

Risk Perception of Tobacco and Nicotine Products: Which Consumer Reported Outcome Measures for Evidence Generation in Support of Regulatory Engagement?



N. Mainy¹; K. Przydzial²; S. Cleanthous²; M. Bajec³; T. Salzberger⁴; S. Cano⁵

¹JT International SA, Rue Kazem Radjavi, 1201, Geneva, Switzerland; ²Modus Outcomes, Stotfold, United Kingdom; ³Bajec Senseworks consulting, Hamilton, L8K 2L7, Ontario, Canada;

⁴Institute for Statistics and Mathematics, Institute for Marketing Management, University of Economics and Business (WU Wien), Welthandelspl.1, 1020, Vienna, Austria; ⁵Modus Outcomes, Cheltenham, United Kingdom.

OBJECTIVES

US Food & Drug Administration Center for Tobacco Products' Premarket Tobacco Product Applications (FDA CTP PMTA) require assessment of the public health impact of New Tobacco Products (NTP) to gain approval via Marketing Granted Orders. PMTA assessment should inform on individuals' risk perception of NTP^[1,2]. Consumer Reported Outcome Measures (CROMs) are central in generating this evidence-base^[3-6,14-16]. The study objective was to evaluate risk perception CROMs for use in real-world evidence (RWE) generation in support of regulatory engagement.

RESULTS

The risk perception CROMs assess absolute or relative risk perception, with the PBI and FDA CTP instruments capturing both (Table 1). With different conceptual coverage, the reviewed CROMs measure domains such as perceived health (Table S1), addiction, social, practical, and risk to others, in adult population of tobacco products users as well as non-users (Table 2). CROMs' item/generation and psychometric validation are presented in Table 3 and Table 4, respectively. Measurement properties in multiple countries/languages, using both modern and classic psychometric validation, were only evaluated for the ABOUT – Perceived Risk instrument^[7,13] (Tables S3-S5).

METHODS

Building upon existing literature review^[7], we investigated the development and validation of three risk perception CROMs, (i) the ABOUT – Perceived Risk instrument^[6,7]; (ii) the Perception and Behavioral Intentions (PBI) survey^[8]; and (iii) the brief measures of tobacco product health risk perceptions (FDA CTP instrument)^[9,10]. We reviewed the reported conceptualization, intended population, item-level matrix, scoring structure, and psychometric performance revealed in empirical studies.

Table 1. Overview of Risk Perception CROMs.

Risk Perception CROM	Intended construct of measurement	Population developed for	Number of items	Response scale	Item stems**	Recall period	Scoring structure***
ABOUT – Perceived Risk ^[7]	Perceived risk of tobacco and nicotine-containing products.	Adult smokers; Former smokers; Never-smokers.	25 (v1.0) 40 (v3.0)	5-point Likert-like scale (0 = 'no risk'; 4 = 'very high risk') + 'I don't know option'		Your lifetime health risk	Separate score for each domain scale - transformed from 0 (no perceived risk) to 100 (very high perceived risk)
PBI Survey ^{[8]*}	Perceptions of general harm, relative risk perceptions, and risk perceptions for tobacco-related health outcomes.	Adult smokers; Adult e-vapor/e-cigarette users; Non-tobacco users.	32	General harm: 5-point Likert scale ('Not at all' to 'Extremely') [§] Relative risk (total health): 10-point Likert scale (0 = 'No risk to health' to 9 = 'Great risk to health') ^{§§} + 'don't know option' Absolute risk of general and specific diseases (% of likelihood): 11-point scale (0% = 'Extremely unlikely' to 100% = 'Extremely likely')		Not specified Using [product] daily To a person who only uses [product] daily	Separate score for each sub-scale
FDA CTP instrument ^[9,10]	Absolute and Relative risk of e-cigarettes.	Adult smokers; Adult e-vapor/e-cigarette users; Non-tobacco users.	21	Absolute risk scales: 5-point Likert scale ('Not at all likely' to 'Extremely likely') Relative risk scales: 5-point Likert scale ('MUCH more likely with [product]' to 'MUCH more likely with [cigarettes/NRT/quitting tobacco]')		If you were to use [product] every day...	Single items + score for each domain scale
	Absolute and Relative risk of smokeless tobacco products.	Adult smokers; Adult smokeless tobacco users; Non-tobacco users.	35	Absolute risk scales: 5-point Likert scale ('Not at all likely' to 'Extremely likely') Relative risk scales: 5-point Likert scale ('MUCH more likely with [product]' to 'MUCH more likely with [cigarettes/NRT/quitting tobacco]')		If you were to use [product] every day...	Single items + score for each domain scale

* The PBI Survey evaluates behavioral intentions, risk perceptions, and attitudes and beliefs about e-vapor/e-cigarette products and was further adapted for other nicotine and tobacco products and adults who use these products: oral tobacco products^[11] and heated tobacco products (heated tobacco capsule system)^[12]. ** Item stems in Table S2; *** There is no total score for these CROMs. § 7-point Likert scale (1 = 'Not at all risky'; 7 = 'Extremely risky') in^[11,12]; §§ 4-point Likert scale (1 = 'Not at all harmful'; 4 = 'Very harmful') in^[12].

Table 2. Summary of Risk Perception CROMs item content.

Risk Perception CROM		Domain					Total number of items	Product Use Behavior [§]				
		Absolute Risk						Relative Risk (compared to other TNPs)	Single use	Dual use	Poly use	
		Health risk	Addiction risk	Social risk	Practical risk	Risk to others						
ABOUT – Perceived Risk ^[7]	v1.0	18 items	7 item**	N/A	N/A	N/A	N/A	25	●			
	v3.0	18 items*	7 item**	7 items	6 items	2 items	N/A	40	●	●§§	●§§	
PBI Survey ^[8,11,12]		9 items (cigarettes) 2 items (e-cigarettes) 11 items ([product name])			N/A	N/A	N/A	10 item scale of different product use behavior ^{§§§}	32	●	●	
FDA CTP instrument ^[9,10]	e-cigarettes	1 item	1 item	N/A	N/A	N/A	17 items (compared to cigarettes) 1 item (compared to NRT) 1 item (compared to cessation)	21	●			
	smokeless tobacco products	5 items	1 item	N/A	N/A	N/A	27 items (compared to cigarettes) 1 item (compared to NRT) 1 item (compared to cessation)	35	●			

* Short version: 9 items (as per user manual); ** 6+1 specific to cessation; § Concurrent use of one (single), two (dual), or more (poly) tobacco products; §§ 'more than one'; §§§ quantity and pattern.

Table 3. Summary of Risk Perception CROMs item generation/refinement.

Risk Perception CROM	Item Generation				Conceptual Framework	Item Refinement / Reduction		
	Participants	Expert Opinion	Literature Review	Pre-existing Instrument		Participants	Expert Opinion	Psychometrics (Quantitative)
ABOUT – Perceived Risk ^[7]	●	●	●		●		●	
PBI Survey ^[8]		●	●		●	?**	●	
FDA CTP instrument ^[9,10]		●	●	(●)*			●	

* The FDA CTP instrument for smokeless tobacco products^[10] was adapted from the FDA CTP instrument for e-cigarettes^[9].

** Unclear from the PBI Survey Validation Study Report^[8].

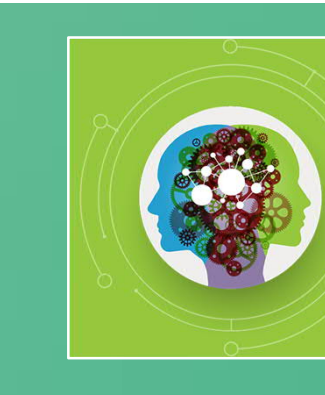
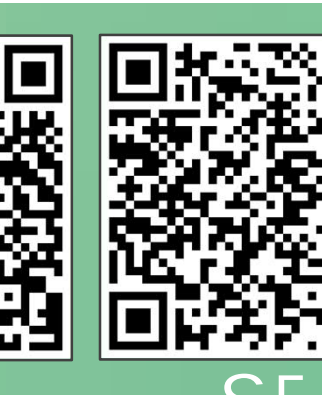
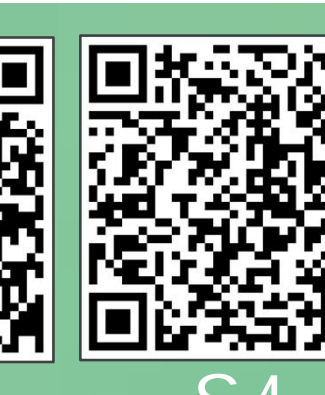
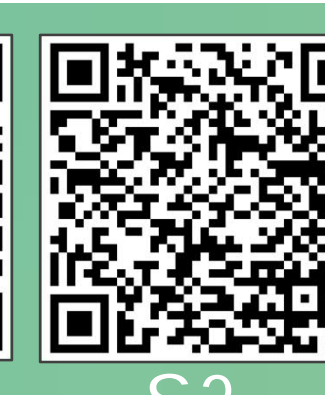
Table 4. Summary of Risk Perception CROMs psychometric validation.

Risk Perception CROM	Data completeness (missing data)	Scaling assumptions (corrected item-total correlations)	Structural validity (factor analysis)	Targeting (floor/ceiling effects)	Reliability (Cronbach's alpha & test-retest)	Construct validity (correlations with scales measuring similar constructs)	Known groups validity (different scores between groups of PPs)	Sensitivity to change
ABOUT – Perceived Risk ^[7]	●	●	(●)*	●	●	●	●	●
PBI Survey ^[8]					●	●		●
FDA CTP instrument ^[9,10]			●		●			

* Structural validity tested based on modern test theory; See psychometric validation output for each Risk Perception CROM in Tables S3-S5.

CONCLUSIONS

Selecting and potentially combining risk perception CROMs for use in assessment studies require considerations of instruments' characteristics, including conceptual overlap, as well as prerequisites pertaining to copyright and translation. Health communication strategies should ensure targeted, effective, non-misleading messaging to empower adults who elect to continue to use nicotine and tobacco products to make informed decision when switching to potentially reduced risk alternatives. Appropriate psychometric CROMs have the potential to capture RWE insights concerning one individual's journey (stages, moments). Characterizing elements that promote a desired behavioral change, such as accurate risk perception, could further support tobacco harm reduction.



Supplementary Tables: Risk Perception CROMs health risks items and item stems.

Supplementary Table 1. Health risks evaluated in Risk Perception CROMs.

Health risks (absolute or relative)	ABOUT – Perceived Risk (v3.0)	PBI Survey	FDA CTP instrument		Number of items across CROMs
			e-cigarettes	smokeless tobacco products	
Breathing	●	●	●	●	6
Coughing	●	●		●	4
Lung cancer	●	●	●	●	4
Mouth cancer	●	●	●	●	4
Heart disease	●	●	●	●	4
Teeth		●	●	●	4
Lung disease				●	3
Emphysema	●	● [§]		●	3
Earlier death	●		●		2
Life-threatening disease	●		●		2
Respiratory infections	●			●	2
Other minor illnesses	●		●		2
Gum	●			●	2
Mouth sores	●			●	2
Asthma				●	1
Exercise capacity	●				1
Fatigue	●				1
Other types of cancer	●				1
Stomach cancer				●	1
Stomach ulcers				●	1
Mouth irritation				●	1
Taste	●				1
Aging	●				1

§ in ^[11,12].

Supplementary Table 2. Risk Perception CROMs item stems.

Risk Perception CROM	Item Stem Formulation*
ABOUT – Perceived Risk (v3.0)	What do you think is YOUR lifetime health risk, because you use [product] ... If you started using [product] again tomorrow, what do you think would be YOUR lifetime health risk of ... What do you think is the lifetime health risk to [product] users of ...
PBI Survey	In your opinion, how harmful are [product] to your general health? In your opinion, to what extent do [product] cause ... Please rate each item for the risk you feel it could pose to a person's health. How likely is it that these things will happen to a person who exclusively uses [product] daily?
FDA CTP instrument	If you were to use [product] every day, how likely is it that you would ... If you either used ... every day, which product would make it more likely that you would ... Imagine you used either ... every day, which product would make it more likely that you would ...

* Exact item stems are dependent on product, product use status (i.e., users and non-users), etc.



Supplementary Tables: Risk Perception CROMs psychometric validation output.

Supplementary Table 3. ABOUT – Perceived Risk psychometric validation output.

Data completeness (missing data)	Scaling assumptions (corrected item-total correlations)	Targeting (floor/ceiling effects)	Reliability (Cronbach's alpha & test-retest)	Construct validity (correlations with scales measuring similar constructs)	Known groups validity (different scores between groups of PPs)
Missing data was 0.1% at most at the item-level (however the proportion of don't know responses was between 11-15%)	Range of corrected item-total correlation Survey 1: Health Risk: 0.89-0.93 Addiction Risk: 0.90 – 0.93 Survey 2: Health Risk: 0.88-0.92 Addiction Risk: 0.92-0.95	Ceiling / Floor Survey 1: Health Risk – 7% / 10% Addiction risk – 8% / 20% Survey 2: Health Risk – 5% / 10% Addiction risk – 6% / 18%	Surveys 1&2: Health Risk: α 0.99 Addiction Risk: α 0.98	For the assessment objects cigarettes, THS 2.2, E-cigarettes and NRT, all correlations between the VAS scores and instrument's measures for both Perceived Health Risk and Perceived Addiction Risk were in the range of 0.52 to 0.68 across both types of risk Assuming a reliability of the VAS of 0.6 and applying the Spearman Brown formula for diattenuation imply correlations in the order of 0.68 and 0.89.	All mean differences were in the expected direction. In terms of the effect sizes (Cohen's d), differences between smokers and never smokers (0.51-0.84) were more pronounced than differences between personal and general risk among current smokers (0.23-0.34) The risk perception of cigarettes was higher than that of IQOS across all countries and years ^[13] . After adjustment for covariates, the relative risk between cigarettes and IQOS was higher in 2018 than in 2019 (0.93; standard error, 0.33; P = 0.005). This was driven by an increase in the risk perception of IQOS over time in Italy (2018: 42.6 [95% CI, 41.6–43.5]; 2019: 44.4 [43.4–45.4]) and Japan (2017: 44.0 [43.1–44.9]; 2018: 45.9 [45.2–46.7]; 2019: 48.6 [47.9–49.4]), while the risk perception of cigarettes remained stable

Supplementary Table 4. PBI Survey psychometric validation output.

Reliability (Cronbach's alpha & test-retest)	Construct validity (correlations with scales measuring similar constructs)	Sensitivity to change
Perceived Harm of MarkTen[®]XL: Validation sample: α .876; ICC .870 (<.001) Cross-validation sample: α .888; ICC.798 (<.001)	Perceived Harm of MarkTen[®]XL: Validation sample: correlation with Behavioral Selection -.309 (<.001) Cross-validation sample: correlation with Behavioral Selection -.387 (<.001)	Correlations between residualised change scores of Perceived Harm of MarkTen[®]XL scales and behavioral selection: Validation sample: Pearson .016 (.784) Cross-validation sample: Pearson .066 (.266)
Perceived Harm of E-Vapor/E-Cigs: Validation sample: α .864; ICC .856 (<.001) Cross-validation sample: α .871; ICC .792 (<.001)	Perceived Harm of E-Vapor/E-Cigs: Validation sample: correlation with Behavioral Selection -.314 (<.001) Cross-validation sample: correlation with Behavioral Selection -.387 (<.001)	Perceived Harm of E-Vapor/E-Cigs scales and behavioral selection task: Validation sample: Pearson .023 (.700) Cross-validation sample: Pearson .067 (.258)
Relative Risk: Validation sample: items Risk1-Risk10 ICC range .527-.747 (<.001); average .603 (<.001) Cross-validation sample: items Risk1-Risk10 ICC range .390-.723 (<.001); average .597 (<.001) Full sample: items Risk1-Risk10 ICC range .462-.731 (<.001)	Relative Risk: Validation sample: correlation with Behavioral Selection items Risk2-Risk6 range -.282 - -.163 (<.001) Cross-validation sample: correlation with Behavioral Selection items Risk2-Risk6 range -.334 - -.214 (<.001)	Relative Risk scales and behavioral selection task (Not Selecting MarkTen[®]XL): Validation sample: items Risk2-Risk6 Pearson range .023-.116 (>.053) Cross-validation sample: items Risk2-Risk6 Pearson range .133-.206 (<.05)
Specific Risk of Cigarettes: Validation sample: items RiskC1-RiskC9 ICC range .637-.795 (<.001) Cross-validation sample: items RiskC1-RiskC9 ICC range .560-.782 (<.001)	Specific Risk of Cigarettes: Validation sample: correlation with being a tobacco user items RiskC1-RiskC9 range -1.580 - -.041 (<.001; RiskC5 p.115) Cross-validation sample: correlation with being a tobacco user items RiskC1-RiskC9 range -.221 - -.075 (<.001; RiskC5 p .005)	Specific risk of MarkTen[®]XL scales and behavioral selection task (Not Selecting MarkTen[®]XL): Validation sample: items RiskV1-RiskV9 Pearson range -.022 - -.103 (>.08) Cross-validation sample: items RiskV2, RiskV3, RiskV4, RiskV9 range .210-.232 (<.001); RiskV6 .197 (.001); RiskV1, RiskV7, RiskV8 range .131-.137 (>.02); RiskV5 .071 (.234)
Specific Risk of MarkTen[®]XL: Validation sample: items RiskV1-RiskV9 ICC range .682-.835 (<.001) Cross-validation sample: items RiskV1-RiskV9 ICC range .652 - .768 (<.001)	Specific Risk of MarkTen[®]XL: Validation sample: correlation with Behavioral Selection items RiskV1-RiskV9 -.298 - -.194 (<.001) Cross-validation sample: correlation with Behavioral Selection items RiskV1-RiskV9 -.378 - -.227 (<.001)	Full sample: items RiskV4, RiskV6, RiskV9 range .114-.130 (<.01); items RiskV1- RiskV2- RiskV3, RiskV8 range .093-.109 (<.05); items RiskV5, RiskV7 .048, .078 (>.05)

Supplementary Table 5. FDA CTP instrument psychometric validation output.

FDA CTP instrument	Structural validity Factorial analyses (EFA/exploratory factorial analysis, CFA/confirmatory factorial analysis), ITC (item-to-total correlation), IRT (item-response theory)	Reliability (Cronbach's alpha & test-retest)
e-cigarettes	Absolute health risk: # factors: 1, % var. explained: 71.6 Factor loadings: .76–.86, Communalities: .57–.74 Health risk of e-cigarettes compared with cigarettes: # factors: 1, % var. explained: 47.4 Factor loadings: .68–.75 (except common cold or flu, pancreatic cancer, diabetes, stomach ulcers, stomach cancer <.3). Communalities: .46–.62 Addiction risk of e-cigarettes compared with cigarettes: # factors: 1, % var. explained: 66.7 Factor loadings: .72–.79, Communalities: .52–.58 Pregnancy risk of e-cigarettes compared with cigarettes: # factors: 1, % var. explained: 70.4 Factor loadings: .61–.66, Communalities: .55–.62 Health risk of e-cigarettes relative to NRT: # factors: 1, % var. explained: 77.2 Factor loadings: .73–.97, Communalities: .56–.72 Health risk of e-cigarettes relative to cessation: # factors: 1, % var. explained: 91.5 Factor loadings: .81–.99, Communalities: .77–.80	Absolute health risk: correlation between this single item and all items = .82 Health risk of e-cigarettes compared with cigarettes: (Final scale: The overall harm item had a correlation with the overall scale of .75, therefore, the core 8-item scale was used to represent the construct. The average of these items has a .93 correlation with the 23 remaining items.) Addiction risk of e-cigarettes compared with cigarettes: α .83 Pregnancy risk of e-cigarettes compared with cigarettes: α .90 Health risk of e-cigarettes relative to NRT: Used overall harm item to represent scale; correlation between this and all items = .92. Health risk of e-cigarettes relative to cessation: Used overall harm item to represent scale; correlation between this and all items = .98.
smokeless tobacco (ST) products	Absolute risk of ST product: Health Risk: 2 factor solution, var. explained: 71.7% Factor loadings: 0.68–0.92, Factor correlation: 0.59 Risk of ST products relative to cigarettes: Health Risk: 2 factor solution, var. explained: 50.7% Factor loadings: 0.64–0.83, Factor correlation: 0.22 Addiction risk: # factors: 1, var. explained: 59.5% Factor loadings: 0.65–0.70 Pregnancy risk: # factors: 1, var. explained: 67.5% Factor loadings: 0.74–0.79 Risk of ST product compared to cessation - Health risk relative to NRT: # factors: 1, Variance explained: 82.4% Factor loadings: 0.76–0.85 Health risk relative to cessation: # factors: 1, var. explained: 87.8% Factor loadings: 0.85–0.88	Absolute health risk of ST product: α 0.75-0.85 Health risk of ST product relative to cigarettes: α 0.93 Addiction risk of ST product relative to cigarettes: α 0.78 Pregnancy risk of ST product relative to cigarettes: α 0.88 Risk of ST products compared to NRT/cessation: α 0.93/0.94 between single items and all items



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