Content validation of a new measure of patient-reported barriers to antiretroviral therapy adherence, the I-Score: results from a Delphi study

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Abstract
Background: Over a third of people living with HIV (PLHIV) have suboptimal adherence to antiretroviral therapy (ART). Measures of barriers to ART adherence often lack comprehensiveness. To help manage ART adherence barriers in HIV care, we are developing a new patient-reported outcome measure (PROM) of these barriers (the I-Score).

Methods: We assessed the content validity of 100 items (distinct barriers) to retain only those most relevant to both PLHIV and HIV health/social service providers. A web-based Delphi was conducted in Canada and France, collecting data from December 2018 to October 2019. Items were evaluated on relevance (the combined rated importance and actionability for HIV care of items among both PLHIV and providers); comprehensibility (rated item clarity); comprehensiveness (examined against our conceptual framework); cross-cultural equivalence (based on comparisons by questionnaire language (English, French) and country of residence). Pearson’s chi-square tests were used for comparisons by language, country, gender, and stakeholder group (PLHIV, providers).

Results: Panelists included 40 PLHIV and 57 providers (66% response rate). Thirty-one items were retained based on consensus thresholds for relevance (minimum: 50% for PLHIV, 60% for providers) and showed good comprehensibility and comprehensiveness, when compared to our conceptual framework (representation of: 6/6 domains, 15/20 sub-domains). No significant difference in relevance based on language or country was found among retained items, suggestive of cross-cultural equivalence. Among all 100 items, only 6 significant differences on relevance were observed for gender. For 62 items, the relevance ratings of PLHIV and providers differed significantly, with providers showing greater endorsement of all items but one.

Discussion: The Delphi led to a much-needed item reduction. Remaining items highlight the panel’s multidimensional priorities for the PROM on ART adherence barriers, with few, if any, differences by language, country, and gender. While the analyses may lack generalizability and power, the sample size is considered adequate for a PROM validation study.

Conclusion: Retained items showed good content validity. The different patterns of item endorsement observed underscore the utility of engaging multiple stakeholder groups in PROM development for use in clinical practice.
Introduction

In the treatment of chronic conditions, not taking medications as prescribed is a widespread and multifactorial problem [1] that is associated with poorer health outcomes and higher healthcare costs [2, 3]. Patient adherence to long-term medications is potentially vulnerable to a wide range of interacting factors related to the health condition; the prescribed therapy; the healthcare team and system; social and economic issues; as well as the patients themselves [4].

Among people living with HIV (PLHIV), the average rate of non-adherence to antiretroviral therapy (ART) worldwide, is estimated to be 37–38% [5, 6]. Addressing adherence barriers in HIV care, while recommended, can be challenging [7]. Impediments include its possible time-intensive nature [8], poor patient-provider communication [9, 10], and inaccurate assessment of patient adherence to ART [11]. The management of adherence barriers may be further challenged by PLHIV and providers having different priorities for HIV care and for addressing adverse health behaviors [12].

To facilitate the identification and discussion of ART adherence barriers that are significant to both PLHIV and providers, our research team is developing the Interference (I)-Score, a new patient-reported outcome measure (PROM) for routine use in HIV care. Two reviews by our team established the need for a more comprehensive measure of these barriers [13, 14]. To this end, a patient-centered conceptual framework was derived from a qualitative synthesis [15] to guide item selection and writing. For use in Canada and France, items were drafted in English and subsequently translated to French, using a multistep process, a multidisciplinary workgroup, and professional translation services (FACITtrans) (see Table 1). All steps were documented including relevant decisional processes which were arrived at collaboratively with FACITtrans or by consensus within the workgroup.

To reduce and evaluate the content validity of the 100 items, a modified Delphi was conducted with a panel of PLHIV and health and social service providers in Canada and France (for full methodological details see [16]). This step as well as our other stakeholder engagement activities [17, 18] recognize that a PROM's content validity is crucial [19] and, when seeking PROM implementation in care, so is involving both patients and clinicians in their development [20]. Content validity, the extent to which an instrument's content reflects its targeted construct, is considered the most important measurement property of a PROM [19]. It refers to its perceived relevance, comprehensiveness, and comprehensibility. The purpose of this paper is thus to present the results of the Delphi's first round of consultations and answer the following research questions:

Keywords: HIV, Patient-reported outcome measures, Adherence, Antiretroviral therapy, Validation, Delphi, Canada, France

Table 1 The I-Score translation process

| Step                                      | Actors involved                                                                 |
|-------------------------------------------|---------------------------------------------------------------------------------|
| Two forward translations into the target language (i.e., French) | FACITtrans translators who are native speakers from Canada and France          |
| Reconciliation of the two forward translations by native speaking translators | A multidisciplinary workgroup composed of four bilingual (French, English)     |
|                                           | I-Score investigators: a physician originally from France (BL), an international |
|                                           | student/statistician living with HIV (SV), and two Canadians with backgrounds   |
|                                           | in the social sciences (KE, DL)                                                |
| Two back-translations of the reconciled version into English by native English speakers who are fluent in the target language | FACITtrans translators                                                          |
| Review and finalization                   | The multidisciplinary workgroup of I-Score investigators reviewed the back-     |
| Formatting of the test version in Word format | translations to finalize the translation                                       |
| Proofreading by two translators working independently from one another and reconciling of proofreading | FACITtrans staff                                                               |
|                                          | Proofreading: One proofreader from FACITtrans                                 |
|                                          | One from the workgroup (KE), who discussed results with the other group        |
|                                          | members for feedback                                                           |
|                                          | Reconciliation: FACITrans                                                      |
1. Which items (i.e. barriers) are deemed by the panelists to be both important and actionable for HIV care?

To what extent:
2. Are these items considered clearly written?
3. Do importance and actionability scores differ by stakeholder group (i.e. are scores consistent across PLHIV and providers as well as gender)?
4. Do the items show cross-cultural equivalence (i.e. are scores consistent across country and language)?

Methods
The first round of the Delphi was conducted with an online survey. Participants completed the survey in their language of choice (English or French). To characterize the panel, they first provided sociodemographic and other descriptive information. Then, for each of the 100 items, they rated its: clarity (“Is the item clearly written/does it make sense?”), importance as a barrier to ART adherence (“Is this an important barrier to adhering to antiretroviral therapy?”), and relevance for HIV care or actionability (“Is this useful information for HIV care?”), with a four-point response scale (1-no, 2-somewhat, 3-quite, 4-very). The precise instructions provided to participants in the survey can be found in Additional file 1: Fig. S1.

Consensus
Round 1 served to class items as: (1) “retained” items: consensus items to consider as core items of the measure; (2) “rejected” items; or (3) “undecided” items to be submitted to Round 2 of the Delphi for consideration as part of an item pool or bank, as done in other work on adherence measures [21]. An item was retained if at least 50% of PLHIV and 60% of providers rated it 3 (quite) or 4 (very) on both importance and actionability. Hence, for retention, the item not only had to be a legitimate barrier to each group, but it needed to be perceived as informative for HIV care. Initially consensus was set at 60% for all panelists. However, the threshold for PLHIV was lowered to 50% as too few items would have been retained. With a 60% threshold, PLHIV would have reached consensus on only 9 items versus 69 items among providers. Furthermore, PLHIV did not achieve a consensus level above 70%. In comparison, with a 50% threshold, consensus among PLHIV is attained for 34 items, reducing the dramatic discrepancy with provider ratings, and improving comprehensiveness. As to rejected items, they were those for which neither group attained the threshold of consensus. Undecided items were those in which the threshold was reached in only one group. As the objectives of the first Delphi round are distinct from those of the second round, a manuscript devoted only to Round 1 is justifiable.

Participants
HIV providers were recruited, with personalized email invitations, from the participating sites of the I-Score Study (or PROM development study) and from the investigators’ networks. Providers from the following categories were sought: physicians, nurses, pharmacists, psychologists/psychiatrists, social workers and community-based organization staff. They needed to have at least 5 years of experience providing services to PLHIV. PLHIV were recruited from the same sites, from included providers, and from community-based organizations. If interested, their emails were forwarded to the research coordinator who emailed them information on the Delphi. This included briefing interested PLHIV on how to complete the survey, to properly orient their responses:

“Please note: In the Delphi, you will be asked to rate the questionnaire items on their importance (i.e. is the particular barrier to adhering to HIV medication important?). When doing so, consider the item’s importance to you and to people living with HIV, in general. Your role is to evaluate the questionnaire, not your own personal barriers to adhering to HIV medication.”

PLHIV were required to be at least 18 years of age, to have at least 12 months of experience on ART, and to self-report difficulty taking their ART in the past 5 years. A minimum of 25% women was established for PLHIV and providers. At least 50% of each group recruited in Canada was to be anglophone. Finally, a minimum of three metropolitan cities needed to be represented within each country.

The survey
The survey was designed with SurveyMonkey Inc. Email invitations were sent to eligible individuals which contained a survey link. A reminder was sent if the survey was not initiated after one week of sending the email. Prior to beginning the survey, participants indicated their informed consent. Item presentation was ordered and contextualized based on the domains and subdomains of the measure’s conceptual framework. After rating each item, a free-text space was provided for comments. All Delphi panelists were compensated for their participation.

Data analysis
The Delphi panelists were described with sociodemographic variables, split into two groups: PLHIV and
providers. These variables were summarized with absolute and relative frequencies.

The observed ratings of the Delphi panelists for each of the 100 items were summarized by the proportion of the panelists who rated an item 3 (quite) or 4 (very), on both importance and actionability. In line with the study objectives, the proportions were split into several pairs for comparison: PLHIV versus providers, females versus males, English versus French questionnaire, and Canada versus France. The proportions were compared with Pearson’s Chi-square test for $2 \times 2$ contingency tables [22], to assess the null hypothesis of no difference between two proportions. For items where more than 20% of the cells of the corresponding contingency table had expected frequencies less than 5, a Fisher’s exact test was used [23]. The $p$-values of the tests are reported for each item, with a significance level of 5%, acknowledging that this may encompass borderline results [24].

Respondent comments were organized by item and by group (PLHIV versus providers) in table form to detect and describe patterns. They are reported, as needed, to help contextualize the quantitative findings.

Results

Response rate
Participants were recruited from December 2018 to October 2019. Of 147 invitations sent, 120 individuals opened the email, while 106 began the survey, and 97 completed it, for a total response rate of 66%. In all, 57 providers and 40 PLHIV formed the panel. It took panelists, on average, 1 h and 44 min to complete the survey.

Panel description
The mean age of PLHIV was 45.1 (SD: 16.1, Range: 20–72) while the mean age of providers was 44.3 (SD: 10.3, Range: 30–68). Additional characteristics of participating PLHIV and providers are presented in Table 2 which also shows that our recruitment goals for gender and language were met. Overall, the panel’s composition included more respondents who completed the questionnaire in French (55%, English: 45%), Canadian residents (58%, France: 42%), and females (62%, males: 36%, trans: 2%).

Table 2 Sociodemographic characteristics of the Delphi panelists (n = 97)

| Characteristic                        | People with HIV n/40 (%) | Service providers n/57 (%) |
|--------------------------------------|--------------------------|---------------------------|
| Country of residence                 |                          |                           |
| Canada                               | 24 (60)                  | 33 (58)                   |
| France                               | 16 (40)                  | 24 (42)                   |
| Gender                               |                          |                           |
| Female                               | 22 (55)                  | 38 (67)                   |
| Male                                 | 16 (40)                  | 19 (33)                   |
| Trans                                | 2 (5)                    | 0 (0)                     |
| Survey language                      |                          |                           |
| English                              | 16 (40)                  | 28 (49)                   |
| French                               | 24 (60)                  | 29 (51)                   |
| Health and social service provider   |                          |                           |
| Nurse                                | –                        | 14 (24)                   |
| Physician                            | 13 (23)                  |                           |
| Pharmacist                           | 13 (23)                  |                           |
| Social worker                        | 6 (14)                   |                           |
| Community organization staff         | 5 (9)                    |                           |
| Psychologist or psychiatrist         | 4 (7)                    |                           |
| City                                 |                          |                           |
| Montreal (Quebec)                    | 21                       | 24                        |
| Toronto (Ontario)                    | –                        | 5                         |
| St-Jérôme (Quebec)                   | 3                        | 3                         |
| Vancouver (British Columbia)         | –                        | 1                         |
| Paris (France)                       | 7                        | 9                         |
| Lyon (France)                        | –                        | 5                         |
| Nantes (France)                      | 2                        | 5                         |
| Clermont-Ferrand (France)            | 5                        | 3                         |
| Tourcoing (France)                   | –                        | 1                         |
| Missing (France)                     | 2                        | 1                         |
| Education                            |                          |                           |
| Primary                              | 4 (10)                   | –                         |
| Secondary                            | 9 (22)                   |                           |
| College/CEGEP/Technical degree       | 13 (33)                  |                           |
| University                           | 11 (28)                  |                           |
| Other                                | 2 (5)                    |                           |
| Missing                              | 1 (2)                    |                           |
| Sexual orientation                   |                          |                           |
| Heterosexual                         | 23 (57)                  | –                         |
| Homosexual                           | 13 (33)                  |                           |
| Bisexual                             | 4 (10)                   |                           |
| History of drug use                  |                          |                           |
| Yes                                  | 10 (25)                  | –                         |
| Years providing HIV care/services    |                          |                           |
| 5–9                                  | –                        | 28 (49)                   |
| 10–14                                |                         | 8 (14)                    |
| 15–19                                |                         | 8 (14)                    |
| ≥ 20                                 |                         | 12 (21)                   |
| Missing                              | 1 (2)                    |                           |

Objective 1: The most important and actionable items

Table 3 provides decisions on the 100 items (i.e. retained, undecided, rejected). Thirty-one items (31%) met the consensus criteria in both PLHIV and providers. These items covered all six domains of the conceptual framework and were distributed across 15 of its 20 subdomains. Two of the four subdomains of the Healthcare services and system domain were not represented by these items (i.e., HIV clinic issues, Pharmacy issues) as were 2 of
the 3 subdomains of the Characteristics of ART domain (i.e., Instructions, Physical features). Panelist comments on the component items of these domains provided little explanation for these results, except for item 98 which five providers remarked was unclear or too vague. The last subdomain not represented was Substance use [composed of two items: Using recreational/party drugs (item 16) and Drinking alcohol (item 15)] within the Lifestyle factors domain. In the panelist comments, for item 16, six providers mentioned the need to consider the quantity and/or type of drug taken (e.g., ‘...a weekend of crystal meth will have a much greater impact on adherence than a joint’ translated from French). Likewise, for item 15, eight provider comments indicated that the key issue for them is the quantity of alcohol consumed (e.g., “Drinking too much?”). Hence, this subdomain’s limited perceived relevance may be explained by some providers’ view that it is the degree of substance use, not necessarily the practice per se, which determines to what extent it qualifies as a barrier.

Twenty-eight items (28%) were rejected, as fewer than 50% of PLHIV and 60% of providers deemed them both important and actionable. They covered all framework domains as well as 14 of its 20 subdomains.

For 41 items (41%), panelists were undecided. For most (n = 39/41, 95%), providers had reached consensus but not PLHIV. All domains were represented by these items as were 17 of the 20 subdomains.

Objective 2: The clarity of retained items

For all 31 retained items, over two-thirds of each group (PLHIV and providers) deemed the item “quite” or “very” clear. The range of proportions was 68–85% for PLHIV and 67–98% for providers. For details see Additional file 2: Table S1. For two retained items, one group achieved a consensus level below 70% (i.e., 67% among providers for item 57 and 68% among PLHIV for item 90). The panelist comments on item 57, “Being too sick or ill”, showed that five providers wanted greater precision (e.g., ‘AIDS? Too sick to take their Rx? Severe acute illness like a gastro[enteritis]?’ Translated from French). Indeed, for 12 of the 31 items (39%), there was at least one provider comment on the need for greater precision (e.g., ‘In what sense? Translated from French, ‘Doesn’t say enough about why’, ‘About something in particular?’). For item 90, “Feeling pressured or powerless with my primary provider in decisions about my health”, PLHIV provided two comments, neither of which helped explain the limited clarity of this item. Hence, it is unknown if these PLHIV clarity ratings signify a problem with item length, terminology (e.g., powerless), or some other issue that complicates understanding.

Objective 3: Stakeholder group differences

Table 3 shows the results of the comparative analyses of the ratings of PLHIV and providers. For 62 items (62%), a significant difference was observed between the proportions of PLHIV and providers who deemed an item both important and actionable. In every case except one, a greater proportion of providers endorsed the item. The exception was item 53, “Getting good tests results (viral load or CD4 cell count)” (PLHIV: 33% versus Providers: 16%, p = 0.05), a rejected item. When examining the comments made by PLHIV on the items in the Delphi, over a third (78/214) were unambiguous descriptions of their personal experience of an ART adherence barrier (e.g., ‘When I am not at home, I do not take my medications because I want to be a normal person,’ ‘I very seldom drink’). PLHIV emphasis on direct experience with a barrier to determine relevance may thus be contributing to this rating differential with providers on importance/actionability.

The comparison by gender yielded six significant differences (for the full results, see Additional file 3: Table S2). In every case, a greater proportion of males versus females considered the item both important and actionable: Item 7-retained (as per Table 3): An irregular or unpredictable schedule (Females: 58% vs. Males: 89%, p = 0.01); Item 22-undecided: Not wanting to think about having HIV (Females: 52% vs. Males: 80%, p = 0.01); Item 56-rejected: Not having symptoms of HIV (Females: 28% vs. Males: 49%, p = 0.05); Item 69-undecided: Having privacy or confidentiality concerns related to HIV at my clinic (Females: 47% vs. Males: 71%, p = 0.02); Item 74-rejected: Anticipating side effects (Females: 35% vs. Males: 66%, p = 0.01); and Item 90-retained: Feeling pressured or powerless with my primary provider in decisions about my health (Females: 60% vs. Males: 83%, p = 0.02).

Objective 4: Cross-cultural equivalence

Comparing the items by language of questionnaire completion revealed three significant differences, again, based on the proportion of those considering the item both important and actionable. The results are as follows: Item 24-rejected (as per Table 3): Worrying about becoming
| Item | Conceptual framework | Domain | Subdomain | Item is important and actionable\(^a\) | p-value | Decision\(^b\) |
|------|---------------------|--------|-----------|----------------------------------------|---------|--------------|
|      |                     |        |           | PLHIV (%) | Providers (%) |            |
| My activities: Lifestyle factors |        |        |           |            |             |            |
| 1    |                     |        | Demands and organization of daily life |          |            |            |
| A change to my daily routine | | | | 33 | 63 | 0.01 | Undecided |
| Travelling | | | | 50 | 56 | 0.55 | Undecided |
| The weekend | | | | 20 | 33 | 0.15 | Rejected |
| Forgetting | | | | 58 | 88 | 0.01 | Retained |
| Work or school | | | | 33 | 40 | 0.43 | Rejected |
| Home or family responsibilities | | | | 38 | 54 | 0.10 | Rejected |
| An irregular or unpredictable schedule | | | | 55 | 79 | 0.22 | Retained |
| Being too busy | | | | 40 | 53 | 0.01 | Rejected |
| Not being at home | | | | 53 | 63 | 0.29 | Retained |
| My medication schedule conflicting with my sleep pattern | | | | 43 | 72 | 0.01 | Undecided |
| My medication schedule conflicting with my eating pattern | | | | 33 | 61 | 0.01 | Undecided |
| Having other priorities in my life than taking my medication | | | | 33 | 82 | 0.01 | Undecided |
| My medication schedule conflicting with my daily activities | | | | 35 | 79 | 0.01 | Undecided |
| Having trouble fitting my medication into my daily life | | | | 40 | 86 | 0.01 | Undecided |
| Substance use | | | |            |             |            |
| Drinking alcohol | | | | 33 | 58 | 0.01 | Rejected |
| Using recreational/party drugs | | | | 40 | 72 | 0.01 | Undecided |
| My thoughts and feelings: Cognitive and emotional aspects | | | |            |             |            |
| Not being informed enough about my medication | | Knowledge | | 55 | 65 | 0.32 | Retained |
| Not being sure how to take my medication | | | | 50 | 75 | 0.01 | Retained |
| Not feeling motivated to take my medication | | Motivation | | 65 | 88 | 0.01 | Retained |
| Wanting control over when I take my medication | | | | 40 | 32 | 0.39 | Rejected |
| Wanting control over if I take my medication | | | | 45 | 61 | 0.11 | Undecided |
| Not wanting to think about having HIV | | Acceptance of HIV | | 40 | 77 | 0.01 | Undecided |
| Having trouble accepting that I have HIV | | | | 53 | 89 | 0.01 | Retained |
| Worrying about becoming dependent on my medication | | Beliefs | | 40 | 30 | 0.30 | Rejected |
| Feeling it is not natural for my mind and body to be taking medication | | | | 43 | 65 | 0.03 | Undecided |
| Feeling I can catch up with missed doses | | | | 35 | 54 | 0.06 | Rejected |
| Feeling medication is only for when you feel sick | | | | 43 | 81 | 0.01 | Undecided |
| Feeling that stopping my medication for a while is only normal | | | | 45 | 74 | 0.01 | Undecided |
| Feeling that I must take my medication my way | | | | 48 | 60 | 0.24 | Undecided |
| Doubting my medication's effects on HIV | | | | 38 | 79 | 0.01 | Undecided |
| Being reminded about HIV when taking my medication | | | | 48 | 67 | 0.06 | Undecided |
| Feeling my medication is toxic or harmful | | | | 55 | 88 | 0.01 | Retained |
| Feeling like I have no control over my health | | | | 50 | 49 | 0.93 | Undecided |
| Worrying about taking my medication with recreational/ party drugs or alcohol | | | | 35 | 54 | 0.06 | Rejected |
| Having trouble trusting my medication | | | | 40 | 65 | 0.02 | Undecided |
| Having trouble trusting the healthcare system | | | | 38 | 65 | 0.01 | Undecided |
| Doubting that I need my medication | | | | 38 | 81 | 0.01 | Undecided |
| Struggling to accept that my medication has both good and bad sides | | | | 50 | 74 | 0.02 | Retained |
| Thinking that HIV is a death sentence | | | | 48 | 42 | 0.60 | Rejected |
| Item | Conceptual framework | Domain | Subdomain | Item is important and actionablea | p-value | Decisionb |
|------|----------------------|--------|-----------|---------------------------------|---------|-----------|
| PLHIV (%) | Providers (%) |
| 40 | Worrying about becoming resistant to my medication | | | | | |
| 41 | Feeling sad or depressed | | | | | |
| 42 | Being afraid | | | | | |
| 43 | Being angry | | | | | |
| 44 | Being worried or anxious | | | | | |
| 45 | Feeling stressed out | | | | | |
| 46 | Having mixed (ambivalent) feelings | | | | | |
| 47 | Feeling discouraged | | | | | |
| 48 | Being tired of taking my medication every day | My health: Health experience and state | | | | |
| 49 | Feeling well | Bodily signals | | | | |
| 50 | Feeling unwell | | | | | |
| 51 | My body telling me I should not take my medication | | | | | |
| 52 | Feeling my body needs a break from my medication | | | | | |
| 53 | Getting good test results (viral load or CD4 cell count) | Medical signs of HIV and general health | | | | |
| 54 | Getting discouraging test results (viral load or CD4 cell count) | | | | | |
| 55 | Having no symptoms of HIV | | | | | |
| 56 | Having symptoms of HIV | | | | | |
| 57 | Being too sick or ill | | | | | |
| 58 | Having medications to take other than those for HIV | Comorbidity | | | | |
| 59 | Having another health condition to deal with (for example, depression, diabetes or heart disease) | | | | | |
| 60 | Not getting the support I need from others | My situation: Social and material context | Relations with others | | | |
| 61 | Feeling isolated or alone | | | | | |
| 62 | Having relationship problems with someone close to me (for example, conflict or loss) | | | | | |
| 63 | Others discouraging me from taking my medication | | | | | |
| 64 | Being with friends or family | | | | | |
| 65 | Feeling unloved or unneeded | | | | | |
| 66 | Not wanting others to notice that I take this medication | HIV stigma and privacy concerns | | | | |
| 67 | Being concerned about stigma or discrimination related to HIV | | | | | |
| 68 | Fearing rejection because of HIV | | | | | |
| 69 | Having privacy or confidentiality concerns related to HIV at my clinic | Challenging material circumstances | | | | |
| 70 | Having financial problems | My medication: Characteristics of antiretroviral therapy | Side effects | | | |
| 71 | Not having a stable or suitable place to live | | | | | |
| 72 | Having trouble getting food or the right kind of food | | | | | |
| 73 | Worrying about the long-term side effects of my medication | | | | | |
| 74 | Anticipating side effects | | | | | |
dependent on my medication (French: 43% vs. English: 23%, p = 0.03); Item 43-undecided: Being angry (French: 60% vs. English: 39%, p = 0.03); and Item 53-rejected: Getting good test results (viral load or CD4 cell count) (French: 15% vs. English: 32%, p = 0.05).

The analyses by country found 7 significant differences, with 6 items endorsed by a greater proportion of Canadian residents. They included Item 14-undecided: Having trouble fitting my medication into my daily life (Canada: 59% vs. France: 78%, p = 0.05); Item 26-rejected: Feeling I can catch up with missed doses (Canada: 59% vs. France: 29%, p = 0.01); Item 36-undecided: Having trouble trusting the healthcare system (Canada: 64% vs. France: 39%, p = 0.01); Item 44-rejected: Being worried or anxious (Canada: 61% vs. France: 39%, p = 0.03); Item 55-rejected: Having no symptoms of HIV (Canada: 52% vs. France: 43% vs. English: 23%, p = 0.03); Item 43-undecided: Being angry (French: 60% vs. English: 39% p = 0.03); and Item 53-rejected: Getting good test results (viral load or CD4 cell count) (French: 15% vs. English: 32% p = 0.05).

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27%, \( p = 0.01 \)); Item 70-undecided: Having financial problems (Canada: 77% vs. France: 44%, \( p = 0.01 \)); and Item 74-rejected: Anticipating side effects (Canada: 59% vs. France: 29%, \( p = 0.01 \)). For the full results of the cross-cultural analysis see Additional file 3: Table S2.

**Discussion**

The general aims of this study were to evaluate the content validity and cross-cultural equivalence of items for a patient-reported measure of barriers to ART adherence through a stakeholder consultation in Canada and France employing Delphi techniques. The content validity of a PROM is essential and relates to its relevance, comprehensiveness, and comprehensibility [19]. Overall, less than a third of items (\( n = 31 \)) met our relevance criteria, based on the importance and actionability ratings of both PLHIV and HIV health and social service providers. As to comprehensibility, these retained items were deemed clear by over two-thirds of each stakeholder group. Finally, judged against our conceptual framework, retained items covered 100% of domains and 75% of subdomains, suggestive of good comprehensiveness.

**Relevance**

Differences in perspectives between PLHIV and their providers have been observed in such areas as HIV care [12], antiretroviral therapy [25], and adherence to ART [11]. For close to two-thirds of items in this study, statistically significant differences were observed in the combined importance and actionability ratings of PLHIV and providers. In almost every case, providers deemed the items more important and actionable. These findings may indicate response bias [26]. For instance, social desirability may lead PLHIV to endorse fewer barriers [27]. Alternatively, as suggested by their comments, many PLHIV may have responded to an item based on whether or not they personally experienced it, thus limiting the number of relevant barriers reported. In contrast, provider responses may reflect years of clinical practice, during which exposure to a wider range of barriers and their impacts is more likely. We addressed this differential and potential threat to our measure’s content validity, by lowering the consensus threshold for PLHIV to 50%, verging on the 51% cutoff recommended by some for Delphi investigations [28]. However, how to respond to and explain such differences between important stakeholder groups in PROM development could be further investigated. Indeed, authors of other Delphi work have underscored the complex elements that can contribute to differences in stakeholder decision-making (e.g., past experience, expectations, cultural factors) and argued for greater attention to this process [29, 30].

Few significant differences in item relevance were based on gender and, when observed, invariably a greater proportion of males endorsed the item. The six items concerned covered all six domains of the conceptual framework. Meta-analyses have established that the male gender is associated with a small advantage in adherence to antiretroviral therapy [31, 32]; however, predictors of adherence in males and females can differ [31]. Further investigation of our PROM with a study powered to analyze the influence of gender is needed to verify these findings. An adequate number of transgender persons could also be included in these analyses. Limited recruitment of this population led to their omission from the comparative analyses in this study. Globally, both transgender men and women are disproportionately burdened by HIV [33] and can face unique barriers to HIV care and adherence to ART (e.g., transphobia, hormone use) [34]. Future research could be designed to assess the content validity of the final PROM specifically among transgender persons.

**Comprehensiveness**

The comprehensiveness of adherence barrier measures, both HIV-specific and generic, is often limited [13, 35], which motivated our development of a new PROM. HIV-specific ART adherence barrier measures, on average, have covered approximately a third of subdomains of our conceptual framework and the involvement of patients in their development is reported for less than a third [13]. Items related to healthcare tend to be underrepresented in such instruments relative to those of other domains such as patient- and medication-related factors [13, 21]. Indeed, in our previous work, we found over three-quarters of HIV-specific barrier measures reviewed included no item on the healthcare system or services [13]. While physicians have been criticized for treating non-adherence as a patient problem and responsibility [36], there was little evidence of this in our results. Retained items covered patient factors well (i.e., 12 (29%) items distributed among cognitive and emotional aspects as well as lifestyle factors) but also addressed PLHIV’s social and material context (7 items), their health experience (4 items), the characteristics of ART (4 items), and the healthcare services and system (4 items), with particular emphasis on the patient-provider relationship.

Interestingly, no item based on substance use (Items 15 and 16) was retained. One was rejected (Item 15: Drinking alcohol) while the other was undecided (Item 16: Using recreational/party drugs). This is puzzling as active substance use is reported to be a major predictor of poor ART adherence in PLHIV [37]. Furthermore, a meta-analysis found 13% of adults with HIV reported alcohol
and/or substance misuse as a barrier to their ART adherence [38]. As the panelist comments suggest, a lack of emphasis on problematic alcohol or drug use (e.g., abuse, addiction) for providers and, among PLHIV, limited personal experience of or willingness to admit these barriers, may be at the source of the items’ dismissal. This will be explored during Round 2 of the Delphi.

**Comprehensibility**
The comprehensibility of the retained items, based on the clarity ratings, appeared good overall. However, over a third of retained items were the object of a provider comment requesting greater precision. Ambiguity is certainly a concern when selecting items [26]; it can arise when content is too general, while content that is too specific can limit relevance. An aim with the new PROM is to help initiate and guide patient-provider conversations on ART adherence barriers, which are expected, in turn, to provide details on the patients’ experiences. In short, the PROM is not intended to provide all the answers. Hence, most items were not modified due to these comments. Our measure’s content will be further assessed based on cognitive interviews with PLHIV who, as the targeted respondents of the instrument, are best suited to evaluate its comprehensibility [19]. These will also gather patient input on such aspects as the measure’s instructions, response scale, recall period, length, and appropriateness.

**Cross-cultural equivalence**
The cross-cultural validity of patient-reported medication adherence measures is rarely assessed [39]. In this study, comparative analyses on the language of questionnaire completion (English, French) and country of respondents (Canada, France) to evaluate the cross-cultural equivalence of the items only identified significant differences in a few rejected or undecided items. Hence, no differences in perceived importance and actionability, as defined, were found among the retained items, providing encouraging evidence of their applicability to and comparability in settings in both Canada and France.

**Limitations**
Several limitations are worth mentioning. Firstly, in this content validation study, as mentioned, the adherence barriers of specific populations with HIV (e.g., gender non-conforming individuals) may not be sufficiently accounted for. Further work will need to evaluate this for the instrument’s widespread applicability. Secondly, statistically, the results we obtained through an analysis of proportions may lack generalizability, due to the moderate sample size and purposive sampling. Non-parametric tests for hypothesis testing were adopted to compensate for this but they can over or underestimate the true difference when the amount of variability differs between the groups and, relative to parametric tests, they have less power. Further research with a larger sample and a parametric approach could help resolve these issues and provide more robust results. Nevertheless, based on criteria advanced by COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) for a PROM content validity study, our sample size is considered adequate [19]. Thirdly, a protocol deviation occurred in this study resulting in differential consensus thresholds between the panel groups. While unconventional, it seemed necessary to preserve the content validity of the instrument. Finally, redundancies may still be present in the 31 retained items (e.g., 4 items address side effects) and a shorter measure may be more appropriate for use in HIV care. Further consideration of these issues and validation of our instrument with stakeholder consultation is thus in order. Cognitive interviews with 12 additional people with HIV will inform next steps as will the Delphi’s second round.

**Conclusions**
This Delphi study provided useful information to reduce the number of items for our measure as well as evidence of the retained items’ content validity and cross-cultural equivalence. It shed light on the ART adherence barriers of greatest interest to both PLHIV and HIV providers in Canada and France which proved multidimensional. Different patterns of item endorsement highlighted the interest of engaging multiple stakeholder groups in measure development [29] but also of further studying their methodological implications.

**Abbreviations**
ART: Antiretroviral therapy; CD4: Cluster of differentiation 4 (CD4 T helper cells are white blood cells); CIHR: Canadian Institutes of Health Research; COSMIN: COnsensus-based Standards for the selection of health Measurement INstruments; CTN: Canadian HIV Trials Network; HIV: Human immunodeficiency virus; IISP: Investigator-initiated study program; PLHIV: People living with HIV; PROM: Patient-reported outcome measure; REB: Research ethics board; Rx: A medical prescription; SD: Standard deviation.

**Supplementary Information**
The online version contains supplementary material available at https://doi.org/10.1186/s41687-022-00435-0.

**Additional file 1.** Instructions provided to Delphi panelists in the Round 1 online survey.

**Additional file 2.** Item clarity ratings of PLHIV and providers.

**Additional file 3.** Item importance and actionability for HIV care by gender, questionnaire language, and country.

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Authors’ contributions
KE designed the study and was responsible for drafting the manuscript and integrating co-author feedback. SV led the quantitative analyses and wrote sections of the methods and discussion. KM participated in data analysis. KE, SV, KM, DL, SA, and BL interpreted the results. SA provided methodological guidance. BL led recruitment for the Delphi. All authors provided important edits to the manuscript and approved the final version.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations
Ethics approval and consent to participate
This web-based study was conducted as a part of the I-Score Study which obtained ethics approval from the Research Ethics Board (REB) of the McGill University Health Centre in Nantes, France (RC17_0310 N° EUDRACT: 2015-2331/14-229 PSY), the site of participant inclusion, and the REB of the University Health Centre’s Research Institute in Montreal, Quebec, Canada. This web-based study was conducted as a part of the I-Score Study, which is supported, in part, by the CIHR HIV Clinical Trials Network (CTN 283) and by a research Grant from the Investigator. KE is supported by a SPOR Mentorship Chair in Innovative Clinical Trials Network (ICTN) funding from CIHR to BL (Grant No. 383427). BL is supported by a career award, LE 250, from the Quebec Ministry of Health for researchers in Family Medicine. The Delphi benefited from methodological expertise and funding from the Quebec SPOR Support Unit-McGill Methodological Developments Platform (Grant No. M006). The Delphi is a subproject of the PROM development study, the I-Score Study, which is supported, in part, by the CIHR HIV Clinical Trials Network (CTN 283) and by a research Grant from the Investigator.

Consent for publication
All participants consented to the use of their data for research purposes, including its publication, as specified in the consent form.

Competing interests
The authors declare that they have no competing interests.

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