Psychometric Evaluation of the Immunoglobulin Patient Experience With Treatment (IgPET) in Primary Immunodeficiency Diseases

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INTRODUCTION

- Primary immunodeficiency diseases (PIDDs) are a group of genetic disorders in which part of the immune system is impaired or absent[1]
- Individuals with PIDDs are at increased risk of infections and typically require immunoglobulin replacement therapy (IgRT)[1]
- IgRT is administered intravenously or subcutaneously, and patients may have a range of options from self-administration of subcutaneous treatment at home to administration of intravenous treatment by a clinician at home or in a clinic
- For patients, IgRT may require substantial time and coordination depending on the route and location of administration
- To the authors' knowledge, no previous study has used a patient-centered measure developed specifically for individuals with PIDD on either subcutaneous or intravenous IgRT to systematically evaluate patients' experiences on IgRT

OBJECTIVE

- To conduct an initial psychometric evaluation of the reliability and validity of the Immunoglobulin Patient Experience with Treatment (IgPET), a new self-reported measure of treatment experience for patients who have PIDD and receive IgRT

METHODS

- Study design and implementation of the psychometric validation of the IgPET are presented in **Figure 1**.
- The IgPET was developed in accordance with the US FDA's guidance for the evaluation and use of patient-reported outcome (PRO) measures[2]
- The IgPET-item set was developed previously from a series of cognitive debriefing interviews conducted in April and May 2017 among 21 patients in the United States who had PIDD and were treated with IgRT (Shire data on file)
- The study protocol was approved by RTI International's Institutional Review Board

Figure 1. Study design and eligibility criteria

Study type	Noninterventional, cross-sectional, web-based survey
Participants	• Adults with self-reported PIDD in the United States • Identified and recruited via email through the Immune Deficiency Foundation (IDF), a US-based patient advocacy organization
Patient recruitment	• Email invitation was sent to IDF to approximately 7,400 members • Email included brief study overview and a unique web link, allowing interested individuals to complete the survey online
Data collection	• 6 weeks from July to August 2017 • Participant characteristics (eg, sex, age, race, and clinical characteristics) were collected, and 3 PRO measures were administered (Table 1)
Eligibility criteria	• Self-reported PIDD and use of IgRT (subcutaneous or intravenous) • ≥18 years old • Could understand and provide consent • Able to complete survey in English

IgRT, immunoglobulin replacement therapy; PIDD, primary immunodeficiency disease; PRO, patient-related outcome.

Table 1. Characteristics of PRO measures administered in the patient survey

Measure	Number of Items	Content	Recall Period	Response Scale	Interpretation
Ig Patient Experience With Treatment (IgPET) questionnaire	19	3 subscales: Convenience, Control, and Impacts and Interference, and 3 informative items	Current experiences	5-point ordered response scales: "strongly agree" to "strongly disagree" or "not at all" to "an extreme amount"	1 to 5; Higher = better treatment experiences
Life Quality Index (LQI)[3]	15	3 subscales: Treatment Interferences, Therapy-related Problems, Therapy Settings	Current treatment satisfaction	7-point scale with different anchors per item	0 to 100; Higher = greater treatment satisfaction
Treatment Satisfaction Questionnaire for Medication (TSMQ-9)[4]	9	3 subscales: Effectiveness, Convenience, Global Satisfaction	"Over the last 2 to 3 weeks or since you last used it [Ig medication]"	5- or 7-point anchors	0 to 100; Higher = greater treatment satisfaction

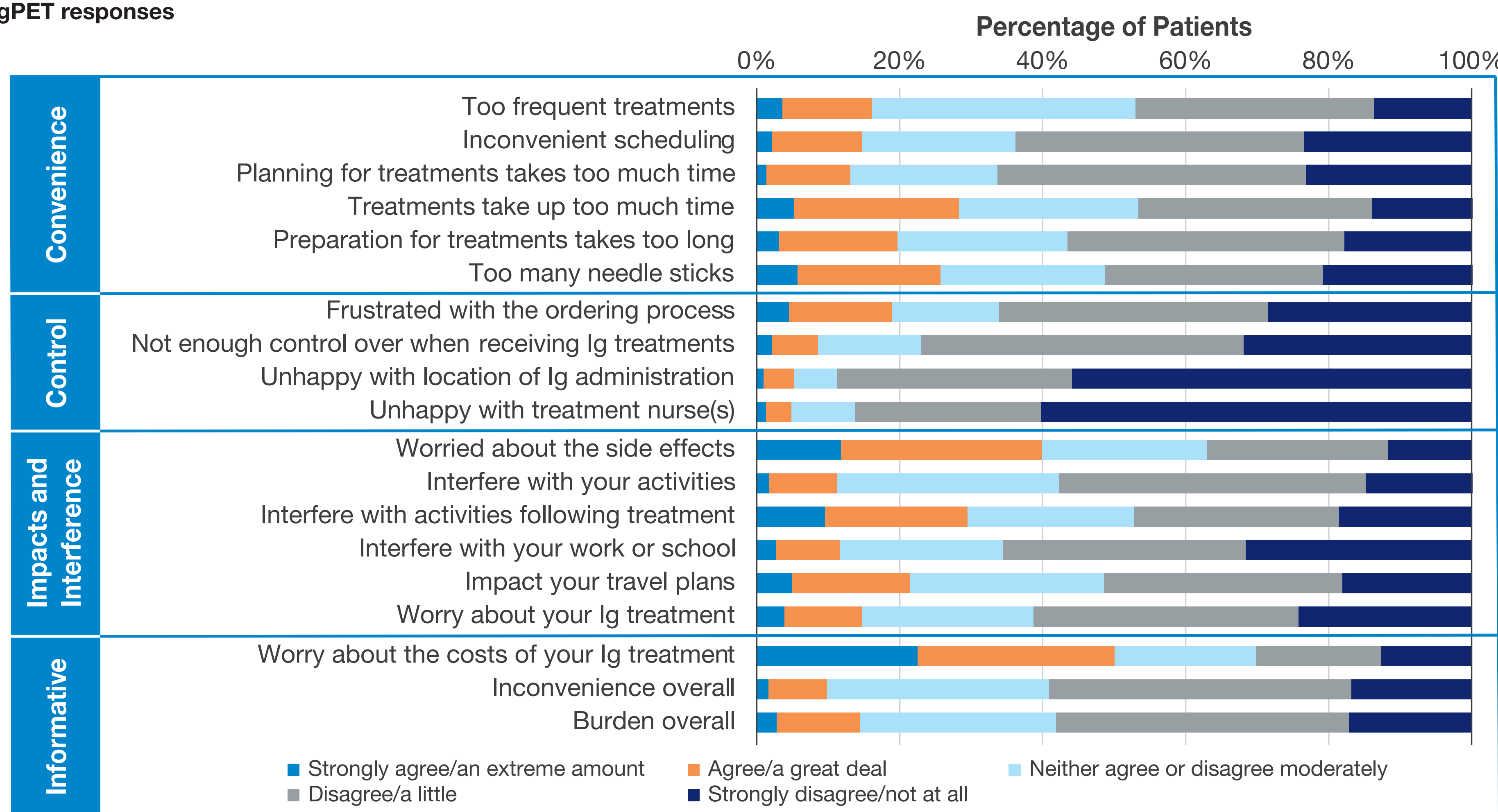Ig, immunoglobulin; PRO, patient-related outcome.

- Psychometric properties evaluated
  - Psychometric tests were conducted to assess item performance, IgPET structure, IgPET scoring, internal consistency reliability, construct validity, and known-groups validity (**Figure 2**)

Figure 2. Psychometric properties evaluated

Psychometric Property	Evaluation
Item performance	• Descriptive statistics (means, standard deviations [SDs], range, missingness) were computed and tabulated

IgPET structure	• Interitem and interscale correlations were computed and tabulated to inform potential IgPET subscales and the relationship between the subscales, respectively
	  – All interitem correlations were hypothesized to be positive
	• Factor analysis
	  – Data were randomly allocated into an exploratory factor analysis (EFA; n=407) or a confirmatory factor analysis (CFA; n=407) sample
	  – The EFA was used to distill agreed-upon concepts from the qualitative development study
	    • The number of factors were based on eigenvalues and scree test results
	    • The number of items within each factor were based on the size and pattern of the factor loadings, interpretability of the factor(s), other item-level psychometric properties, and results from the qualitative development of the IgPET
	  – The conceptual framework was then evaluated with the CFA, in which the comparative fit index,[5] the Tucker-Lewis Index,[6] and the root mean square error of approximation[7,8] were used to assess the model fit

IgPET scoring (missing rules)	• The maximum tolerable number of missing items were calculated for all IgPET scales using a threshold for Cronbach's alpha of 0.70
Internal consistency reliability	• Internal consistency reliability of the IgPET subscales was assessed by computing Cronbach's alpha • An alpha in the range of 0.70 to 0.90 was considered indicative of a strongly related set of items, able to support a unidimensional score structure without redundancy[9]

Construct validity	• A priori hypotheses were proposed regarding the relationships between items and/or subscales with similar constructs within the IgPET items, IgPET subscales, TSMQ-9 subscales, and LQI items. For example:
	  – Positive correlations were expected between all IgPET items and the LQI subscales and between IgPET items and TSQM-9 subscales
	  – Specific correlations between IgPET items and LQI subscales and between IgPET items and TSQM-9 subscales were expected to be at least moderate in strength (indicated in Table 5)
	• Construct validity correlations were also computed between IgPET subscales and between the LQI and TSQM-9 scores

Known-groups validity	• Analysis of variance testing was used to assess a priori hypotheses regarding the direction of mean scores on IgPET between patient groups:
	  – Patients with lower values on the TSQM-9 Global Satisfaction subscale would have worse IgPET scores than those with higher values on the TSQM-9 Global Satisfaction subscale
	  – Patients who had been on their current Ig treatment for >1 year were compared with those who had been on their current Ig treatment for ≤1 year
	• All statistical tests were 2-tailed, and a type I error rate of 5% (alpha = 0.05) was applied to each significance test, unless otherwise stated

IgPET, Immunoglobulin Patient Experience with Treatment; IgRT, immunoglobulin replacement therapy; LQI, Life Quality Index; PIDD, primary immunodeficiency disease; TSQM, Treatment Satisfaction Questionnaire for Medication.

RESULTS

- Demographic and clinical characteristics for the 814 patients who met eligibility criteria and completed the survey are shown in **Table 2**

Table 2. Patient demographic and clinical characteristics

Patient characteristic	Frequency	Percent*
Age, years		
18 to 30	56	6.9
31 to 64	576	70.8
≥65	182	22.4
Sex		
Male	128	15.7
Female	683	83.9
Prefer not to answer	3	0.4
Ig administration		
Subcutaneous	479	58.8
Intravenous	335	41.2
Hispanic		
Yes	13	1.6
No	792	97.3
Prefer not to answer	9	1.1
Race/ethnicity (select all that apply)		
White	779	96.7
African-American or Black	5	0.6
American Indian	10	1.2
Asian	2	0.2
Mixed race (1 or more races)	17	2.1
Other or prefer not to answer	18	2.2
Current employment status (select all that apply)		
Full-time	279	34.3
Part-time	93	11.4
Student full-time or part-time	30	3.7
Not employed but looking for employment	19	2.3
Not employed due to disability	176	21.6
Retired	188	23.1
Other or prefer not to answer	51	6.3
Highest grade or level of education		
Less than high school	4	0.5
High school diploma or equivalent (GED)	48	5.9
Some college, associate degree, or technical school	252	31.0
College degree (eg, BA or BS)	264	32.6
Professional or graduate degree (eg, MS, MD, PhD, JD)	236	29.1
Other or missing	10	1.3
Type of health insurance coverage (select all that apply)		
Private insurance or health plan	631	77.5
Medicare	272	33.4
Medicaid	45	5.5
Military-related health care	39	4.8
Other or not sure	31	3.8

*Percentages are calculated out of valid responses for each item. Missing percentages are calculated out of the total (N = 814).

Item performance

- Respondents used the entire range of the IgPET scale from 1 ("strongly agree"/"an extreme amount") to 5 ("strongly disagree"/"not at all") when they considered each item (**Figure 3**)
- Mean scores for each IgPET item ranged from 2.7 (IgPET item 17: "How much do you worry about the cost of your Ig treatment?") to 4.4 (both IgPET item 8: "I am unhappy with where I receive my Ig treatments [home or clinic]" and IgPET item 9: "I am unhappy with my treatment nurse[s]")

IgPET structure

- Based on fit and interpretability, a 3-factor solution, including IgPET items 1–16, was selected as the best-fitting exploratory factor analysis (EFA) model (item-scale relationship presented in **Figure 3**)
- Confirmatory factor analysis (CFA) factor loadings ranged from 0.56 to 0.82, indicating that the subscales sufficiently described the relationships between items and concepts
- Results from the root mean square error of approximation indicated a fair fit (0.08), and the CFI and TLI results indicated a good fit (0.95 and 0.95, respectively)

IgPET scoring method

- The maximum tolerable number of missing IgPET items for each subscale was 2 for "Convenience" and "Impacts and Interference" and 1 for "Control" (**Table 3**)
  - The IgPET items "I am frustrated with the process needed to order my Ig treatment and supplies," "I am unhappy with my treatment nurse(s)," and "In general, how much does your Ig treatment interfere with your work or school" included checkboxes to enable the respondents to indicate that the item was not relevant to their therapy; if these boxes were checked, the item was considered missing for the analysis

Figure 3. IgPET responses

Response choice: items 1–11/items 12–19.
Ig, immunoglobulin; IgPET, Immunoglobulin Patient Experience with Treatment.

Table 3. Maximum tolerable number of missing responses by IgPET subscale

IgPET Subscale	Items/Scales Removed in Order of Removal	Number of Items/Scales Removed	Final Cronbach's Alpha	Maximum Tolerable Number of Missing Responses[a]
Convenience	6, 3	2	0.72	2
Control[b]	0	0	0.75	1
Impacts and Interference	12, 13	2	0.75	2

[a]Includes checkbox items.
[b]The Control subscale allows 1 missing answer due to checkbox items.
IgPET, Immunoglobulin Patient Experience with Treatment.

- IgPET subscale scores were calculated as follows:
  - Each subscale score was calculated as the mean of the non-missing items
  - If more than 2 items were missing on the "Convenience" or "Impacts and Interference" subscales or more than 1 item was missing on the Control subscale, the subscale was considered missing
- IgPET items 12–19 were reverse scored such that higher scores indicated better treatment experiences
- IgPET subscale scores ranged from 1–5, with higher scores indicating better treatment experiences

Reliability

- Cronbach's alphas were within the recommended range (0.70–0.90) for all subscales, indicating that each set of items was strongly related and capable of supporting a unidimensional scoring structure, without being redundant (**Table 4**)

Table 4. Cronbach's coefficient alpha results

IgPET Subscale	Alpha	n
Convenience	0.83	814
Control	0.75	196[a]
Impacts and Interference	0.84	481

[a]Listwise deletion of observations with missing values was conducted in the calculation of Cronbach's coefficient alpha. The "Control" scale contains 2 items with checkboxes to indicate "not applicable," therefore, the available sample for which to calculate alpha was relatively smaller than the other scales.
IgPET, Immunoglobulin Patient Experience with Treatment.

Construct validity

- Most of the item-level hypotheses were met (ie, the correlation was at least moderate in strength) (**Table 5**)

Known-groups validity

- IgPET mean scores were higher among respondents in the top quartile of the TSQM-9 Global Satisfaction Subscale (indicating higher patient satisfaction) and lower for respondents in the bottom quartile of the TSQM-9 subscale scores (P<0.05 for all IgPET items and subscales)
- Respondents who had been on Ig therapy >1 year also had higher mean IgPET item-level scores compared with those who had been on Ig therapy ≤1 year (P<0.05 for IgPET items 3, 4, 5, 8, 11, 13, 16, and 18, and the "Control" and "Impacts and Interference" subscales)

Table 5. Construct validity correlations for the TSQM-9 Convenience and Satisfaction subscales and LQI items

Cells with a bold outline indicate correlations that were hypothesized to be at least moderate in strength.
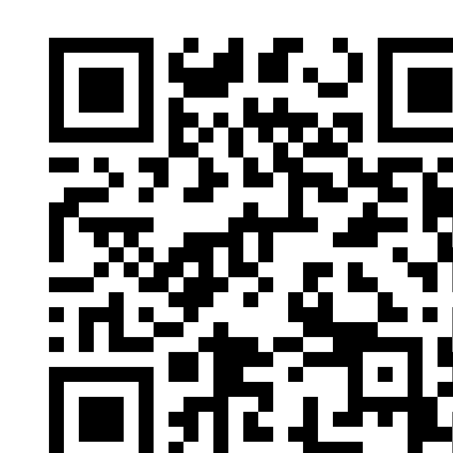Ig, immunoglobulin; IgPET, Immunoglobulin Patient Experience with Treatment; LQI, Life Quality Index; TSQM-9, Treatment Satisfaction Questionnaire for Medication.

SUMMARY

- The IgPET is an appropriate measure of patient experience with IgRT for use in individuals with PIDD
- Limitations:
  - The results may not be generalizable to populations outside of the US
  - Respondents were recruited through an advocacy organization and, therefore, were more likely to be engaged with their care and proactive about treatment
- Future studies may be warranted to evaluate the IgPET measurement properties using longitudinal study designs to assess responsiveness (the ability to detect expected changes) and test-retest reliability (the ability to provide consistent measurements when no change is expected). They should also include populations outside the US to ensure comparability across countries

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