PCR218: Supplementary materials

Title: Content Validation of the Most Bothersome Symptom – Essential Tremor Questionnaire (MBS-ET): A Cognitive Debriefing Study

MBS-ET V1.0 – Overview of content

- Patient reported outcome (PRO) instrument designed for administration in electronic format
- Designed for use in adult populations with essential tremor (ET)
- Developed by Sage Therapeutics. Included concepts were based on the content of The Essential tremor Rating Assessment Scale (TETRAS)[1-3]
- 'Symptoms' module: Consists of tremor locations (head, voice, right arm/hand tremor, left arm/hand tremor, right leg/foot tremor, left leg/foot tremor, other)
- 'Activities of Daily Living (ADL)' module: Consists of tremor-related ADL impacts (eating, drinking, hygiene, dressing, pouring, using computer/smartphone, carrying items, writing, working, using keys, other)
- At baseline administration, respondents identify up to three symptoms and three ADLs that they find most bothersome, indicate the one symptom and ADL impact that is most bothersome and indicate the level of bother experienced
- Level of bother is assessed on a numeric response scale (NRS; 0-10 integers; with illustrative verbal anchors: 0 = 'Doesn't bother me at all', 5 = 'Bothers me sometimes', 10 = 'Bothers me all the time')
- At post-baseline assessments, respondents complete only the items assessing bother on their 1-3 most bothersome symptoms and 1-3 most bothersome ADLs indicated at baseline
- Most items use a recall period of 'the past 7 days', apart from item stems 2 & 5 (Most bothersome symptom/ADL) where no recall period was specified.

Methods

Institutional Review Board (IRB) approval statement:

- This study was reviewed and approved by the WIRB-Copernicus Group (WCG) IRB on 19th October 2022 (tracking number: 20225601), with subsequent amendments as detailed below:

- Amendment 1 (3rd November 2022): Study contact information revised
- Amendment 2 (2nd March 2023)/Amendment 3 (3rd April 2023): Unrelated to current poster
- Amendment 4 (31st May 2023): MBS-ET V1.1 approved
- Amendment 5 (12th July 2023): MBS-ET V1.2 approved

Table 1. Participant inclusion/exclusion criteria

Inclusion	Exclusion

• Aged 18-80 years
• Live in the US
• Fluent in spoken and written English
• Clinician confirmed diagnosis of essential tremor defined by the following criteria:
  ○ Isolated tremor syndrome consisting of bilateral upper limb action tremor, with or without tremor in other locations
  ○ At least 3 years duration
• Had a severity of tremor score of 2 (mild) 3 (moderate) or 4 (severe) on the Clinician Global Impression Scale – Severity of illness (CGI-S)
• Had a severity of activities of daily living score of 2 (mild problems), 3 (moderate problems), 4 (severe problems), or 5 (unable to do) on the Patient Global Impression of Severity - Activities of Daily Living (PGI-S ADL) at screening
• Absence of other neurological signs, such as dystonia, ataxia, or parkinsonism, isolated focal tremors (e.g., voice, head), task- and position-specific tremors, sudden tremor
	• Onset of tremor was associated with direct or indirect injury or trauma to the nervous system
	• Previous procedure for the treatment of essential tremor, deep brain stimulation, brain lesioning, or magnetic resonance (MR) guided procedure, e.g., MR-guided focused ultrasound
	• Individual had botulinum toxin for treatment of upper limb tremor within 6-months of screening
	• Historical or clinical evidence of tremor with psychogenic origin
	• Participant had currently active and medically significant or uncontrolled hepatic, renal, cardiovascular, pulmonary, gastrointestinal, hematological, immunologic and / or metabolic disease
	• Participant was currently undergoing treatment for oncologic disease at screening or is planned to commence treatment within the next 30-days, excluding skin cancers
	• Participant had a history of substance or

Inclusion	Exclusion
onset or evidence of stepwise deterioration of tremor • Willing and able to provide consent to take part in a 60-minute audio-recorded interview	alcohol dependence in the last 6-months • Was enrolled in a clinical trial at the time of recruitment • Previously enrolled in a clinical trial sponsored by Sage Therapeutics

Participant ID codes

IDs were allocated in chronological order as participants were consented (starting from P001). IDs contained participants PGI-S ADL score (MLD = 2 / Mild; MOD = 3 / Moderate; SEV = 4 / Severe).

Interview Process

- Participants completed a background questionnaire at the start of the interview. Interviews lasted approximately 60-minutes and included a concept elicitation section (first n=2 interviews only) followed by the cognitive debriefing of the MBS-ET (and one other PRO instrument). The current poster summarises the cognitive debriefing of the MBS-ET only
- Cognitive debriefing interviews followed a structured interview guide. Participants completed the MBS-ET using a 'think-aloud' technique
- Interviews assessed participant comprehension of the instructions, item wording, response options and recall periods utilised
- The patient-relevance of included concepts was evaluated
- Feedback on conceptual comprehensiveness and responder burden (i.e., length) or the MBS-ET was also obtained

Results

Table 2. Sample demographic characteristics for the MBS-ET cognitive debriefing interviews

Demographic Characteristic	R1 (n=4)	R2 (n=2)	R3 (n=4)	Total (N=10)
		Mean (range)		
Age (years)	57.2 (38-68)	59.5 (46-73)	64.5 (54-69)	60.4 (38-73)
		Median		
	62	59.5	67.5	67.5
		N (%)		
Age				
≤65 years	2(50)	1(50)	1(25)	4(40)
66-80 years	2(50)	1(50)	3(75)	6(60)
Sex				
Male	3 (75)	-	2 (50)	5 (50)
Female	1 (25)	2 (100)	2 (50)	5 (50)
Transgender				
No	4 (100)	2 (100)	4 (100)	10 (100)
Race				
White	3 (75)	1 (50)	3 (75)	7 (70)
Black or African American	1 (25)	-	1 (25)	2 (20)
Ethnicity				
Hispanic/Latino	-	1 (50)	-	1 (10)
Highest level of education				
College or university degree	3 (75)	2 (100)	1 (25)	6 (60)
Graduate degree	1 (25)	-	1 (25)	2 (20)
High school diploma	-	-	1 (25)	1 (10)
Vocational school or other trade certificate	-	-	1 (17)	2 (20)
Employment status[1]				
Retired	1 (25)	1 (50)	1 (25)	3 (30)
Self-employed	2 (50)	2 (100)	2 (50)	6 (60)
Employed full-time	1 (25)	1 (50)	1 (25)	3 (30)
Employed part-time	1 (25)	-	-	1 (10)

Note: R1/2/3 = Round 1/2/3; [1]The sum of counts exceeds the total as participants were able to select multiple responses. The sum percentages may be less or greater than 100 as all percentages are rounded to the nearest whole number (0.d.p).

Table 3. Sample clinical characteristics for the MBS-ET cognitive debriefing interviews

Clinical Characteristic	R1 (n=4)	R2 (n=2)	R3 (n=4)	Total (n=10)
		Mean (SD, Range)		
Time since diagnosis (years)	5.7 (4.0, 3.08 - 11.67)	7.2 (5.7, 3.17-11.25)	5.2 (0.7, 4.50 - 5.75)	6.03 (3.5, 3.08 - 11.67)
		N (%)		
PGI-S ADL[1]				
Mild problems	2 (50)	-	1 (25)	3 (30)
Moderate problems	1 (25)	2 (100)	1 (25)	4 (40)
Severe problems	1 (25)	-	2 (50)	3 (30)
PGI-S[2]				
Mild problems	2 (50)	-	1 (25)	3 (30)
Moderate problems	1 (25)	2 (100)	1 (25)	4 (40)
Severe problems	1 (25)	-	2 (50)	3 (30)
CGI-S ADL[3]				
No problem	-	1 (50)	1 (25)	2 (20)
Mild problems	2 (50)	-	1 (25)	3 (30)
Moderate problems	1 (25)	1 (50)	-	2 (20)
Severe problems	1 (25)	-	2 (50)	3 (30)
CGI-S[3]				
Mild problems	2 (50)	-	-	2 (20)
Moderate problems	1 (25)	2 (100)	2 (50)	5 (50)
Severe problems	1 (25)	-	2 (50)	3 (30)

Note: [1]Patient-reported in participant screener; [2]Patient-reported in participant background questionnaire; [3]Clinician-reported in participant screener; CGI-S / PGI-S = Clinician / Patient Global Impression – Severity (Tremor); CGI-S ADL / PGI-S ADL = Clinician / Patient Global Impression – Severity (Activities of Daily Living); SD = Standard deviation; R1/2/3 = Round 1/2/3

Figure 1. Patient understanding and relevance of the MBS-ET symptom module

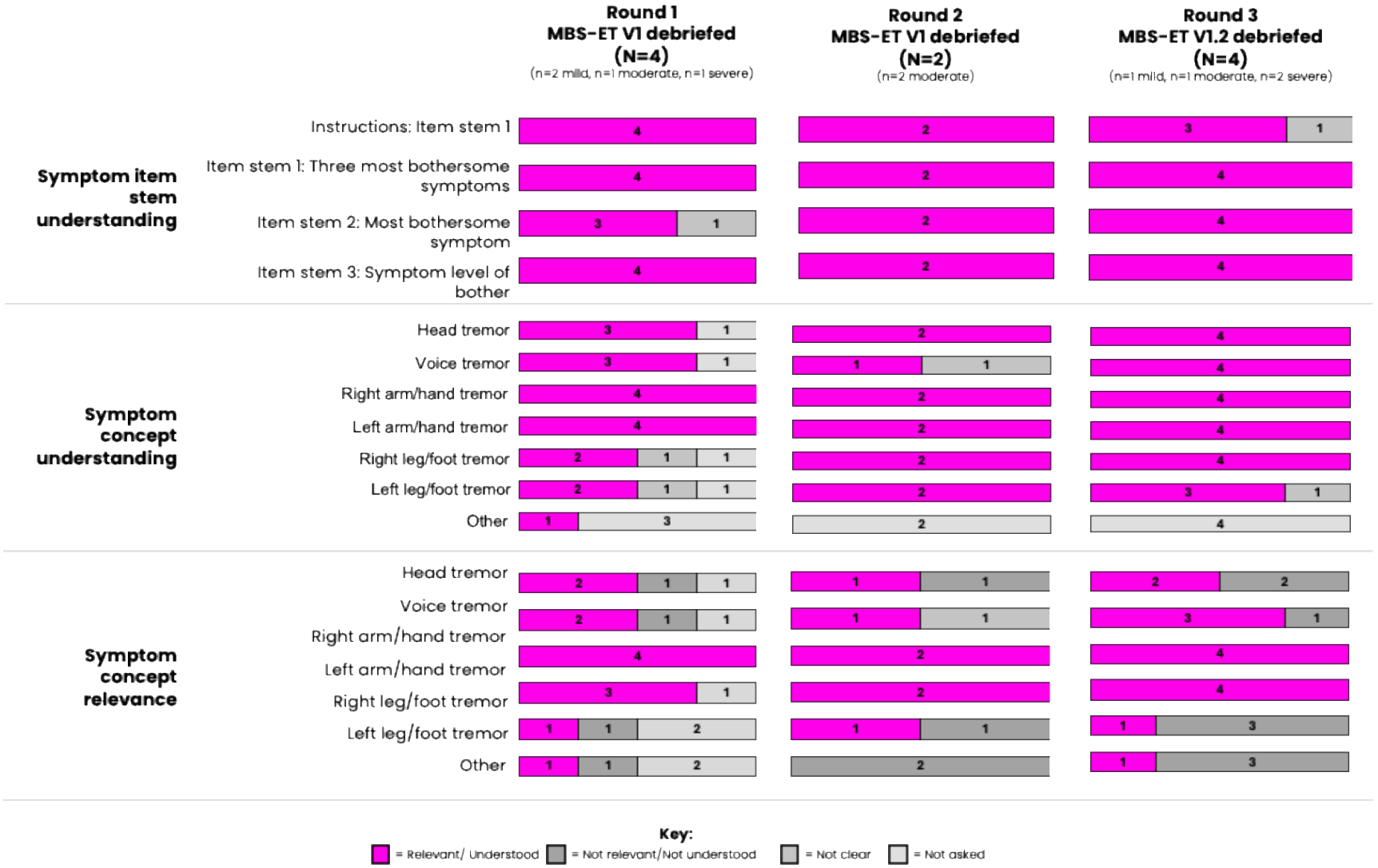

Figure 2. Patient understanding and relevance of the MBS-ET ADL module

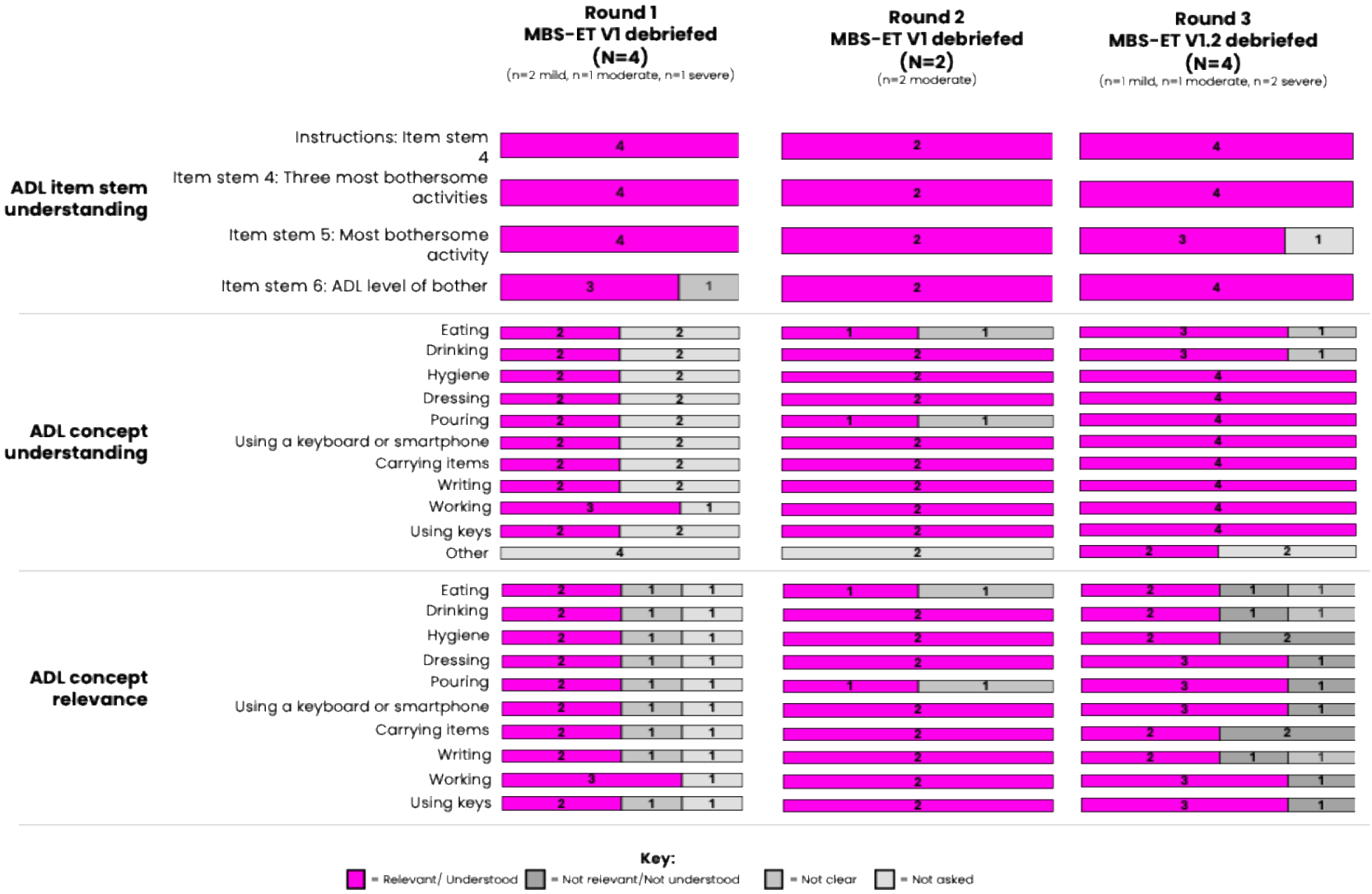

Table 5. Summary of feedback on MBS-ET: Response options, recall period, missing concepts and responder burden

MBS-ET V1.0 (Round 1; N=4)	MBS-ET V1.1 (Round 1; N=2)	MBS-ET V1.2/2.0 (Round 3; N=4)
Response scales		
Three most bothersome (symptom/ADL impacts) ranking question		
Understood by all participants.	Understood by both participants.	Understood by all participants.
One most bothersome (symptom/ADL) ranking question		
Understood by most participants (n=3). P007-MLD did not clearly understand as they selected two symptoms when ask to select their 'Most bothersome symptom' (item stem 2).[1] Two participants indicated it was challenging to select just one response as multiple concepts were equally relevant.	Understood by both participants.	Understood by all participants.
Numeric Response Scale (0-10 integers)		
Understood by most participants (n=3). P017-SEV did not clearly understand as they indicated that it was difficult to select a response, as the level of bother experienced when completing an ADL was variable (item stem 6).	Understood by both participants.	Understood by all participants, but P022-MOD noted that interpretation of this scale may be subjective.
Recall period		
Item stems 1, 3, 4 & 6 in the MBS-ET V1.0 used a 7-day recall period. Two participants reported using a recall period of 7-days. P004-MLD reported using a recall period of 4-	Item stems 1, 3, 4 & 6 in the MBS-ET V1.1 used a 7-day recall period. P019-MOD reported using a 7-day recall period on all items. P020-MOD reported using a 7-day	All items in the MBS-ET V1.2/2.0 use a 7-day recall period. Two participants reported using a 7-day recall period for all items. P021-MLD reported using a recall period of "since

MBS-ET V1.0 (Round 1; N=4)	MBS-ET V1.1 (Round 1; N=2)	MBS-ET V1.2/2.0 (Round 3; N=4)
5 years. One was not asked.	recall period for all items but item stem 5 (Most bothersome ADL) which does not specify a recall period. P020-MOD also indicated a 1-month recall period may be preferable to 7-days.	tremors began" for item stems 1 (Three most bothersome symptoms) and 2 (Most bothersome symptom) but used a 7-day recall period for all other items. P022-MOD reported using a variety of recall periods across items, but did not use a 7-day recall for any items.
Missing items / concepts		
Two participants indicated that the MBS-ET was conceptually comprehensive. When prompted, P004-MLD suggested including items to assess driving (ADL) and sexual relationships (wider HRQoL). P018-MOD suggested including an item to assess difficulty reaching (gross motor skill).	Both participants indicated that the MBS-ET was conceptually comprehensive.	Two participants indicated that the MBS-ET was conceptually comprehensive. When prompted, two participants reported concepts they perceived to be missing: 'Driving' (ADL; P024-SEV) and 'Social and leisure activities' (Wider HRQoL; P023-SEV).
Responder burden (length)		
Three participants considered the length of to be acceptable. One was not asked.	Both participants considered the length to be acceptable.	All participants considered the length to be acceptable.

HRQoL = Health-related quality of life; N=Number of participants; MBS-ET = The Patient Attainment Scale-Essential Tremor

[1]Interviews were conducted using 'live' PDFs of the MBS-ET rather than ePRO devices. The issue of trying to select multiple responses to a single response item is unlikely to be encountered when administered in ePRO format.

Table 6. Item tracking matrix - Revisions to MBS-ET following Round 1 (MBS-ET V1.0 to V1.1)

MBS-ET V1.0	Revision made	Rationale for revision	MBS-ET V1.1
Item stem 3 & 6: response options NRS (0-10 integers) Descriptive label: • 0 = Doesn't bother me at all • 5 = Bothers me sometimes • 10 = Bothers me all the time	• Removal of descriptive label 'Bothers me sometimes'	• n=2/4 participants in round 1 reported that the 'Bothers me sometimes' descriptor was ambiguous.	Item stem 3 & 6: response options NRS (0-10 integers) Descriptive label: • 0 = Doesn't bother me at all • ~~5 = Bothers me sometimes~~ • 10 = Bothers me all the time
Blue text indicates wording or formatting revisions			

Table 6. Item tracking matrix - Revisions to MBS-ET following Round 2 (MBS-ET V1.1 to V1.2/V2.0)

MBS-ET V1.1	Revision made	Rationale for revision	MBS-ET V1.2/V2.0
Item stem 2 & 5: Item 2: Please select the one symptom that bothers you the most Item 5: Please select the one activity that bothers you the most	• Addition of 7-day recall period	• P020-MOD selected 'Writing' as the most bothersome ADL in item stem 5 (no recall period specified), but indicated it was less bothersome that the two other ADLs selected when responding to item stem 6 (ADL level of bother) which utilizes a 7-day recall period. • The 7-day recall period was added to item stems 2 & 5 for consistency with all other item stems.	Item stem 2 & 5: Item 2: Please select the one symptom that has bothered you the most in the past 7 days Item 5: Please select the one activity that has bothered you the most in the past 7 days
Blue text indicates wording or formatting revisions			

References

Supplementary materials

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Poster

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