Identification of response shift at the item level on Patient-reported outcomes changes using Rasch Measurement Theory models

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Background

- A better understanding of the experience of patients using ***Patient reported outcomes (PRO)*** ⇨ essential to assess the effectiveness of health care

- **PRO** ⇨ directly reported by the patients without interpretation of their responses by a clinician or anyone else
  - Measures of perceived health, QoL, fatigue, well-being…

- **Measurement and interpretation of PRO ⇨ conceptual, methodological, interpretational and practical issues**

Background

- Measurement and interpretation of PRO – Some issues
  - Cognitive processes involved in completing PRO are **complex**
  - PRO are often **multidimensional** with multiple items and dimensions
  - **Missing data** are often **non-ignorable** *(e.g. patients might be too tired to fill in the fatigue questionnaire)*
  - Measurement non-invariance

⇨ Patients might not respond to PRO consistently & might not be comparable *between groups (Differential Item Functioning, **DIF**)* and *over time (Response Shift, **RS**)*

Measurement non-invariance

- **Measurement non-invariance between groups & over time**
  - PRO data include *patients' perceptions of the items* which cannot be directly measured but can influence their responses
  - DIF: perception varies between groups *(e.g. gender, age)* ⇨ can alter the properties of questionnaires such as reliability, validity or ability to detect "true" differences
  - RS: perception varies over time *(e.g. change in meaning, in life priorities)* ⇨ erroneous conclusions for the detection of "true" change

Response Shift & clinical interpretation

- Should Response Shift be only reduced to measurement bias?

Example: in the context of cancer

- Likely that patients might regularly adapt to their illness ⇒ might give different answers to the questionnaires over time…
- Not only because their health has changed, but also because their ***perception*** of what QoL means to them has changed

Sprangers M & Schwartz C. *Soc Science Med* 1999;48:1507-15.

Methods for Response Shift

- **Mostly "sample-level" methods**
  - *Dimension-level* ⇨ *e.g.* Structural equation Modeling (*SEM*), Classification and Regression Trees (*CART*)
  - *Item-level* ⇨ *e.g.* Rasch Measurement Theory / Item Response Theory (*RMT/IRT*)

- Assume that the *whole sample* has been affected by the *same changes* in the perception of QoL over time BUT among a sample
  - Only some individuals might be affected by RS, ≠ types of RS might affect ≠ individuals to ≠ extent, might depend on known or unknown covariates

Oort F. *Qual Life Res* 2005;14:587-98. Lix et al. *Qual Life Res* 2013;22:695-03.
Guilleux et al. *Qual Life Res* 2015;24:553-64. Salmon et al. *Cancer Med* 2017;6:2562-75.

Methods for Response Shift

Alternative approaches

- *Dimension or item-level subgroup RS analyses*
  - Multigroup SEM, Growth Mixture Modelling (*GMM*) ± SEM, RMT and Guttman errors

- *Pros and cons*
  - Investigating differential RS in subgroups *± DIF simultaneously*
  - Known and unknown covariates (latent classes) *interpretation sometimes tricky*
  - *Multiple testing issues + MNAR data*

Sawatzky et al. *Qual Life Res* 2017 in press; Wu et al. *HQLO* 2017;15(1):102; Gadermann et al. *Qual Life Res* 2017;26:1463-72. Blanchin et al. *Qual Life Res* 2016;25:1385-93; Salmon et al. *Cancer Med* 2017;6:2562-75.

Objectives & Motivations

Objective

- Assessing the impact of know covariates on DIF and RS at item-level on PRO changes using longitudinal Rasch models

Statistical motivations

- Rasch models ⇨ specific objectivity property *(robust to MNAR data, simulation studies)*, interval measurements, item-level
- DIF and RS ⇨ jointly in the same modelling process *(latent regression)*
  ⇨ DIF stability over time + differential RS in subgroups
- Multiple testing ⇨ accounted for

Blanchin et al. *Stat Med* 2011;30:825-38; Blanchin et al. *Int J Appl Maths & Stats* 2011;24:SI-11A
De Bock et al. *Stat Methods Med Res* 2016;25:2067-87; De Bock et al. *Qual Life Res* 2015;24:19-29

Objectives & Motivations

Clinical motivation

- The term “cancer” includes various diseases and may generate ≠ social beliefs about prognosis and perceived dangerousness
- *Breast cancer & melanoma patients* might experience QoL changes and adaptation to their illness in a ≠ way during and after treatment ⇨ ≠ healthcare needs

Clinical objective

- Assess the impact of breast cancer and melanoma on DIF, RS and QoL changes *(Emotional Functioning, EF)*

Bourdon et al. *Qual Life Res* 2016;25:1969-79.

Statistical methods – ROSALI2

- Extension of the "RespOnse Shift ALgorithm for Item-level" (ROSALI) to incorporate covariates for assessing:
  - DIF between groups (breast cancer and melanoma)
  - Covariate effect on DIF, RS and QoL changes between 2 measurement occasions *(RS differentially estimated between groups)*

- Cross-sectional and longitudinal Partial Credit Models (PCM) to detect non-uniform and uniform recalibration RS
  - Iterative steps: DIF detection $\rightarrow$ RS detection $\pm$ DIF including *Bonferroni correction*

Guilleux et al. *Qual Life Res* 2015;24:553-64.

DIF detection – PCM at T1

Step A
DIF measurement model

$$P\left(X_{ij} = h \mid c_i, \theta_i, \delta_{j1}, \ldots, \delta_{jm_j}, \gamma_{j1}, \ldots, \gamma_{jm_j}\right) = \frac{\exp\left(h\theta_i - \left[\sum_{p=1}^{h} (\delta_{jp} + \gamma_{jp} c_i)\right]\right)}{\sum_{l=0}^{m_j} \exp\left(l\theta_i - \left[\sum_{p=1}^{l} (\delta_{jp} + \gamma_{jp} c_i)\right]\right)}$$

DIF parameters

- X_{ij}: response of patient i to item j
- Θ ~ N(0, σ^2); θ_i: latent trait level of patient i
- (δ_{jp}): item difficulties of item j
- m_j: number of positive response categories for item j
- c_i: group covariate
- γ_{jp}: DIF parameter *(uniform if* $\gamma_{jp} = \gamma_j \; \forall p; non\text{–}uniform\ otherwise)$

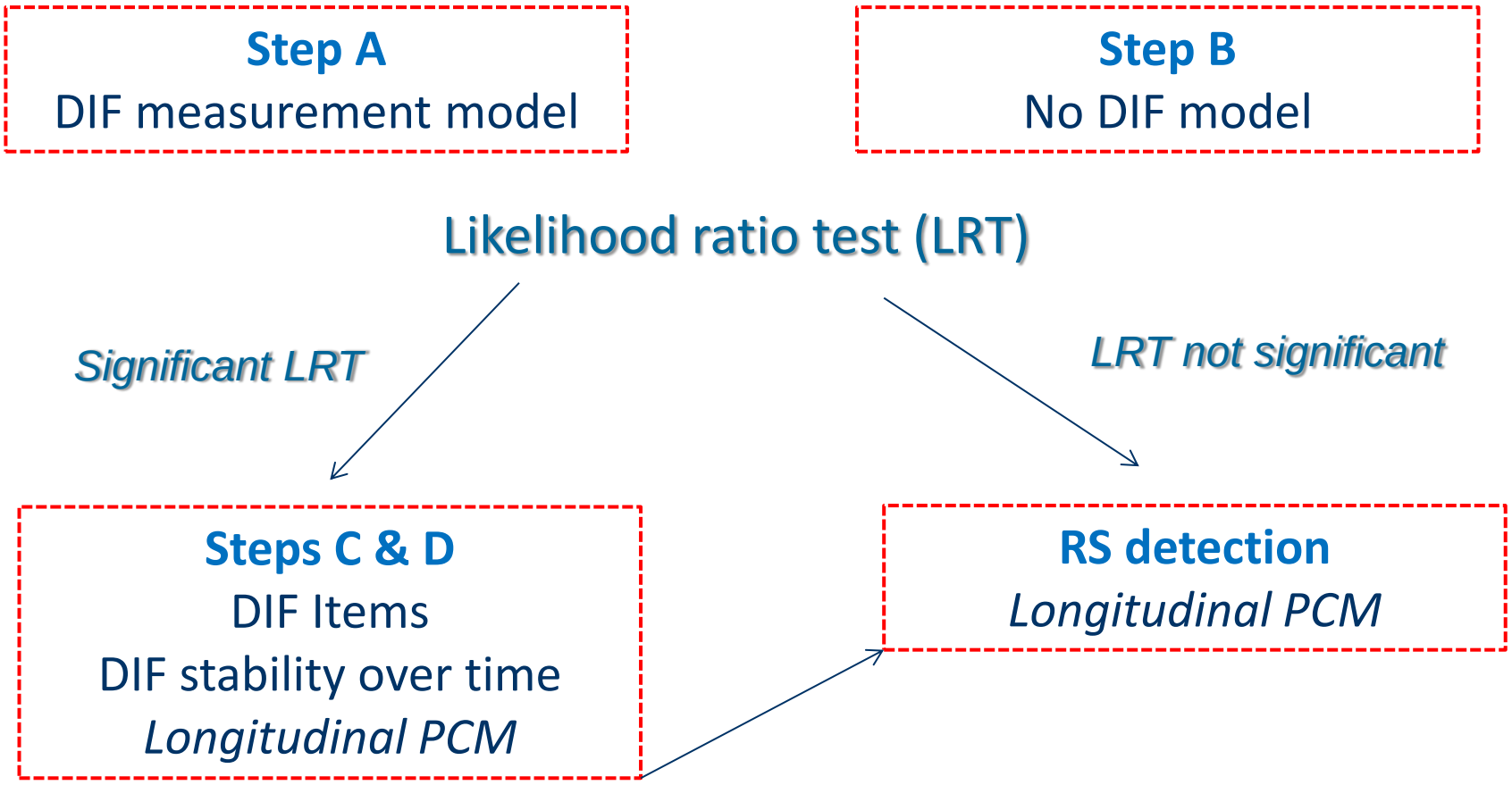
DIF detection – PCM at T1

Step B
No DIF model

$$P\left(X_{ij} = h|\beta, c_i, \theta_i, \delta_{j1}, \ldots, \delta_{jm_j}\right) = \frac{\exp\left(h(\beta c_i + \theta_i) - \sum_{p=1}^{h} \delta_{jp}\right)}{\sum_{l=0}^{m_j} \exp\left(l(\beta c_i + \theta_i) - \sum_{p=1}^{l} \delta_{jp}\right)}$$

- X_{ij}: response of patient i to item j
- Θ ~ N(0, σ^2); θ_i: latent trait level of patient i
- $\left(\delta_{jp}\right)$: item difficulties of item j
- m_j: number of positive response categories for item j
- c_i: group covariate
- β: regression parameter

DIF detection → RS detection



RS detection – Longitudinal PCM T1/T2

Step 1
RS measurement model ± DIF

$$\begin{bmatrix}\Theta^{(1)}\\ \Theta^{(2)}\end{bmatrix} \sim N\left(\begin{bmatrix}0\\ 0\end{bmatrix};\ \Sigma\right)$$

$$P\left(X_{ij}^{(t)} = h|\beta,\ c_i, \theta_i^{(t)}, \delta_{j1}, \dots, \delta_{jm_j},\ \eta_{j1}^{(t)}, \dots, \eta_{jm_j}^{(t)}, \gamma_{j1}^{(t)}, \dots, \gamma_{jm_j}^{(t)}\right)$$

$$= \frac{\exp\left(h(\beta c_i + \theta_i^{(t)}) - \left[\sum_{p=1}^{h}(\delta_{jp} + \eta_{jp}^{(t)} + \gamma_{jp}^{(t)}\, c_i)\right]\right)}{\sum_{l=0}^{m_j}\exp\left(l(\beta c_i + \theta_i^{(t)}) - \left[\sum_{p=1}^{l}(\delta_{jp} + \eta_{jp}^{(t)} + \gamma_{jp}^{(t)}\, c_i)\right]\right)}$$

Recalibration RS parameters

Constraints

$\eta_{jp}^{(1)} = 0\ \forall j, p$

Based on steps C & D

- No DIF: $\gamma_{jp}^{(1)} = 0\ \forall j, p$
- Uniform DIF: $\gamma_{jp}^{(t)} = \gamma_j^{(t)}$; Non-uniform DIF: $\gamma_{jp}^{(1)} = \gamma_{jp}^{(2)}$

RS detection – Longitudinal PCM T1/T2

Step 2
No RS model ± DIF

$$\begin{bmatrix}\Theta^{(1)}\\ \Theta^{(2)}\end{bmatrix} \sim N\left(\begin{bmatrix}0\\ \mu^{(2)}\end{bmatrix};\ \Sigma\right)$$

$$P\left(X_{ij}^{(t)} = h|\beta, \beta_{time*group}^{(t)}, c_i, \theta_i^{(t)}, \delta_{j1}, \dots, \delta_{jm_j}, \eta_{j1}^{(t)}, \dots, \eta_{jm_j}^{(t)}, \gamma_{j1}^{(t)}, \dots, \gamma_{jm_j}^{(t)}\right)$$

$$= \frac{\exp\left(h(\beta c_i + \beta_{time*group}^{(t)} c_i + \theta_i^{(t)}) - \left[\sum_{p=1}^{h}(\delta_{jp} + \gamma_{jp}^{(t)} c_i)\right]\right)}{\sum_{l=0}^{m_j}\exp\left(l(\beta c_i + \beta_{time*group}^{(t)} c_i + \theta_i^{(t)}) - \left[\sum_{p=1}^{l}(\delta_{jp} + \gamma_{jp}^{(t)} c_i)\right]\right)}$$

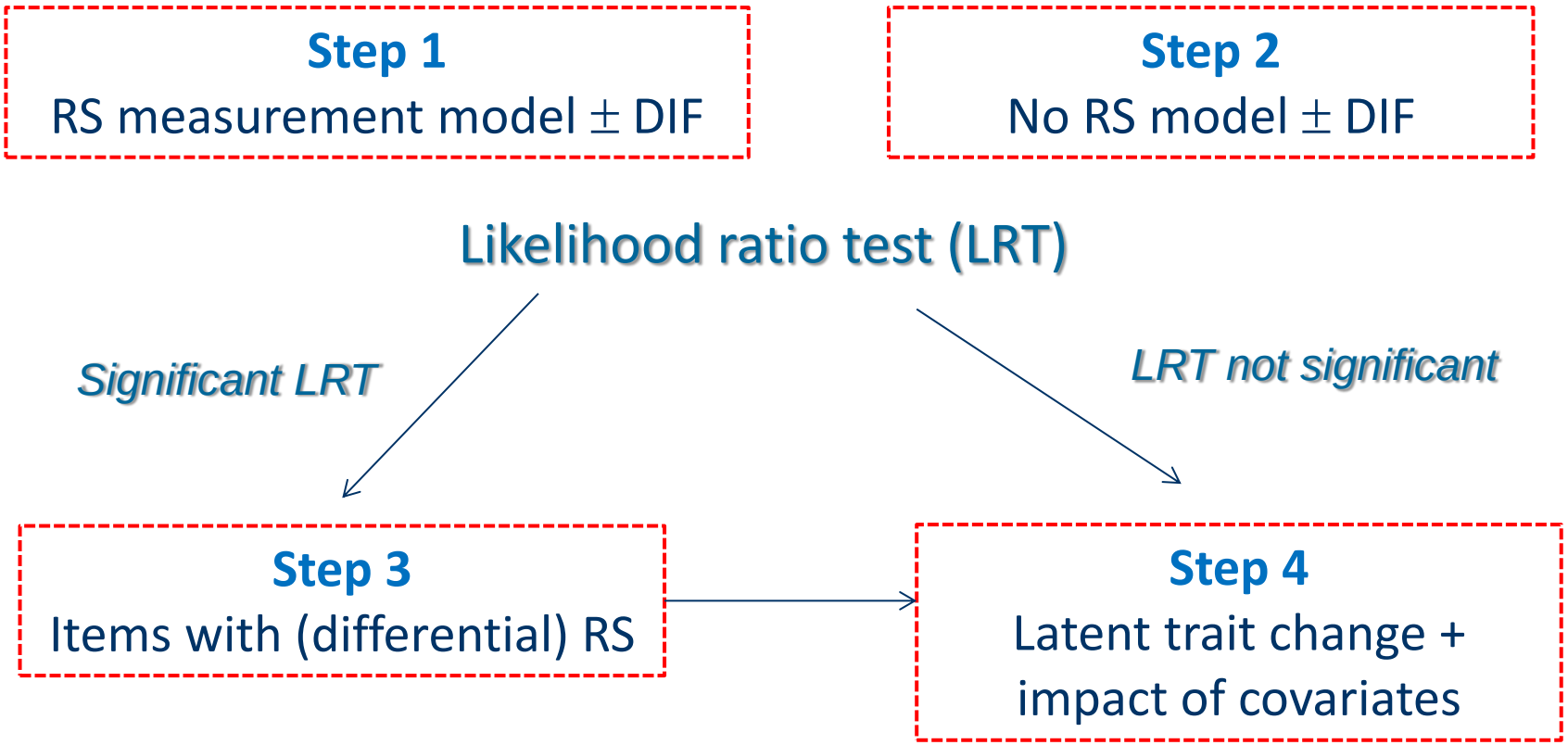
Constraints

$\eta_{jp}^{(t)} = 0\ \forall j, p, t$

Based on steps C & D

- No DIF: $\gamma_{jp}^{(1)} = 0\ \forall j, p$
- Uniform DIF: $\gamma_{jp}^{(t)} = \gamma_j^{(t)}$; Non-uniform DIF: $\gamma_{jp}^{(1)} = \gamma_{jp}^{(2)}$

DIF detection → RS detection



Material & methods – ELCCA study

Study design

- Prospective longitudinal study, 2 year-follow-up: *within 1 month after diagnosis (T1), 12 (T2) and 24 (T3) months after* $\rightarrow$ *focus on first year*

Inclusion criteria

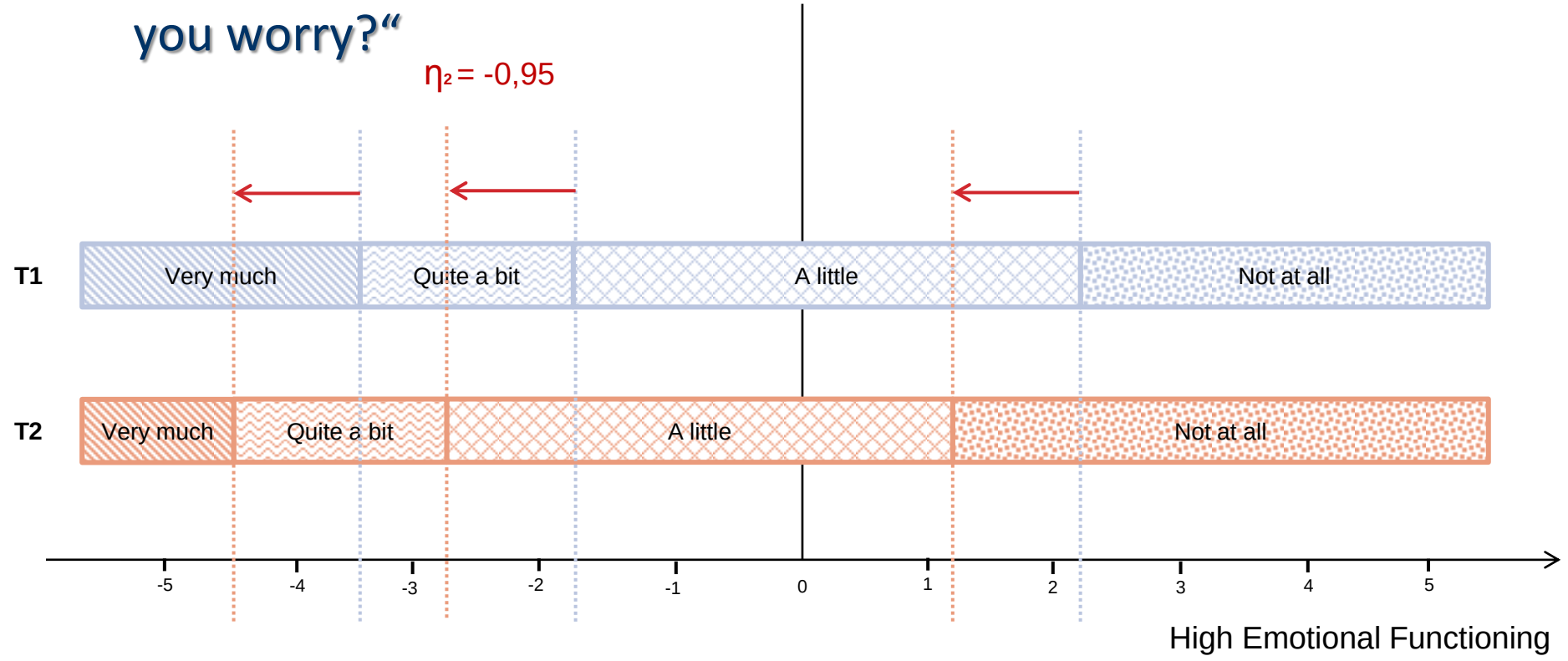
- Adults, early stage non-metastatic (stages I and II) melanoma and breast cancer (BC), informed consent

PRO Measures

- Cancer-specific Quality of Life Questionnaire (QLQ-C30 version 3.0), emotional functioning (EF) scale with 4 items
  - *During the past week:* Did you feel tense? Did you worry? Did you feel irritable? Did you feel depressed?
  - *4-point Likert scale:* Not at all, A little, Quite a bit, and Very much

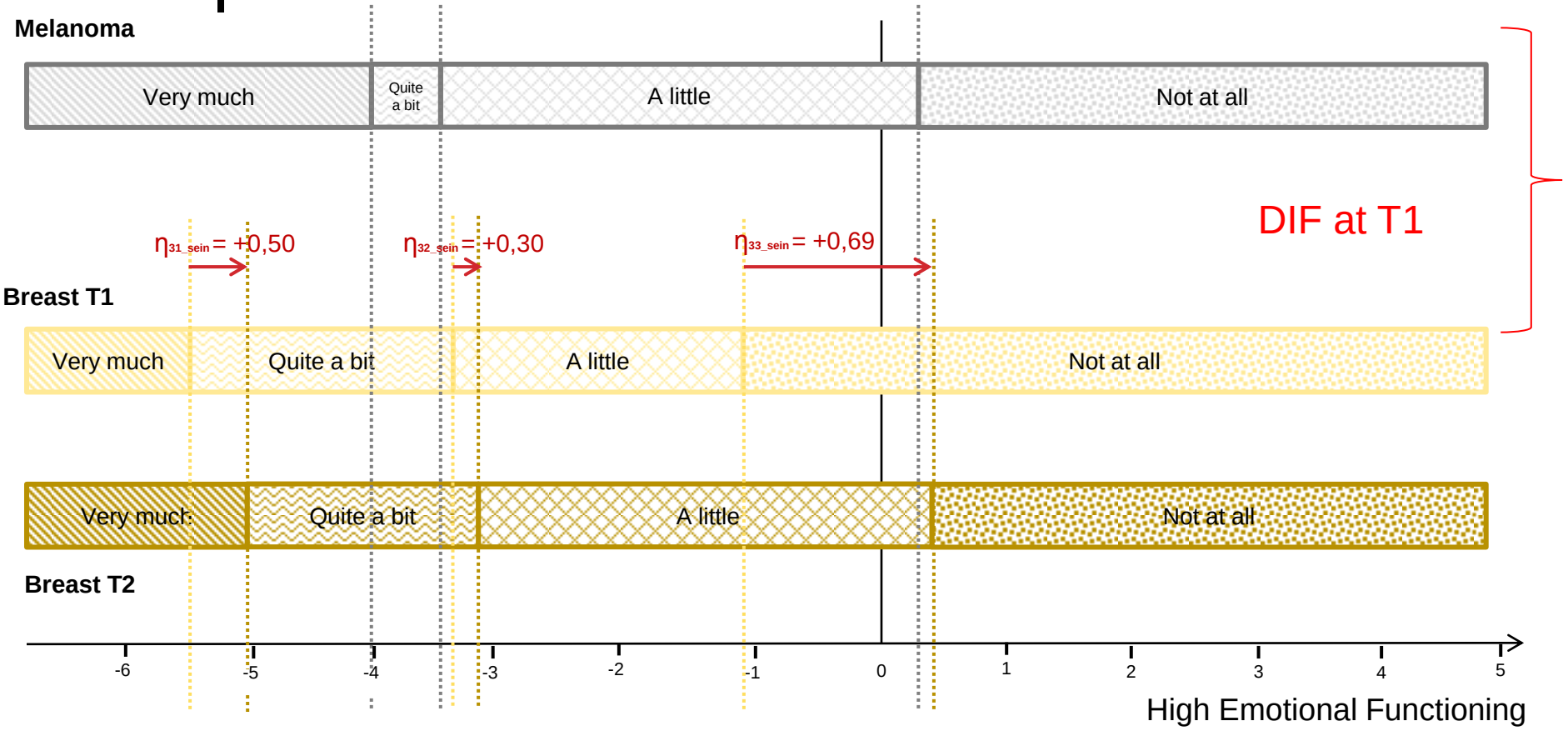
Results – One (T1) and 12 (T2) months after diagnosis

- Breast cancer & melanoma ⇨ Uniform recalibration - Item “Did you worry?“



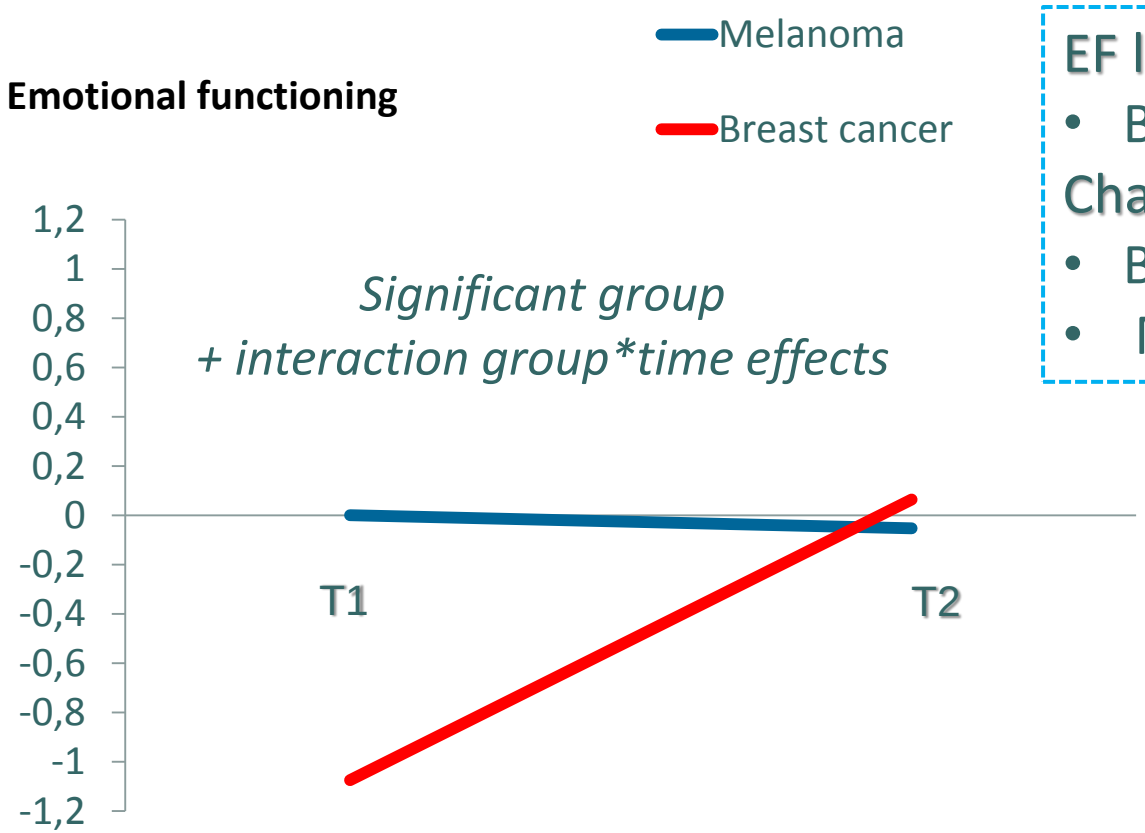
⇨ For a same level of emotional functioning, patients reported lower worry levels at T2 as compared to T1

Results – Breast cancer only ⇨ Non-uniform recalibration - Item “Did you feel irritable?“



⇨ For a same level of emotional functioning, breast cancer patients reported higher irritability levels at T2 as compared to T1

Results – Latent trait change



EF levels at T1

- Breast cancer < Melanoma

Change in EF levels

- Breast cancer → Increasing
- Melanoma → Stable

Discussion

- **DIF & Recalibration RS**
  - DIF at T1: for a same level of EF, higher irritability levels for melanoma as compared to BC patients → not stable over time (no DIF at T2) → RS
  - Similar RS *(worry)* and differential RS *(irritable)* evidenced for breast cancer (BC) and melanoma patients
- **QoL change**
  - Increasing for BC → reaching the QoL level of melanoma patients which remained stable during the first year
- **Interpretation of RS "effect sizes"**
  - What is a meaningful RS effect? What is the MCID of RS?

Discussion

Recalibration RS → Reprioritization & Reconceptualization?

- Statistical perspective
  - Reprioritization → Generalized PCM with discrimination parameters → IRT not RMT anymore, *no specific objectivity*
  - Reconceptualization → Multidimensional RMT or IRT models → convergence problems, large sample sizes

- Conceptual perspective
  - Reprioritization → Interpretation at dimension-level (e.g. social >> physical); does it makes sense at item-level?

Conclusion

- Perspectives
  - Enhance the development of methods for identification of RS at more individual levels
  - ROSALI2: differential impact of covariates on RS and latent trait change at item-level
  - Combine methods for the analysis of RS at dimension and item-level
  - Simulation studies are needed to assess the performance of the methods