



An introduction to Rasch analysis for Psychiatric practice and research

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ABSTRACT

This article aims to present the main characteristics of Rasch analysis in the context of patient reported outcomes in Psychiatry. We present an overview of the main features of the Rasch analysis, using as an example the latent variable of depressive symptoms, with illustrations using the Beck Depression Inventory. We will show that with fitting data to the Rasch model, we can confirm the structural validity of the scale, including key attributes such as invariance, local dependency and unidimensionality. We also illustrate how the approach can inform on the meaning of the numbers attributed to scales, the amount of the latent traits that such numbers represent, and the consequent adequacy of statistical operations used to analyse them. We would argue that fitting data to the Rasch model has become the measurement standard for patient reported outcomes in general and, as a consequence will facilitate a quality improvement of outcome instruments in psychiatry. Recent advances in measurement technologies built upon the calibration of items derived from Rasch analysis in the form of computerized adaptive tests (CAT) open up further opportunities for reducing the burden of testing, and/or expanding the range of information that can be collected during a single session.

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1. Introduction

The use of patient reported outcomes in health care in general, and psychiatry in particular, has seen a rapid expansion over recent years. The ascertainment of latent constructs such as anxiety, depression and self harm has seen a steady increase in the number of instruments designed to measure such attributes (Bowen et al., 2008; Brunner et al., 2007; Fliege et al., 2009; Gamez et al., 2007; Garlow et al., 2008; Honarmand and Feinstein, 2009; King et al., 2008; Klonsky et al., 2003; Latimer et al., 2009; Parker et al., 2005; Pedersen, 2006; Pomerleau et al., 2003; Terluin et al., 2006; Tuisku et al., 2009). While some instruments are administered by professionals, the majority are self completed 'patient reported outcomes' and are widely used in both clinical practice and research (Bech, 2008; Chan et al., 2010; Chandler et al., 2010; Counts et al., 2010; Hawton et al., 2002; Norris and Aroian, 2008; Steinhausen et al., 2009). The obvious value of such instruments is

that they can minimize the burden of assessment upon patients, and can be applied to large numbers, which may be more restricted, or not feasible in the case of structured clinical interviews.

However, the use of such scales has been the subject of some debate. Marshall et al. (2000), examining a number of controlled trials in schizophrenia, found that the intervention was more likely to be effective when unpublished scales were used, in opposite to validated ones. Another issue, which has been rarely considered, is that the majority of instruments derive ordinal scores, which indicate rank relationships (Stevens, 1946). Such scores are not capable of supporting mathematical calculations such as change scores, or parametric effect sizes (Smith, 2001). Consequently using ordinal scores in sophisticated parametric analyses could lead to misinference of the findings (Merbitz et al., 1989). However, ordinal scales, which provide a magnitude of the trait under consideration, are perfectly acceptable when the object is to identify a cut point, or magnitude of the trait, such as found in many instruments, for example, to ascertain depression. This application just relies on a specific magnitude, which is available from an ordinal scale. Thus, the problem is not necessarily the scale themselves (although it may be), but rather the way in which they are analysed.

In the formation of patient reported outcomes, the usual procedure has been to generate a scale with a certain number of

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items that intend to assess some observable behaviours related to the construct of interest (Tesio, 2003). Therefore, when setting out to measure such a construct we look for indicators (items) which are related to the construct, preferably in a way to be specified by an underlying theory. When someone responds to a certain question or item, the probability of the subject to endorse the item should depend on their level of the latent trait or ability (Baker, 2001). For example, it is expected that a more depressed subject will endorse an item regarding hopelessness more frequently than a non-depressed one. While this particular item does not directly measure depression (it addresses hopelessness), it helps in the construction of the depression score, together with other related items, which are designed to measure the latent variable (depression in this case).

In order to put together a set of items with the expectation that they measure the target construct, a set of psychometric requirements must be satisfied, and these requirements can be grouped into those associated with Classical Test Theory (CTT), and Modern Test Theory (MTT) (although in practice there is considerable overlap between the two). The present article aims to briefly review the former, and then go on to describe the potential contributions of the latter, in particular Rasch analysis, with respect to the development and testing of instruments. The Beck Depression Inventory (BDI) will be used as a practical example of this purpose.

2. Classical Test Theory

The measurement properties of most patient reported outcomes to-date have been evaluated from the CTT perspective. This has entailed publication of evidence concerning the reliability and the validity of the instrument. Reliability concerns whether or not the instrument has consistency, both internally (Cronbach's alpha) and over time (test–retest). Validity is often reported to comprise three central aspects, namely construct validity, criterion and content validity. These represent appropriate targeting, its relationship with a gold standard (e.g. a structured clinical interview), and whether the items appear to be consistent with expectations of an underlying theory (Nunnally, 1978). In practice, validity falls into two primary components, internal and external (Loevinger, 1957). The former concerns whether or not it is valid to add together the set of items and, within the framework of CTT, is primarily concerned with factorial validity. The latter is concerned with whether or not the instrument measures what is intended, and would include criterion validity. Reliability sits between these two, as in order to test reliability the summed score must be valid (i.e. internal validity). In order to test external validity, both the summed score and reliability must be shown to be adequate. Thus, the focus of CTT lies on the summed score, and its decomposition into true score and measurement error, the estimation of reliability, and the correlation between that summed score and other comparator measures, whether they are judged to be a gold standard, or not.

The Beck Depression Inventory – second edition (BDI-II) is one such example of a well-known instrument used to quantify depression (Beck et al., 1996) which has been developed using CTT. When a patient completes the BDI-II, a set of 21 items (scored 0–3) indicate the level of depression of this patient on a score which ranges from 0 to 63. A score of 29 and above is indicative of severe depression. A considerable body of evidence exists with regard the reliability and validity of this instrument (and the original version) (Beck et al., 1996; Hayden et al., 2010; Helm and Boward, 2003; Levin et al., 1988; Osma et al., 2004; Siegert et al., 2010). However, some concern has been expressed about the unidimensionality of the scale, and whether or not it is valid to add together all the items (Storch et al., 2004). Concerns have also been expressed (with regard the earlier version) about the reliability (test–retest) of the

instrument (Ahava et al., 1998). While there is a myriad of adaptations of the BDI into different languages, and for different diagnoses, some have raised issues about the absence of relevant scales in certain diagnoses or with particular groups, such as older people with cancer (Nelson et al., 2010). Nevertheless, such group/diagnosis-specific reliability and validity is fundamental, and has been recognized as a requirement for some time (Loevinger, 1957). Scales should have evidence of reliability and validity in every group for which their use is intended.

Although there are a few exceptions, one interesting aspect of the CCT approach is that every item is given an equal weight with respect to their contribution to the summed score. For example, an item that assesses suicidal ideation is given the same weight (raw score) as one that assesses inattention. Nevertheless, it is known that clinically a depressive syndrome with suicidal ideation is more severe and that this item alone indicates higher intensity of depression (Alexandrino-Silva et al., 2009; Clark et al., 1983; Pompili et al., 2008; Selvi et al., 2010; Van Gastel et al., 1997). Yet surprisingly, there are circumstances when the simple raw score is a sufficient statistic for the estimate of the persons underlying level of the trait. This notion of 'sufficiency' has also been around for a long time (Fisher, 1921) and implies that the raw score contains all the information required to estimate the persons level of, in our example, depression. It is also equivalent to a stochastically consistent ordering of all item pairs (Fischer and Molenaar, 1995). To ascertain whether or not this is the case, we can invoke Modern Test Theory and, specifically, the Rasch measurement model.

3. Modern Test Theory (MTT) and the Rasch model

The first MTT models (under the generic label of Item Response Theory –IRT) appeared in the 1950s in the education area based on the need to build tests that would be at the same time simple, valid and with high discrimination power (Embretson and Reise, 2000). IRT represents a group of several distinct models, which share in common an assumption that the response to any particular item is a function of the difference between the ability of the person (or in our example their level of depression) and the characteristics of the item which, in the Rasch model, is the difficulty of the item (or in our case, the level of depression implied by the item). Other IRT models have additional characteristics of items, but lose the key characteristics of sufficiency in doing so.

The Rasch Model is a one-parameter IRT approach that has been increasingly utilized in the health field (Reise and Waller, 2009; Rocha et al., 2012; Tennant et al., 2004a,b). In this model, the parameter of discrimination is fixed in the value of 1 for all the items, and then only the parameter of *difficulty* varies. As a consequence, the Rasch model is frequently considered a model of 1 parameter (*difficulty*) (Baker, 2001; Rasch, 1960). The main strength of this model is that it allows for testing if the simple summed raw score is a sufficient statistic (which cannot be done with other models) and also tests whether or not the data are consistent with the axioms of conjoint measurement, so providing a transformation to interval scaling, which also cannot be done with other models (Karabatos, 2001; Mitchell, 2003). By fitting data to the Rasch model, we can assume that the estimated latent measure, when generated by an instrument that fits Rasch Measurement Model requirements, is interval scaled. As such, given appropriate distributional properties, this estimate may be suitable for parametric operations, including basic aspects such as the calculation of change scores, and group comparisons using a *t*-test, as well as more complex models (such as structure equation modelling), given other requirements are also met (O'Connor and Tennant, 2008).

IRT in general, including Rasch analysis, explores the performance of each individual item rather than the total test score as in

CTT. All explorations are based on the assumption that the probability of someone endorsing an item (in the Rasch dichotomous case) depends *only* on the difficulty of the item and on the subject's ability. This probabilistic relationship is tested by a series of fit statistics, which examine the comparison between the theoretical item performance (i.e., subjects with more ability should get right answers, and more difficult items should be correctly answered by those who have higher ability) and the observed data (Andrich, 1988). Results are reported as a series of chi-square statistics and fit residuals. All are concerned with the amount of discrepancy between expected and observed data for that particular item. For example, where an item fits the Rasch Model, a chi-square probability should exceed 0.05 (that is no significant deviation), and a fit residual should be within a specified range (e.g. ± 2.5) (Pallant and Tennant, 2007).

4. An example using the BDI

To illustrate how data are fitted to the Rasch model, data were collected from a sample composed of 122 chronic patients, of whom 66 (54.1%) were male, and 56 (45.9%) were female. The most frequently reported health problems were hypertension (18%), heart diseases (15.6%), neoplasm (13.1%), diabetes (13.1%), emphysema/asthma/bronchitis (11.5%), autoimmune diseases (8.2%), and kidney diseases (8.2%). They were recruited in a tertiary hospital in Porto Alegre-RS-Brazil, in the different clinical and surgical inpatient units and outpatient clinics. The Ethics Research Committee of Hospital de Clínicas de Porto Alegre approved this investigation.

Table 1 shows the results of fitting the data from the BDI to the Rasch model. Thus, used the RUMM2020 software package (Andrich et al., 2004). With a Bonferroni correction to the Chi-Square item probability, all items are shown to fit the model, except the item 19 "Weight loss", which was excluded because of misfit (fit residual = 3.08; chi-square = 10.3; $P = 0.016$). Furthermore, all fit residuals are within the (99%) range of ± 2.5 . Note also the location of the items. These indicate the severity of depression associated with the item. Thus, a disturbed sleep pattern and loss of energy are associated even with low levels of depression, whereas suicidal thoughts would be affirmed by those only with very high levels of depression.

Table 1
Measures of fit and location (SE) of BDI items.

BDI items ^a	Location	SE	FitResid	ChiSq	Prob
16 Sleep pattern	-1.186	0.18	1.226	1.742	0.628
15 Loss of energy	-1.163	0.134	-0.118	0.536	0.911
20 Excessive worrying about health	-1.124	0.192	0.035	2.893	0.408
17 Tiredness or fatigue	-1.077	0.193	-1.122	5.237	0.155
21 Loss of interest in sex	-0.85	0.173	-0.761	5.168	0.160
6 Punishment feelings	-0.816	0.25	0.516	0.385	0.943
14 Appearance	-0.72	0.179	1.06	4.751	0.191
8 Self-criticalness	-0.704	0.143	2.063	8.685	0.034
10 Crying	-0.589	0.187	0.519	2.888	0.409
4 Loss of pleasure	-0.522	0.191	-2.322	9.848	0.020
13 Indecisiveness	-0.101	0.203	-0.238	3.109	0.375
2 Pessimism	-0.03	0.215	-1.388	5.178	0.159
18 Changes in appetite	0.048	0.18	1.486	10.542	0.014
11 Irritability	0.098	0.215	0.471	7.954	0.047
5 Guilty feelings	0.1	0.226	-0.568	3.339	0.342
1 Sadness	0.18	0.212	-2.084	10.214	0.017
12 Loss of interest	0.979	0.257	-1.381	4.607	0.203
7 Self-dislike	1.797	0.226	-0.82	1.738	0.628
3 Past failure	2.748	0.277	-1.5	5.403	0.145
9 Suicidal thoughts or wishes	2.931	0.423	0.805	2.372	0.499

^a Collapsing categories and excluding item 19 "Weight loss" because of misfit: fit residual >2.5.

Item fit can also be evaluated graphically by the Item Characteristic Curve (ICC), sometimes called the Item Response Function. It is based on the fact that individuals with more ability (latent trait) have more chance of succeeding the item. As we can observe the slope is a sigmoid and reminds us of an "S" (Baker, 2001). Fig. 1 shows the ICC of the item "Indecisiveness" of the BDI. Axis X indicates the latent depression estimate on an interval 'logit' scale and the Y axis represents the expected response value of the item. The sigmoid is the relationship expected by the model, and the dots on the line, represent the average response for groups at different ability (depression) levels (Andrich, 1978; Rasch, 1960). It can be seen that in this instance, the dots closely follow the expected curve, and so the item represents a good fit to the model expectations. Consequently the fit statistics, as reported at the top of the graph in the form of the fit residual, and the chi-square probability, each indicate a good fit to the model. These fit statistics are also reported in Table 1.

The BDI has a polytomous response structure, which is why the expected response ranges from 0 to 3 (the Rasch programmes always set the first category to 0). It is important to note that, in such circumstances, the distances between response options are not equal with respect to the underlying trait. For example, in the case of the BDI these distances vary considerably (Fig. 2) which is consistent with the partial credit parameterization of the Rasch model.

Also, sometimes the categories may not be ordered properly, and this may contribute to misfit. This is where the transition point between categories (threshold) does not follow an increasing level of the underlying trait. Such 'disordered thresholds' may arise because of ambiguity in response option wording, or by respondents having difficulty discriminating between options (perhaps when the category semantics are too close to one another). This can be accommodated within the Rasch model framework by collapsing categories until they are all ordered. Fig. 2 shows the item set after collapsing categories, where necessary. The way in which categories are collapsed is shown in Fig. 3 which illustrates an item with a disordered threshold together with its new Rasch-generated well-performing format. Thus, the Rasch model allows for testing potential alternative response formats, as well as for checking if these alterations improve the overall scale (Chachamovich et al., 2009; Chachamovich et al., 2008). In our case, originally only 6 out of the 21 BDI items showed ordered categories. Mostly, in 15 out of 21 BDI items, categories "1" and "2" which represents less severe symptoms, had to be collapsed. The resulting variability in scoring range across items is another reason to use the Partial Credit Model in the present analysis.

In addition, summary fit statistics indicate how well the scale, as a whole satisfies Rasch model expectations. Initially, in this sample,

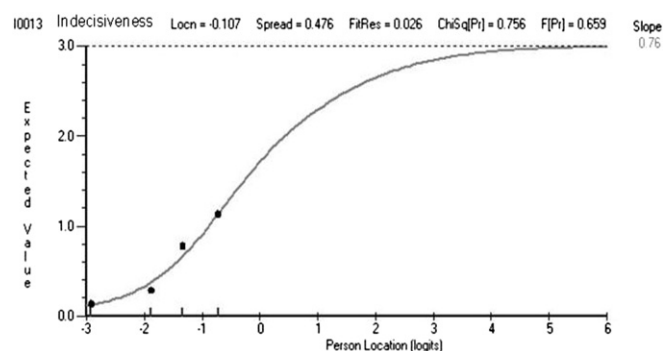


Fig. 1. Item characteristic curve of item 13 (Indecisiveness) of the Beck Depression Inventory (BDI).

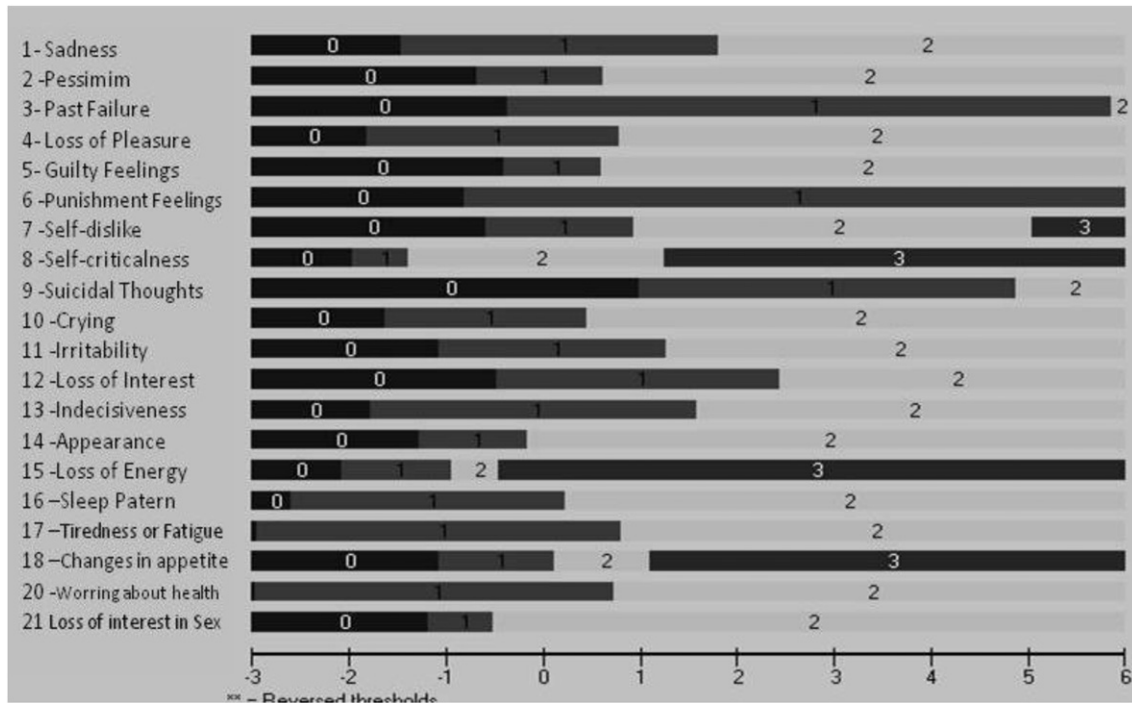


Fig. 2. Threshold map for BDI items.

before rescaling disordered thresholds, the BDI shows poor fit to model expectations, as indicated by a summary Chi-Square significance value that was very low, and a summary item residual standard deviation of 1.39 (Table 2). After rescaling, fit improved, but item 19 ‘Weight loss’ showed significant misfit to and so it was deleted. This improved the summary fit statistics and no individual item showed misfit to the model (Bonferroni corrected).

Where comparisons are desired, it is also required that an item is invariant across different subjects, such male/female, older/younger, ill/health, etc. As a consequence, a well-performing item should not show differential item functioning (DIF) (Tennant et al., 2004a,b). For example, when DIF is present, the probability of a subject endorsing an item (or category) when they have the same amount of depression differs according to group membership (e.g. gender). Thus, the estimation of depression level will be biased (e.g. by the gender of the subject) (McKenna et al., 2007). The process of Rasch Analysis also allows for a test for the presence of DIF, and provides information regarding item invariance and indicates which items require alterations or deletion in order to generate a DIF-free scale. In practice, the BDI items showed no DIF for gender, as is shown in Fig. 4 which plots the ICC for both males and females, as well as the model expectation.

Depending upon the application, the targeting of persons to items is an important feature of validity, and another additional feature of Rasch analysis. As the process plots both persons’ ability and items’ difficulty on one metric logit scale, a comparison (both visual and statistical) of the location of persons and items is possible, including the magnitude of difference between the mean person and item location, giving the overall targeting of the scale (Fig. 5).

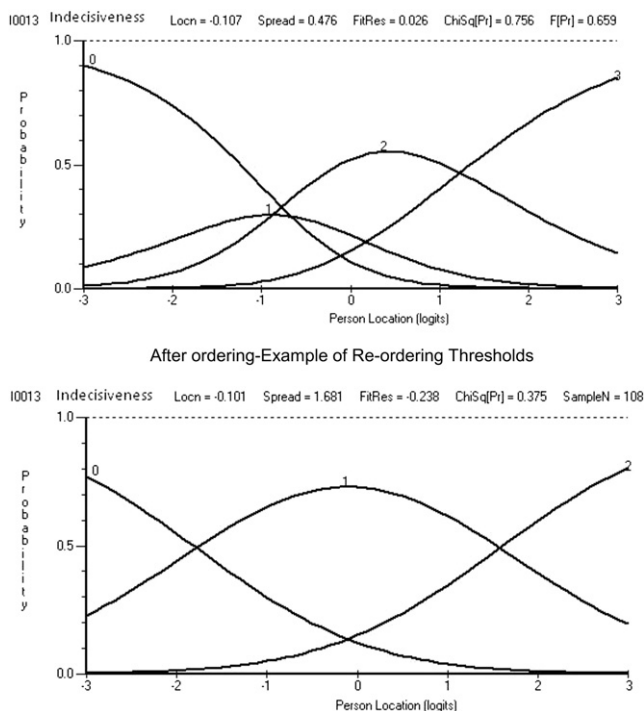


Fig. 3. Probability categories curves of the item 13 (Indecisiveness) of the BDI-example of disordered thresholds.

Table 2
Summary of measures of Rasch model fit for BDI items.

Measures of fit	Basal model	Adjusted model ^a	Subtest model ^b
Item fit residual (SD)	-0.13 (1.39)	-0.21 (1.22)	-0.17 (1.27)
Person fit residual (SD)	-0.13 (0.90)	-0.25 (0.99)	-0.22 (0.92)
Total item × 2	122.15	96.59	90.74
Chi-square P	0.000012	0.002	0.002 ^c
PSI	0.82	0.86	0.85
t-test P (IC 95%)	7.02% (6%–12%)	6.5% (2%–11%)	7.5% (3%–12%)

^a Collapsing categories and excluding item 19 “Weight loss”.

^b Subtest analysis: subtest1 items 5&7 5 ‘Guilty Feelings’ & 7 ‘Self-dislike’; subtest 2 13&16 13 ‘Indecisiveness’ & 16 ‘Changes in sleep pattern’; subtest3 6&20 6 ‘Punishment feelings’ & 20 ‘Excessive worrying about health’.

^c Bonferroni adjusted Chi_Square 0.002.

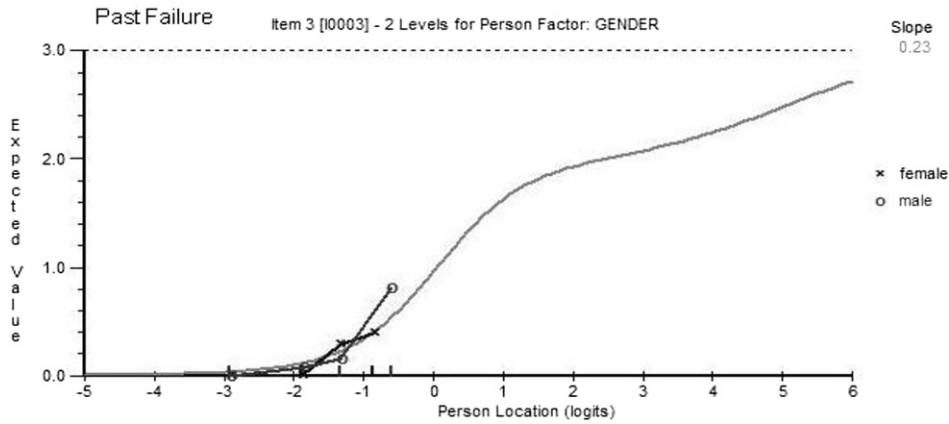


Fig. 4. DIF-free item from the BDI "Past failure".

In Fig. 5 the offset of persons (upper half) to items (lower half) may suggest a poorly targeted scale. Unless a substantial increase in depression is expected, this skewed distribution (with a floor effect) would not serve well as an outcome measure as considerable deterioration would be needed before any points were added to the scale score. The patients are a long way below the operational range of the scale (although from a probabilistic perspective they may nevertheless gain some points). Thus when a task is to measure the spectrum of depressive symptoms, new items around the low- and high extremes would improve the measurement range. By doing this, the amount of information around the clinical cut-point may decrease, but the knowledge about the whole spectrum will increase significantly (Bond and Fox, 2007). If, on the other hand, the scale is used as a screening instrument for depression among those not expected to have the condition (or a general population) then this distribution may be expected. What is a concern under these circumstances is that the clinical cut points are associated with the maximum degree of precision of the scale (usually at zero logits).

Dropping of one item and the collapsing of categories of 15 items have, as a consequence, changed the operational range of the scale, rendering the existing cut points invalid. However, within the framework of the Rasch analysis it is possible to equate tests. Thus, the calibrations of those items which were unchanged in the revised scale (that is not rescored) were used to anchor the revised metric to the original metric. In that way, the logit value of the original cut point (e.g. 29) can be used in the revised scale to

determine what the equivalent raw score would be. Thus, the original cut points of 19 and 29 would become 15 and 26 on the revised scale (Fig. 6).

Other requirements of the Rasch model are unidimensionality and local independence of items. Although some items (5 'Guilty Feelings' & 7 'Self-dislike'; 6 'Punishment feelings' & 20 'Excessive worrying about health'; 13 'Indecisiveness' & 16 'Changes in sleep pattern') were shown to be highly correlated in the residuals, suggesting potential redundancy (correlations >0.3 in residual correlation matrix), when these items were grouped (Subtest analysis) this procedure did not improve fit. Unidimensionality was confirmed by a post hoc *t*-test (% outside range 7.5%); binomial IC% (3–18%) (Table 2).

As such, by assessing these requirements, it is assured that, for example, the BDI measures exclusively depression (unidimensionality), and that the value attributed to each question (item) of the scale can be adequately added to the value of the other; that each item is measuring a relevant aspect and, given the level of depression of the person, does not depend on another item to have this information (local independence), and even if this item is administered to other respondent belonging to a different group it will continue measuring the same ability (invariance) (Tesio, 2003).

5. Discussion: Rasch applications in clinical research

This paper is an introductory paper to stress the potentialities of Rasch analysis for Psychiatric practice and research. The BDI was

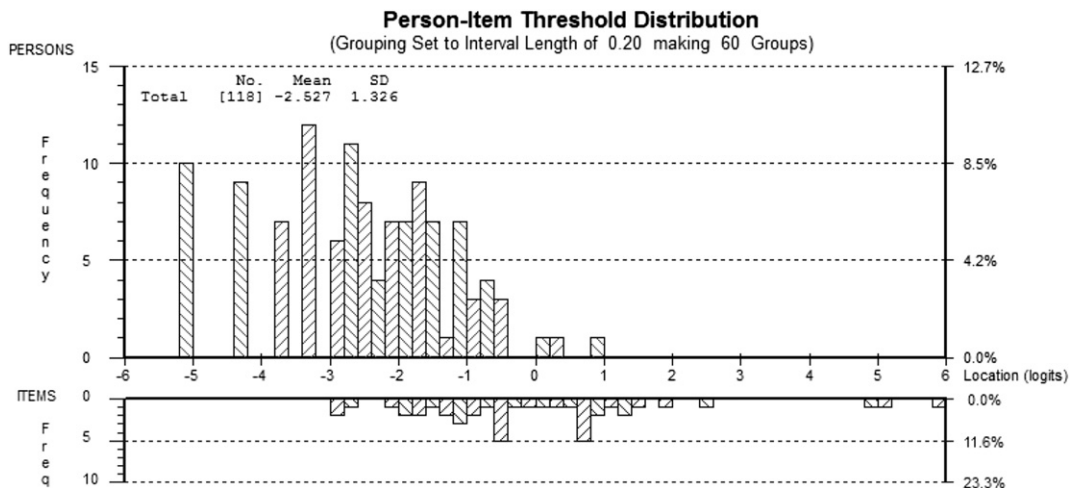


Fig. 5. Person-item distribution map.

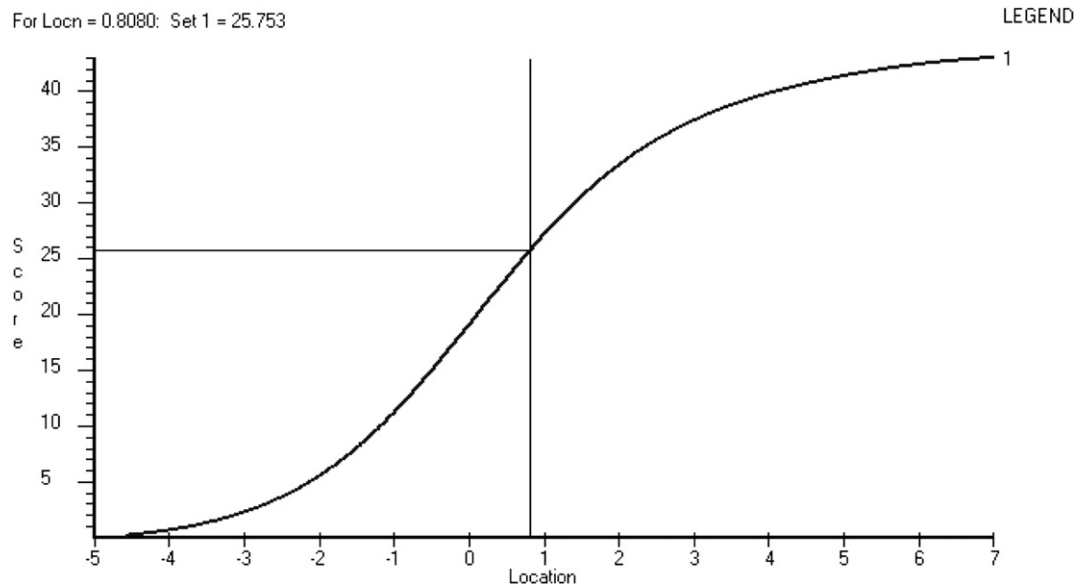


Fig. 6. Equating the original cut point (raw score 29) of logit value 0.808 to give the new raw score cut point for the revised scale.

used here merely as an example. The BDI has been shown to satisfy Rasch model expectations after some adjustments, in a mixed diagnostic sample of a tertiary hospital. Designed to be used in a clinical sample of depressed patients to ascertain the severity of that depression, the distribution of thresholds across the continuum of depression is consistent with that purpose. The removal of item 19 “weight loss” is consistent with the confounding of co-morbidity that may be expected when applied to other diagnostic groups, and this type of confounding has been found in other depression scales (Gibbons et al., 2011). In the present example, it reflects the fact that weight loss does not share a probabilistic structure with the other items in the scale. A purpose beyond our paper is to make definitive conclusions about the psychometric properties of BDI.

Rasch analysis represents the current quality standards in measuring outcomes (Sloan and Mandrekar, 2005; Tennant et al., 2004a,b). It complements Classical Test Theory by providing detailed analysis of how items work within scales, and whether or not their summed score is valid (Chachamovich et al., 2008). Ultimately, it examines scales and items in depth, and statistically tests the theoretical requirements. Where data are shown to fit the Rasch model, a transformation to interval scaling is available through exporting the latent estimate from the Rasch analysis programme. Consequently, Rasch analysis has been applied to several distinct areas and specialties, such as quality of life, pain, rheumatology, rehabilitation, neurology and ophthalmology (Hagell et al., 2003; Lamoureux et al., 2008; Pesudovs et al., 2010; Sloan and Mandrekar, 2005; Tennant and Conaghan, 2007; von Steinbüchel et al., 2010; Wolfe, 2003).

Increasingly, the development (Adler and Brodin, 2011; Cinnamon et al., 2011) and reviews of existing measures widely used in psychiatry are being published in appropriate journals (Castro-Costa et al., 2008; Kendel et al., 2010; Kørner et al., 2012; Licht et al., 2005; Pallant et al., 2006; Shea et al., 2009; Smith et al., 2006.)

There are several distinct advantages of applying the Rasch model to outcome scales in Psychiatry. Besides ensuring that the best quality standards for measurement are attained for any outcome scale, the process adds a layer of diagnostic information which is not available in CTT, and which may have clinical relevance. For example, just as much as items may misfit model expectations, so may persons. Consequently, persons whose responses differ from model expectations may indicate some

unknown pathology or co-morbidity which affects those responses. Where different scales are used in the same diagnostic groups, clinical caseness may vary solely because different scales result in different prevalence, for example, of depression (Covic et al., 2009). Rasch analysis allows for direct comparison of scale cut points under a common person equating study (same people fill out different scales at same time), so adding to the knowledge of the true variability of depression, and other conditions, as opposed to the potentially spurious variability derived from different scale-specific case ascertainment. Furthermore, an interesting application of this method would be its use for the definition of more homogeneous syndromes (Bouman and Kok, 1987), since the heterogeneity of depression construct for several types of settings: clinical, psychiatric or general population samples.

When items from different scales are calibrated on the same metric, an ‘item bank’ is formed (Forkmann et al., 2009). This opens up the possibility of Computer Adaptive Testing (CAT). CAT makes use of the calibrated items to provide ‘tailored testing’ for the individual. Often starting at the item representing an average level of depression, response to that item will determine the next item to be administered, and so on. In this way, relatively few items need to be administered, so providing a useful way to screen patients in, for example, a busy out-patient clinic.

Rasch analysis can also help adjust for cross-cultural differences where data is pooled, for example, in international clinical trials (Tennant et al., 2004a,b). It has frequently been used to explore cross-cultural properties of several well-known instruments and, again, whether the format demands adaptations for certain cultural contexts (Rocha et al., 2012; Ravens-Sieberer et al., 2007; Tennant et al., 2004a,b).

In summary, the present article briefly reviews the Rasch Measurement Model, its practical applications and potential for psychiatry. It is now widely adopted in many specialties, and has the potential to provide high quality measurement for everyday practice, and for research.

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Contributors

All authors managed the literature searches. Neusa Rocha and Alan Tennant undertook the statistical analysis, and Neusa Rocha, Eduardo Chachamovich and Marcelo Fleck wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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