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Supplementary Material:

The 12-item Hypoglycaemia Impact Profile (HIP12): psychometric validation of a brief measure of the impact of hypoglycaemia on quality of life among adults with type 1 or type 2 diabetes

Supplementary Material 1: Developing the HIP12

Adaptations were made by members of Hypo-RESOLVE Consortium with expertise in hypoglycaemia, QoL, and PROM development/validation. Five members of the Hypo-RESOLVE Patient Advisory Committee (PAC) (60% male, 80% with T1D), provided input into this process from a lived experience perspective. Input from PAC members took place over two, 1-hour video conference calls in October 2020 and February 2021. The first call began with a broad discussion about how hypoglycaemia impacts on QoL and which areas of life are essential to explore. Subsequently, the original DIDP was presented to discuss the strengths and limitations of the measure, and its suitability for adaptation into a hypoglycaemia-specific measure. In the second call, the first draft of the HIP12 was presented, and PAC members provided feedback on the comprehensibility and content of the measure. PAC members further provided written feedback on the full 'Your SAY: Hypoglycaemia' survey and protocol and the recruitment advertisements for the study.

Development of the HIP12 involved the following specific changes or additions to the DIDP:

1. The question stem was changed from "how does diabetes currently impact the following aspects of your life?" to "how do your experiences with or worries about hypoglycaemia (low blood glucose or 'hypos') impact the following aspects of your life?".
   a. To eliminate ambiguity, the word "currently" was removed. Feedback from the PAC indicated that the timeframe was unclear; "currently" can be interpreted literally (e.g., at this moment) or in a more general sense (e.g., over the past few days/weeks).
   b. The word "hypoglycaemia" could not simply replace the word "diabetes", as this would leave it unclear whether the focus was limited to *episodes* of hypoglycaemia, or included broader experiences (e.g., planning/prevention, episodes, recovery, and thoughts/feelings about risk of hypoglycaemia). A balance needed to be struck to ensure that the breadth of people's experiences of hypoglycaemia was captured by the questionnaire, without including lengthy/wordy explanations about the scope of the measure.

2. Five items were added to reflect additional domains of life where hypoglycaemia may have an impact: sleep, independence, ability to be spontaneous, ability to be fit/active, and sex life. These additions were:

a) based on suggestions by the PAC and the research team, and on past research on the personal impact of hypoglycaemia (e.g., (1-3)).

b) included only if they were likely to be broadly applicable to most people with insulin-treated diabetes.

Supplementary Material 2: Measures used for validation purposes

DAWN2 Impact of Diabetes Profile

The DIDP (4, 5) assesses the impact of diabetes on six domains of life: physical health, finances, relationships, leisure activities, work or studies, and emotional wellbeing. A modified version of the DIDP contains a seventh item about dietary freedom (6). Items are rated on a 7-point scale (from 1 = *very positive impact* to 7 = *very negative impact)* or participants can select "not applicable". Composite scores are calculated by averaging scores across applicable items, with scores <4 indicating a positive impact, a score of 4 no impact, and scores of >4 a negative impact of diabetes on QoL.

WHO-5 Wellbeing Index

The WHO-5 is a 5-item positively worded measure of general emotional wellbeing over the past 2 weeks (7). Participants indicate how frequently they have experienced each statement (e.g., "I have felt calm and relaxed") on a 6-point Likert scale (from 0= *At no time* to 5 = *All of the time)*. Item scores are summed, with a total raw score of <13 indicating likely depression (8).

The Hypoglycaemia Confidence Scale

The 9-item Hypoglycaemia Confidence Scale (HCS) measures the degree to which people feel confident in managing hypoglycaemia in various scenarios (e.g., while physically active, driving, asleep) (9). Each item is scored on a 4-point scale (from 1 = *Not confident at all* to 4 = *Very confident)*, and a composite score is calculated with higher scores indicating greater confidence. Applicable only to people with partners/spouses, the ninth item asks the person with diabetes to estimate how confident their partner is in the ability of the person with diabetes to manage hypoglycaemia.

The Hypoglycaemia Fear Survey - Short form (worry subscale)

The 6-item worry subscale of the Hypoglycaemia Fear Survey - Short Form (HFS-SF) (10) assesses how often respondents have worried about certain aspects of hypoglycaemia over the past 6 months. Items are rated on a 5-point Likert scale (from 0 = *Never* to 4 = *Almost always)*. Item scores are summed, with higher scores indicating greater fear of hypoglycaemia.

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Hypoglycaemia history and awareness

Eleven items from the Hypoglycaemia Awareness Questionnaire (HypoA-Q) (11) were included. Six items assessed frequency of severe and self-treated hypoglycaemia (while awake and asleep) over the past 12 months. The five-item Impaired Awareness subscale assessed hypoglycaemia awareness, where items were rated on a scale ranging from *Never/Strongly disagree* to *Always/Strongly agree*. Items are summed to generate composite scores, where higher scores indicate more impaired awareness. The single-item Gold score (12) was administered to enable categorisation of participants by awareness status (intact versus impaired).

Demographic and clinical information

Participants self-reported demographic information (including age, gender, native language, country, employment, financial status, and education) and clinical information (including diabetes duration, diabetes management strategies, HbA1c, medical complications, and COVID-19 history). They also provided ratings of the overall impact of the COVID-19 pandemic on their QoL (from 1= *very negative impact* to 7 = *very positive impact*).

Supplementary Material 3: Statistical Analyses

Statistical analyses were conducted using SPSS version 28 and R Studio version 2021.09.1. All statistical analyses (unless otherwise indicated) were conducted separately for adults with T1D and adults with T2D. Structural validity and internal consistency analyses were further conducted separately for native and non-native English speakers.

Descriptive data are presented as Mean±SD, median(IQR), or valid percent (n), as applicable. Missing data was generally low (<5.4% across questionnaires), but pairwise deletion was used to maximise use of available data. Non-parametric statistical tests were used where Kolmogorov-Smirnov tests and histograms indicated non-normal distributions. P values <0.05 were considered statistically significant.

For the HIP12, acceptability, applicability, and response patterns were examined descriptively. High overall completion rates (by ≥90% of the sample) were taken as evidence of acceptability (4). Floor and ceiling effects (i.e., ≥15% of responses at either the highest or lowest value on the response scale (13)) and response patterns, including item applicability, were explored. Free-text responses for additional domains of life nominated by participants were coded and grouped into semantically related categories. The approach followed principles of thematic analysis (14) but rather than moving from codes to broader themes, all phases were undertaken at the code-level. The process involved the following phases:

1. Familiarization with free text responses (i.e., multiple read-throughs of all data before taking action) (MB)
2. Initial coding of each free text response (MB)
3. Review and discussion of initial codes (MB, HC, JS, FP, US)
4. Finalisation of code labels to reflect "domains" of life (MB, HC, JS, FP, US)

Once category labels were finalized, the associated impact rating for each category was calculated and summarized across participants. For participants who nominated additional domains of life, their composite scores on the HIP12 were calculated both with and without ratings from added domains, and were compared using a Wilcoxon signed rank test.

Inter-item correlations (Spearman's Rho) were calculated to identify item pairs with associations that were very low (r_s<0.2) or very high (r_s>0.9) (15). The determinant value was used to explore multicollinearity, with a value ≥0.00001 indicating no multicollinearity (16). A Kaiser-Meyer-Olkin statistic of ≥0.6 indicated sampling adequacy for confirmatory factor analysis (CFA) (17). A minimum of 120 participants per CFA were required to meet the suggested 1:10 item-to-participant ratio (13). A Full Information Maximum Likelihood estimation strategy was applied to make use of all available data (i.e., to include available data from participants who may have indicated N/A on one or more items). CFA determined whether the expected one-factor solution demonstrated for the original DIDP was supported by the data. Factor loadings of ≥0.5 were deemed acceptable. Tucker Lewis index (TLF) >0.95, Comparative Fit Index (CFI) >0.95, Root-Mean-Square Error of Approximation (RMSEA) <0.06, and the Standardized Root-Mean-Square Residual (SRMR) <0.08 (17, 18) model fit parameters were taken as indication of good model fit. In case of suboptimal model fit on the CFAs, follow-up EFAs were conducted to explore alternative latent structures. McDonald's Omega (ω) was calculated as a measure of internal consistency, with ω>0.7 indicating good internal consistency. McDonald's ω has been suggested to be superior to Cronbach's alpha, resulting in fewer underestimations of internal consistency (19). To determine how many missing responses could be accepted before internal consistency was compromised, items with the highest factor loadings were removed iteratively until ω<0.7.

Construct validity can be ascertained by demonstrating theoretically expected relationships between the target measure and existing measures of similar constructs (convergent validity) or unrelated constructs (divergent validity) (13). Spearman's rho correlations were calculated between HIP12 scores and measures of similar constructs (HFS, HCS, DIDP, and WHO-5) and constructs expected to be unrelated (self-reported diabetes duration and HbA1c). A large correlation (r_s>0.5) was expected between the HIP12 and the DIDP. Moderate correlations (r_s>0.3) were expected between the HIP12 and other psychological

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measures to demonstrate convergent validity. Small correlations ($r_s < 0.3$) were expected on measures to demonstrate divergent validity.

Known-groups validity can be ascertained by demonstrating the capacity of the target measure to discriminate between groups that are expected to differ on the measure (13). This was assessed using Mann-Whitney U tests, comparing HIP12 (composite and item) scores between those: 1) who had experienced at least one episode of severe hypoglycaemia in the past 12 months versus those who had not, 2) who had experienced 0-1, 2-4, or ≥5 episodes of hypoglycaemia (of any severity) over the past week, and 3) with impaired versus intact awareness of hypoglycaemia. Effect sizes (rank serial-biserial correlations (20)) are interpreted as follows: 0.1 = *small*, 0.3 = *medium*, 0.5 = *large* (21).

Supplementary Material 4: Comprehensiveness of the HIP12

Most participants (73%) did not use the free-text options to nominate any additional domains of life, while 27% (n=345) provided 590 responses (i.e., each nominating at least one domain of life). Of these, 67 responses were deemed to be invalid (as they referred to causes of hypoglycaemia rather than domains of life impacted by hypoglycaemia, or they could not be interpreted without clarification from participants). After their removal, there were 523 valid responses: 454 from 280 (26%) participants with T1D, and 69 from 42 (22%) participants with T2D.

Coding resulted in 30 categories, 12 of which aligned with the existing items of the HIP12 (e.g., a free-text response of "mental health" was categorized as "emotional wellbeing"). Two-hundred and three responses aligned with existing domains, and the remaining 320 responses were categorised into 17 domains of life not currently assessed by the HIP12. Category labels, a brief description of each category, and the rated impact of hypoglycaemia on each by diabetes type, are presented in Supplementary Table 1.

Figure 1 (in the main manuscript) shows the average reported impact of hypoglycaemia on each domain of life (HIP12 items, Nominated (already included), and Nominated (new)) across the sample. No added domain was nominated by more than 7% of the total sample. For the 322 participants who rated the impact of at least one additional domain there was a marginal but statistically significant (p<.001) difference between original composite scores (5.13±0.76) and composite scores that incorporated the rating of the added domain/s (5.19±0.75). This was consistent across diabetes types.

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Supplementary Table 1: Additional areas of life nominated by participants and their rating of the impact of hypoglycaemia

Domain of Life	Description of domain	Type 1 diabetes		Type 2 diabetes	
		N	Impact Mdn (range)		Impact Mdn (range)
Cognitive function	Concentration, focus, thinking clearly, memory, decision-making	28	6 (5-7)	7	6 (5-7)
Confidence	Self-confidence, general confidence	8	6 (5-7)	-	-
Daily activities	Non-leisure activities (e.g., grocery shopping, housework); appointment keeping; general productivity; interruptions to/having to stop activities	26	6 (1-7)	3	6 (5-7)
Diabetes	Glucose & insulin management; awareness of hypoglycaemia	19	7 (5-7)	3	7 (6-7)
Driving	Driving; ability to drive; access to driver's license	79	6 (2-7)	9	5 (2-7)
Energy	Energy levels, stamina, feeling tired or fatigued	12	6 (5-7)	3	6 (3-7)
Feelings about the future	Feelings of uncertainty; future goals/dreams	4	5.5 (2-6)	-	-
Healthcare experiences	Experiences with healthcare professionals and the hospital system	3	7 (5-7)	2	7 (7-7)
Other people	Others' (mainly family members) sleep and emotional well-being	8	7 (6-7)	-	-
Others' reactions	Public perception, blame, judgement from others, feeling watched or criticized by others	6	6 (5-7)	2	7 (7-7)
Parenting/ caregiving	Parenting & raising children; looking after others (e.g., grandchildren), babysitting	15	6 (5-7)	1	7
Perceived control	Ability to control one's life; sense of feeling in control	4	7 (1-7)	-	-
Safety	Physical safety and feelings of safety	4	7 (5-7)	-	-
Social life/interactions	Socializing, ability to have a social life; communication/interaction, social embarrassment, public speaking	21	6 (5-7)	1	7
Travel/holidays	Air travel/international travel, vacations/holidays, ability to travel	29	6 (4-7)	6	6 (5-7)
Weight/body image	Weight gain, body image, body positivity	9	6 (5-7)	2	7 (7-7)
Women's health	Menstruation, pregnancy, breastfeeding	6	6 (6-7)	-	-

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