Formulário de acesso a dados do Registo Nacional de Doentes Reumáticos (Reuma.pt) da SPR

1. Title

Variation in patient-reported outcomes for patients with Inflammatory Rheumatic diseases: evidence from Portugal

2. Introduction

2.1. Literature review

The main goal of the most health care systems is to improve patients' health, but how can patients' health be measured? Instead of using measures of mortality or readmission rates which can reveal little about the health status of the vast majority of patients, more comprehensive and sensitive patient-reported outcomes measures (PROMs) have recently been used in health care systems around the world to represent the patients' views of their health status. PROMs explore different health dimensions and can provide a score of the patient's health-related quality of life. Patients are often the best judges of how they feel, and the introduction of PROMs in clinical decisions reflects a growing recognition that the perspective of the patient is highly relevant to efforts to improve the quality and effectiveness of health care. Ultimately, PROMs are likely to become a key part of how all health care is funded, provided and managed. One concern often noted is that PROMs data are not adequate or appropriate to guide clinical decision-making since they are subjective (they rely on patients' views and feelings). Even though the ideal scenario would be the one where PROMs could be complemented with objective, clinical measures of the physiologic and/or biochemical status of patients, ultimately the health care system should focus on what really matters for patients.

The potential of PROMs in conjunction with more traditional clinical measures is enormous: measure the effectiveness and risks of interventions, assess the performance of clinicians and organisations, promote practice improvement and establish value-based payments, among others. Ultimately, PROMs can improve patient choice and increase provider accountability if information is publicly available and easy to interpret. The first step in achieving the potential benefits of PROMs is to make sure PROMs data are collected (typically patients are given one or more questionnaires to complete), and then put together in a simple and informative way so that hospitals/clinicians can use that information as feedback on the care they have provided and to improve clinical performance (if needed), and patients could potentially choose where to receive treatment and what treatment is the best for them. It has been recognised that in order for PROMs to be effective, they must capture factors that are important to both patients and clinicians.

To conclude, PROMs reflect a new paradigm in health care and a fundamental rethink about what hospital efficiency means and how it can be measured. It represents a change from focusing on activities

and processes to focus primarily on outcomes. Traditional analyses on hospital efficiency have focused on identifying variations between hospitals, and the factors associated with those variations, in the production of *health care* whereas by using PROMs data it is possible to explore the variations between hospitals in the production of *health* and this way assess the extent to which hospitals achieve improvements in population health given their inputs, resource use and other relevant characteristics (both related to patients and providers). Even though risk-adjusted PROMs analyses will not identify the factors that have led to a good/bad performance, the analysis of the variation in PROMs should be seen as a starting point for organisations and providers, after which a discussion around why some hospitals/providers appear to perform better/worse than others should take place, and then a bespoke plan should be drawn with what they need to do in order to improve. Even though the objective is still to measure performance in order to promote quality improvement, the fact that PROMs are reported by patients along with the new patient-centre approach to care have promoted the share of this information publicly with patients to improve provider accountability and patient choice, ultimately creating a more transparent and collaborative environment [1, 2].

2.2. Previous work

PROMs are being increasingly used worldwide to assess the quality of services provided and encourage systematic quality improvement. In particular, they "have been used to compare and reward the performance of healthcare providers in England, the USA, Australia and Sweden, and their potential to improve quality has also been recognised in Canada and the Netherlands" [3]. As an example, Spire Hospitals (formerly Bupa Hospitals) which is the second largest provider of private healthcare in the UK, used PROMs to change clinical practices in its hospitals. In one hospital, lower scores than the average encouraged a change in its care pathway for hysterectomy. In another hospital, higher scores than the average following hip replacement prompted an investigation which noted that, at that specific hospital, the physiotherapy department had started to run an intensive pre-operative training session for patients who were to be submitted to a hip replacement surgery, which resulted in patients being better prepared both for their procedure and recovery periods.

In 2009, the English National Health Service (NHS) has mandated the routine collection of PROMs before and after 4 specific interventions – hip replacement, knee replacement, varicose vein and groin hernia surgery in England. In 2012, Nils Gutacker et al. [4] looked at PROMs for patients who were submitted to a hip replacement surgery and explored the change in PROMs between baseline and follow-up on 5 health dimensions (EQ-5D) and the extent to which the treatment impact varied across 153 hospitals. They concluded that some hospitals were better than others in improving health across particular EQ-5D dimensions, demonstrating that when assessing hospital performance, it is important to evaluate each EQ-

5D dimensions separately. After this study, Nils Gutacker and Andrew Street [5] explored PROMs data further and created a tool https://www.york.ac.uk/che/patient-outcome-tool/ where patients can understand the likely benefits associated to each intervention. Physicians can also understand whether they are above or below the average performance (in regard to different metrics) for England at http://www.njrsurgeonhospitalprofile.org.uk. The PROMs initiative is a truly remarkable development for the NHS and reflects a key theme in the NHS reforms, namely to "improve the responsiveness of the NHS to patients' views, preferences and choices". Patient value information on the quality of care provided by hospitals and providers when deciding, for example, where to receive a surgery. However, until recently this information was not publicly available for patients.

In Portugal, Reuma.pt included since the beginning, PROMs such as visual analogue scales of pain and disease activity, EQ5D, SF36 and HAQ. These instruments can be a fundamental tool to capture self-reported quality of life and disability, in addition to validated and worldwide adopted composite disease activity scores such DAS 28, ASDAS or BASDAI.

2.3. Hypothesis

The objective of the current study is to determine the change in PROMs for patients with Rheumatoid Arthritis (RA), Spondyloarthritis (SpA) or Psoriatic Arthritis (PsA) between baseline (starting the first biologic drug) and follow-up at 6 months and 1 year on different health dimensions (EQ-5D / SF-36) and the extent to which the treatment impact varies across hospitals in Portugal. As data and knowledge around normal/expected variance grows, it will become clearer if there is a specific level of performance under which action must be taken for specific conditions. However, for the current project, the approach is to look at the variance around the average performance of Centers in terms of PROMs. Furthermore, a composite score of disease activity (DAS28, ASDAS or BASDAI, as appropriate) will be also considered in order to corroborate the conclusions provided by PROMs, ultimately increasing the confidence in the results. Finally, since there are characteristics of the patients (e.g. sex, age, education, severity of disease, comorbidities, employment status, etc.) and Centers (size, location, etc.) that are beyond the control of the hospital, care will be used when selecting the factors to adjust for (more details in 'Methods').

To conclude, understanding how much the outcomes vary for patients with inflammatory rheumatic diseases across different rheumatology Centers in Portugal will be very important for organisations and providers as feedback on the care they have provided. These results might lead to discussions around why some hospitals appear to have patients reporting better/worse outcomes than others, ultimately motivating quality improvement at the practice level.

Additionally, we also want to know the relation between PROMs and disease activity, namely when patients are in very active states or in remission and how the control of inflammation reflects on PROMs.

Are there groups of patients in remission and poor results in PROMs (namely EQ5D and HAQ)? What are the main characteristics that distinguishes these patients from subjects in remission with high scores in QoL (and less disability)?

2.4. Innovation and significance

In a recent Commission group led by Nigel Crisp [6], a former Chief Executive of the English National Health Service, areas that required particular attention of the Portuguese national health system were explored. On one side, the Commission noted the excellent clinical skills of Portuguese health professionals. On the other side, they pointed out a "lack of data compared to other Western European countries, poor quality in what was available, and lack of transparency". In their final recommendations, they emphasized the importance of evidence supported by data, openness and systematic quality improvement, and also, the switch from hospital-centred based system to a patient-centred based one where patients contribute actively to the system. This study aims to tackle some of these aspects by looking at PROMs to assess the variation in outcomes across hospitals for patients with RA.

Previous research on hospital performance in Portugal has focused mostly on processes [7], ignoring improvements in patients' health-related quality of life. To the best of our knowledge, this is the first study that systematically explore variation in different Centers' outcomes based on PROMs in Portugal. Another important contribution relates to the fact that the current study aims to use individual-level data (instead of hospital-level data) and focus on patients with a specific condition, reducing the risk of ecological fallacy and increasing the likelihood of obtaining statistically significant results when dealing with a small number of organisations (as per the study [8]). Publishing these results could be seen as a step towards a more transparent and open approach to health care in Portugal.

3. Specific aims

3.1. Primary aim

- Determine the change in PROMs for patients with RA, SpA or PsA between baseline (drug start) and follow-up (at 6, 12 and 18 months) on different health dimensions (EQ-5D / SF-36) and the extent to which the treatment impact varies across Rheumatology Centers in Portugal (with the appropriate case-mix adjustment applied)
- Corroborate these results with results of variation in disease activity scores between baseline and follow-up
- Ultimately, to take advantage of the entire potential offered by PROMs data, these findings need to be shared with patients in a simple and succinct format (as it is currently done in the English NHS), and this study aims to explore the political, organisational and financial factors

that might enable that to happen and ultimately promote greater patient choice and involvement in the Portuguese national health system.

3.2. Secondary aim

- Explore potential reasons for variation in PROMs.
- Study the health-related quality of life of patients with RA, PsA and SpA and compare with the Portuguese general population.
- Explore the associations between health status and sociodemographic variables.

4. Methods

4.1. Study design

This will be an econometric study (longitudinal study) including all patients with RA, SpA or PsA in the Reuma.pt registry starting a biologic (naïve patients and/or patients who had used the same biological product before and/or patients who required to switch to a different biological product).
Inclusion criteria: patients with RA, SpA and PsA included in Reuma.pt

4.2. Variables description and analysis plan

The key variables are listed below. These variables need to be collected for every patient for all Centers included:

- Patient-reported outcomes (measured by EQ-5D or SF-36 questionnaires) at baseline and after treatment being initiated – outcome variable
- Disease Activity (DAS28, ASDAS or BASDAI) at baseline and after treatment being initiated – outcome variable
- Center – independent variable
- Disease duration - controls
- Sex – controls
- Age – controls
- HAQ – controls
- Level of education - controls
- Comorbidities – controls
- Employment status – controls
- Co medication: corticosteroids, DMARD -Methotrexate, leflunomide, sulphasalazine - controls

Other variables (if available) will allow for controlling for other parameters in regression (better case-mix adjustment)

- Measures of the physiologic and/or biochemical status of patients – controls
- Socio-economic status – controls
- Education – controls
- Mortality

When analysing variation in PROMs, the following points will be considered:

- Compare baseline disease activity data across hospitals in order to assess the 'threshold' decisions made by clinicians that might be indicative of different hospital patient management systems and clinical decision-making (e.g. when to treat the patient) which will ultimately have consequences not only for the patient (in terms of equity of access and capacity to benefit from treatment), but also for the health care system (in terms of the efficient use of resources).
- Look for patterns of patients' responses after 6 months. For example, a scenario where many patients report high/low score for a specific dimension (e.g. mobility, pain, anxiety) of health might be indicative of where to focus to improve the patients' quality of life.
- When exploring potential reasons for variation in PROMs, consider results from traditional research on hospital performance in terms of mortality, treatment failure in terms of increasing diseases activity, adverse events rates which have reported that a significant proportion of the variation can be explained by low numbers of physicians per Center, high workload and other factors related to providers.

Brief description of statistical analysis:

Kim Olsen and Andrew Street [8] studied the hospital efficiency among a small number of organisations by exploiting patient-level data. The statistical methods used in their work will be applied in the current study to assess the variation in PROMs across different Rheumatology Centers. As mentioned before, there are characteristics of the patients (e.g. sex, age, disease duration, severity of disease (disability), etc.) and hospitals (size, location, etc.) that are beyond the control of the hospital. If hospital A has a younger population than hospital B, this is likely to impact the outcomes and it has nothing to do with hospital performance, and therefore needs to be controlled for in the model. Therefore, attention will be put into selecting the factors to adjust for, but this will also be dependent on the variables available in the Reuma.pt data base. The two-level multilevel model that takes into account the clustering of patients within hospitals is given by:

$$PROMs\_change_{ij} = \alpha + \beta\ controls_{ij} + u_j + v_{ij},\ \ i = 1,\ldots, I\ ;\ j = 1,\ldots, N$$

where $PROMs\_change_{ij}$ is the change in PROMs between baseline and follow-up (when clinically appropriate; to be confirmed) of patient *i* at hospital *j*; $controls_{ij}$ is a matrix of covariates defining the characteristics of patient *i* in hospital *j*; v_{ij} is the normal residual assumed to be iid with zero mean and constant variance; and u_j is the hospital effect. Several estimators can now be used to estimate the hospital effect u_j: fixed-effects, random effects and generalised least squares. All these 3 methods will be used and compared, and the pros and cons of each model explained. The hospital with the highest u_j will likely be the one with the highest performance when it comes to treat patients with RA (according to PROMs).

4.3. Sample size

There is no specific power calculation for this type of study. The higher the number of patients, the more robust the model will be. Therefore, the current request is for data from all Reuma.pt patients with a diagnosis of RA, SpA or PsA starting a biologic (naïve patients and/or patients who had used the same biological product before and/or patients who required to switch to a different biological product). It might not be possible to include in the analysis hospitals that do not have PROMs data for a sufficient number of patients, but we would like to request access to all hospitals and then decide based on the total number of patients per hospital.

5. Limitations and expected results

Expected results:

This study will show some or none variation in patients with RA across hospitals in Portugal. These findings are expected to be of interest to the organisations under study and the Portuguese population in general, and ultimately, they might lead to discussions around why some hospitals appear to have patients reporting better/worse outcomes than others, ultimately motivating quality improvement at the national level.

Limitations:

Depending on the number of missing data, in particular, affecting the key variable of the model "PROMs", the model might not be robust.

6. Timeline

6.1. Primary aim

Access to Reuma.pt data base after scientific approval from *as soon as possible* to start getting familiarized with the data, up until 28th August.

The quantitative analysing will be performed in the first 1,5 months (June-mid July) and the remaining 1,5months (mid July-August) will be to write the MSc thesis.

Publication: MSc thesis on 28th August; potentially an article in a Journal afterwards

6.2. Secondary aim

The analysis will be performed as soon as the data is available. We expect to publish an article in an indexed scientific journal. The first draft of the article will be ready for submission by the end of 2018.

7. Research team and institutions

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8. Funding and conflicts of interest

We declare no conflicts of interest.

The project has no funding.

The names of the Centers will not be disclosed publicly. Each Center will be assigned a code in order to respect anonymity.

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