recruited from May 2020 through October 2020. The study team sent potential participants an invitation to participate in the study with a link to the survey. The study link sent via email provided a description of the study and gave patients the opportunity to provide consent for the study.

### Measures

Demographic data included race, ethnicity, gender, household income, education status, marital status, work status and age. Clinical data included hematologic diagnosis, type of transplant and time since transplant. Patient reported data was collected using the following measures a) Patient Reported Outcomes Measurement Information System (PROMIS) - Anxiety b) PROMIS- Depression c) Brief Coping Orientation to Problems Experienced (COPE) inventory d) Daily Inventory of Stressful Events (DISE), and e) Distress thermometer. Data reported is based on 46 survey questions. Participants had the option to complete the survey over several sessions, so the exact time to completion is unknown.

#### PROMIS anxiety

The PROMIS anxiety was used to measure anxiety and features eight statements associated with anxiety, with each response on a Likert scale from 0-5: 0 being 'never' and 5 being 'always'. This measure has been widely used and has demonstrated high reliability and consistent psychometric properties with a Cronbach's alpha of 0.95.<sup>17</sup>

#### PROMIS depression

The PROMIS depression was used to measure depression and features eight statements associated with depression, with each response on a Likert scale from 0-5: 0 being never and 5 being always. This instrument has been widely used and is reliable and valid with a Cronbach's alpha of 0.95.<sup>17,18</sup>

#### Brief COPE

The Brief COPE questionnaire was used to assess coping strategies that were used by the participants. Eight different domains were assessed and each domain comprised of two questions rated on a 4-point Likert scale with total scores from 2-8 as a continuous variable (higher scores denoting more frequent use). The instrument has good construct, concurrent, and predictive validity in relation to emotional well-being and adjustment in different clinical populations including cancer patients.<sup>19-21</sup>

#### Daily Inventory of Stressful Events (DISE)

Participants were asked to appraise the extent to which COVID-19 pandemic as a stressor impacted certain aspects of their life on a 4-point scale from "none at all" to "a lot."<sup>22</sup> This measure was not used in its entirety for this study.

#### Distress thermometer (DT)

The Distress thermometer is a self-report measure to assess the level of distress patients may have experienced. The scale measures

distress on a scale from 0-10, with 0 being no distress and 10 being extreme distress. This is an extensively used and validated measure in cancer patients.<sup>23,24</sup> It has a problem list which is an inventory of issues that could have attributed to the distress experienced. The problem list was modified for purposes of this study wherein the patient answered “yes/no” to indicate the type of problem experienced since the pandemic.

#### Access to health care and resources

The survey had 4 questions related to changes in scheduled procedures and access to medical care, and the participants responded “yes/no” to indicate their experience. Two questions related to impact of pandemic on transportation and caregiver support were included on the survey, wherein participants responded on a 5-point scale from “strongly disagree” to “strongly agree”.

#### Telemedicine

HCT participants were asked questions about their televisit preferences, wherein participants responded on a 5-point scale from “very unlikely” to “very likely”.

#### Susceptibility and pandemic recommendations adherence

The survey included questions on the extent to which HCT participants were worried about family and self-susceptibility to COVID-19. The questions were rated on a 5-point scale from “not at all worried” to “extremely worried”.

#### Data Analysis

Descriptive statistics were run for all data to assess quality assurance and describe distributions. The survey and demographic data were descriptively analyzed (means/variances for continuous variables and frequencies/percentage for categorical variables).

## Results

#### Sample characteristics

Demographic information and clinical variables are presented in [Table 1](#). Sixty-six participants responded to the study survey, with 54 participants completing the entire survey and included in the descriptive analysis. The majority of the participants were white, unemployed, >60 years old, and had at least a baccalaureate degree. Diagnoses were categorized as lymphoid neoplasia [acute lymphoblastic leukemia (ALL), Non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma (HL), multiple myeloma (MM)] or myeloid neoplasia [acute myeloid leukemia (AML), chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML), myelofibrosis, myelodysplastic syndrome (MDS)]. There was an equal distribution of male and female participants.

#### PROMIS anxiety and depression

The mean for anxiety was 13.67 (SD 5.86) and 45% of participants stated that the pandemic contributed to their anxiety levels. The mean for depression score was 12.50 (SD 5.02), 37% of participants attributed their depression to be impacted by the pandemic ([Table 2](#)).

#### Brief COPE

The mean score of all domains in the Brief COPE scale are shown in [Table 2](#). Coping domains can be divided into two major categories: approach coping (active coping, positive reframing, planning, acceptance, emotional support, and seeking informational support) and

**Table 1**  
Characteristics of demographic and clinical variables

Variable	N (%)
<b>Diagnosis</b>	
Lymphoid neoplasia	29 (15)
Myeloid neoplasia	21 (39)
Multiple diagnosis	3 (5)
Other	1 (2)
<b>Treatment type</b>	
Autologous	23 (43)
Allogeneic	22 (41)
Awaiting Transplant	9 (16)
<b>Age</b>	
18-40	5 (9)
41-50	7 (13)
51-60	11 (20)
61-70	25 (46)
>70	6 (11)
<b>Gender</b>	
Female	28 (52)
Male	26 (48)
<b>Education</b>	
Bachelors or above	46 (85)
< Bachelors	7 (13)
Others	1 (2)
<b>Race</b>	
White	51 (94)
Others	3 (6)
<b>Ethnicity</b>	
Not of Hispanic, Latino or Spanish origin	52 (96)
No data	2 (4)
<b>Employment status</b>	
Unemployed	29 (54)
Employed - full time	13 (24)
Employed - On medical leave	8 (15)
Employed- part time	4 (7)

**Table 2**  
Characteristics of depression, anxiety and coping measures

	Mean	Std Dev
<b>PROMIS</b>		
Depression	12.5	5.02
Anxiety	13.67	5.86
<b>Brief COPE</b>		
Acceptance	7.13	1.33
Religion	5.15	2.4
Positive reframing	5.07	1.85
Planning	4.89	1.86
Emotional support	4.74	2.03
Self-distraction	4.69	1.78
Active coping	4.67	1.69
Humor	3.89	1.84
Instrumental support	3.63	1.86
Venting	3.22	1.27
Self-blame	2.61	0.96
Substance use	2.43	0.88
Denial	2.37	0.92
Behavioral disengagement	2.09	0.4

avoidant coping (denial, substance use, venting, behavioral disengagement, self-distraction and self-blame).<sup>25</sup> In the current study, patients endorsed utilizing acceptance, religion and positive reframing (approach coping) more often, and conversely endorsed utilizing substance use, denial and behavioral disengagement (avoidant coping) less frequently.

#### DISE-Stress Appraisal

Participants were asked to indicate the extent to which the pandemic impacted their health, future plans, daily routine, health of

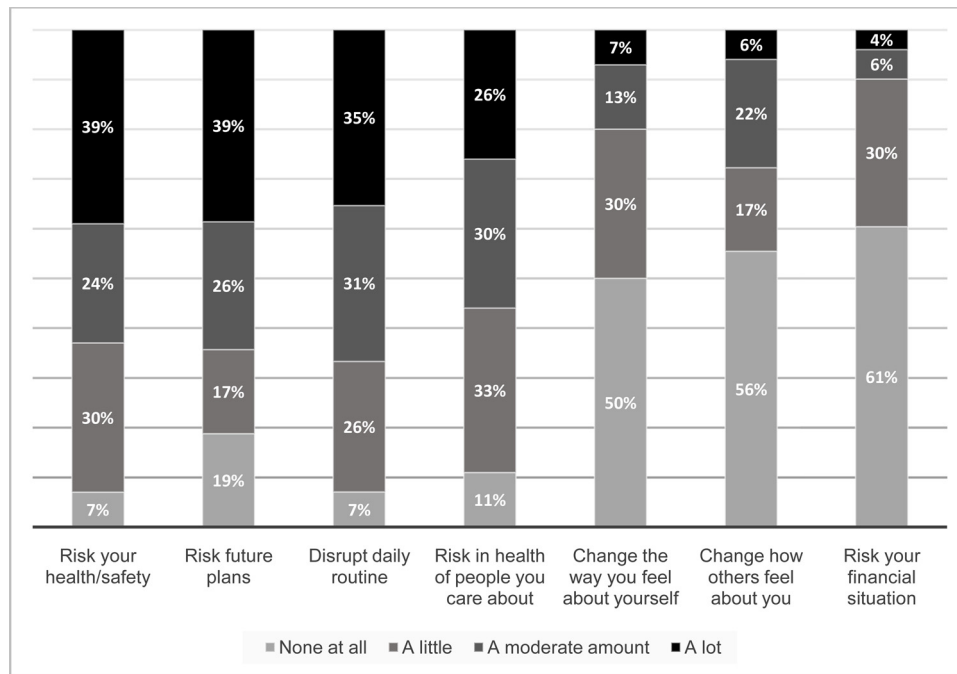


Figure 1. Appraisal of COVID-19 pandemic as a stressor

loved ones, and financial situation as well as others' perception about them. Approximately 40% of HCT participants stated that the pandemic significantly impacted their health and future plans, and 35% indicated that the pandemic disrupted their daily routine 'a lot'. The frequencies for the DISE-stress appraisal measure are presented in Figure 1.

Distress thermometer

The mean distress score in this study population was 3.22 (SD 2.49). Respondents indicated issues contributing to their distress under three main categories: practical problems, cognitive effects and social effects. Table 3 lists responses for all three categories. Eighty percent of the participants agreed that their 'ability to socialize' was a practical concern and 54% participants stated that 'ability to perform usual physical activity' was a physical concern attributing to their distress. Among cognitive effects, 56% and 48% of the participants agreed that 'worry' and 'fear' respectively contributed to their distress. 'Family health problems' was reported as a social issue contributing to distress by 35% of the participants. (Table 3) For the current cross-sectional study involving HCT patients at different points in their transplant process a clinical cut-off of 3 was considered since it is an optimal cut off score in adult cancer patients where DT scores significantly differ at different time points during the treatment trajectory.<sup>26</sup>

Access to healthcare and resources

The pandemic resulted in changes in access to healthcare with specific restrictions in place to address the spread of the COVID-19 infection.<sup>27</sup> Participant responses regarding access to healthcare and other resources such as transportation and caregiver support are summarized in Table 4. Twenty-eight percent of participants stated that they received less medical care (routine clinic visits or preventive care appointments) than usual; however, 98% of the participants stated that they were able to access medical care for a transplant-related complication. Eighteen percent of the participants had their medical procedures such as chemotherapy, surgery or stem cell

Table 3 Distribution of problems listed on the distress thermometer

	N (%)	
	Yes	No
Practical problems		
Child care	4 (7)	50 (93)
Housing	2 (4)	52 (96)
Insurance	4 (7)	50 (93)
Finances	7 (13)	47 (87)
Work/school	20 (37)	34 (63)
Treatment decisions	19 (35)	35 (65)
Ability to eat healthy	9 (17)	45 (83)
Dependable transportation	2 (4)	52 (96)
Ability to socialize	43 (80)	11 (20)
Ability to get your usual physical activity	29 (54)	25 (46)
Cognitive effects		
Depression	13 (24)	41 (76)
Fears	26 (48)	28 (52)
Nervousness	21 (39)	33 (61)
Sadness	15 (28)	39 (72)
Worry	30 (56)	24 (44)
Loss of interest in usual activities	11 (20)	43 (80)
Social effects		
Dealing with children	14 (26)	40 (74)
Dealing with partner	12 (22)	42 (78)
Family health issues	19 (35)	35 (65)

collection postponed; 13% had their medical procedures canceled. Approximately one-third of the participants agreed that they hesitated to go the medical provider due to fear of COVID-19. Only 6% of the participants experienced an impact on transportation for transplant-related care and visits. Less than 10% participants stated that the pandemic impacted the ability of their caregivers to provide the required support and care.

Telemedicine

During the initial phase of the pandemic, many healthcare settings transitioned to online models of care and established televisits

**Table 4**  
Access to Healthcare and Resources

	N (%)		N (%)				
	Yes	No	Strongly agree	Agree	Neutral	Disagree	Strongly Disagree
Medical procedure cancelled	7 (13)	47 (87)					
Medical procedure postponed	9 (17)	45 (83)					
Unable to access medical care for a BMT related complication	1 (2)	53 (98)					
Less medical care than usual	15 (28)	39 (72)					
Hesitated to go to a medical provider	7 (13)	12 (22)	6 (11)	13 (24)	16 (30)		
Impacted access to transportation	3 (6)	0 (0)	2 (4)	5 (9)	44 (81)		
Impacted ability of caregivers to provide care	1 (2)	3 (6)	7 (13)	13 (24)	30 (56)		

to incorporate necessary pandemic related preventative measures and to reduce exposure of individuals to the hospital setting. 83% of individuals were likely to participate in televisits with their provider during the pandemic and 67% were likely to participate even after the COVID-19 pandemic.

#### *Susceptibility and pandemic recommendation adherence*

Ninety-three percent of participants shared that they were worried (to varying extents) about getting sick with COVID-19 and 91% were worried about their family getting infected. Despite the worry, the majority of the participants (79%) agreed that as an HCT patient it was easy to follow recommended precautions such as social distancing, handwashing, staying away from sick individuals during the pandemic.

#### **Discussion**

In this descriptive, cross-sectional study conducted during the acute phase of the COVID-19 pandemic, HCT patients showed high distress levels secondary to inability to socialize and perform routine physical activity as well as concern about COVID-19 susceptibility. Respondents also reported that the pandemic had an impact on their stress and anxiety and that they primarily relied on approach-based coping styles. The data suggest that although the pandemic abruptly disrupted the healthcare system in general, most HCT participants were able to receive transplant-related care and caregiver support, with about one-third indicating disruptions to their routine medical care. Most participants also found it easy to follow COVID-19 restrictions and had a general willingness to continue participating in telehealth even following lifting of restrictions.

In patients with cancer, psychological distress results in poor treatment outcomes leading to poor QoL.<sup>28</sup> Physical activity and exercise are known to often serve as feasible and effective interventions for managing stress, anxiety and depression in cancer patients.<sup>29,30</sup> Results from our study align with this notion since participants reported increased levels of distress and also frequently cited an inability to do physical activities as one of the reasons contributing to their distress. Prior research has identified that early-phase transplant patients demonstrate clinically significant anxiety and depression, with the number of depressed patients increasing two-fold with just two weeks of preventive routine isolation.<sup>31,32</sup> Though the current study enrolled HCT participants in different phases of the transplant process, it is important to note that the pandemic resulted in increased isolation policies for many individuals - including HCT patients - which likely contributed to the increased anxiety and depression reported by the respondents.

Patients queried in the current study noted frequent use of approach-based coping strategies. Given that a lower level of symptom related distress is associated with the use of approach-focused coping strategies,<sup>33,34</sup> it is possible that they were experiencing fewer HCT

related symptoms at the time of the survey, though this was not explicitly assessed. Coping can also be dynamic across the disease continuum. In the initial phases, patients with cancer may draw from their existing coping strategies to manage distress and psychological well-being followed by the development of additional strategies to lead a meaningful life as they continue along their cancer trajectory.<sup>35</sup> Some of these respondents may have adapted strategies over time and identified enhanced ways to deal with the transplant process including remaining positive, maintaining normal life routines, finding acceptance, and engaging in religious coping.<sup>36,37</sup> Some of these strategies were identified in our study and may have resulted in enhanced coping amidst a pandemic compared to the general population.

Most HCT participants in the current study were able to receive care for any transplant-related condition, indicating that access to transplant care was not a concern for these participants. It is also important to acknowledge that technology has played a vital role in healthcare during the pandemic and positive experiences have been reported by oncologists and patients.<sup>38,39</sup> In addition to avoiding non-essential admissions to the hospital, telehealth has helped in providing psychological support for patients.<sup>27,40</sup> Respondents in our study shared their willingness to participate in televisits even after the pandemic, providing transplant providers with novel opportunities to provide intervention for supportive care and consultation services in the future.

Surprisingly, most HCT participants did not have any disruptions in caregiver support. It is possible that caregivers resided in the same household and therefore patients had easy access to their caregiver with no disruption due to the pandemic. Considering that participants were at different phases in their transplant process, caregiver support may have distinctively impacted patients who were undergoing transplant and hospitalized during the pandemic (course of the study) with additional guidelines and visitor restrictions in place, versus a long term HCT survivor.

During the pandemic, there were several recommendations and preventive measures that were in place to ensure public safety and impede the spread of the disease. As expected, most HCT participants in our study (about 80%) stated that it was easy to follow the suggested recommendations and measures as an HCT patient. This is likely secondary to the fact that HCT patients are accustomed to taking infection prevention measures even in the absence of the pandemic due to their immunocompromised status. This is similar to other research concluding that immunocompromised adults and adults with chronic diseases in general were more likely to adhere to recommended COVID-19 preventive behaviors, such as hand washing and maintaining social distance.<sup>41,42</sup>

#### **Limitations**

The study's findings are limited in several respects. First, this cross-sectional study represents a heterogeneous sample of HCT patients at various phases throughout the transplant process who

were recruited from a single transplant center, limiting the generalizability of the data. Response to recommendations and patients' perspectives may vary based on the regional policies and regulations that were in place. Second, since the study does not capture pre-pandemic transplant history or coping strategies and other assessments during respondents' transplant process, we are limited in our ability to infer impact of the pandemic alone. However, this study highlights experiences of this unique HCT population during the peak of the COVID-19 pandemic. Third, recruitment from a single site during the acute phase of the pandemic also resulted in a relatively small sample size.

### Implications for practice

Despite these limitations, this study provides valuable information regarding perceptions and experiences of HCT patients during the pandemic, suggesting that these data could provide additional insight into coping responses to a wide variety of stressors HCT patients may encounter. We have identified frequently reported factors affecting distress levels and frequently used coping strategies in HCT population. Future studies on identifying types of interventions and resources that HCT patients need to address distress in alignment with coping strategies would be an important next step.

### Conclusion

In sum, HCT patients reported experiencing relatively high levels of distress during the initial phase of the COVID-19 pandemic in 2020 but were also likely to use healthy, approach based coping methods to deal with this stress. This dynamic should be further explored with healthcare providers and patients together, both for use in future health emergencies but also to best help immunocompromised patients manage their stress, their mental health, and the current COVID-19 pandemic, of which the consequences are likely to persist with differential effects.

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### Declarations of Competing Interest

None

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