Author’s response to reviews

Title: HIV/AIDS length of stay in Portugal under financial constraints: a longitudinal study for Public hospitals, 2009-2014

Authors:

Gonçalo Figueiredo Augusto (figueiredo.augusto@ihmt.unl.pt)

Sara Dias (sara.dias@nms.unl.pt)

Alexandre Abrantes (aabrantes@ensp.unl.pt)

Maria do Rosário Martins (mrfom@ihmt.unl.pt)

Version: 1 Date: 28 Sep 2018

Author’s response to reviews:

Overall response from authors:

The authors would like to thank all reviewers for their valuable comments. The manuscript was deeply reviewed, changed and improved in all sections. Also, relevant references were added and the model was re-analysed in order to meet the reviewers’ thoughtful comments.

Technical Comments:

Please combine Ethics approval and Consent to participate under one heading and change the first heading from Introduction to Background.

We have made the requested changes.

Editor Comments:

In addition to the referee comments below, can you please also address the following Associate Editor comments:

The manuscript entitled “HIV/AIDS length of stay in Portugal under financial constraints: a longitudinal study for public hospitals, 2009-2014” presents an analysis of the relation between
Although this study presents some interesting results, the performance of the regression model is not indicated. We agree with this comment. We can obtain statistics like BIC and AIC to compare the simple Poisson model with this more complex approach. However, because of the complexity of the model, the usual statistics based on residuals are more complicated to obtain. Poisson specification with Random effects is largely used to analyse LOS, as can be seen in previous research:

Liming Xiang1; 2, Kelvin K. W. Yau2, Andy H. Lee1;*, † and Wing K. Fung. Influence diagnostics for two-component Poisson mixture regression models: applications in public health, Statistics in medicine, 24(19), 3053-3071.


Peiming Wang, Martin L. Puterman, Iain Cockburn, Nhu Mixed Poisson Regression Models with Covariate Dependent Rates Biometrics, Vol. 52, No. 2 (Jun., 1996),

The authors should also clarify how the various covariates were preselected, in particular co-infections. And why is it important to include co-infections?

Co-infections are a relevant indicator in on the health status of HIV patients. Therefore, we selected main co-infections (TB, Hep B, Hep C and Pneumocystis pneumonia) based on other studies on this issue and on international literature. We included that information in the Methodology section.

Stages of HIV infection may have an impact on the length of stay. Should not they be included in the analysis?
It would have been very interesting to include stage of HIV infection, but this variable was not recorded on DRG data source used for this analysis.

The quality of the data is not discussed (e.g. missing values, outliers).

DRGs are mandatory in Portuguese NHS hospitals and therefore there are no missing values in the variables used to this study.

Regarding outliers, LOS has several outliers given its nature, reason why Poisson regression model is a model that fits these data. HIV/AIDS DRGs outliers varies between 0% and 9%, and the majority of cases is around 6-7% (Dias & Martins, 2015). We have performed boxplot for our data:

### LOS

```r
> summary(aids$los)

    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.  
 0.00   6.00  11.00   17.85  22.00  363.00
```

### AGE

```r
> summary(aids$idade)

    Min. 1st Qu. Median  Mean 3rd Qu. Max.  
 18.00   37.00 44.00  45.41  52.00  95.00
```

How were readmissions considered for discharges occurring by the end of December 2014?

As 31 December 2014 was the end of the study period, readmissions within 30 days of cases discharges by the end of 2014 were not considered for the current analysis.

Reviewer reports:

Julian Perelman (Reviewer 1):

The paper is relevant, generally clear and well-written. There are however several issues that must be accounted for so that the paper is suitable for publication, in particular regarding the rationale and objectives of the paper, and the interpretation of results. I also feel the analysis could be further developed to increase the paper relevance for an international audience. These comments are detailed here-below.

Introduction

1. The rationale/objective of the paper is presented in a way that is misleading. At first sight, it seems the study is about HIV, but then it seems it is more about how the economic crisis and austerity measures reduced LOS. I suggest starting the paper focusing on measuring the crisis/austerity impact, and then present HIV as a relevant case study to evaluate this issue.

We improved the introduction section.

2. Theoretical considerations and literature review are missing regarding why austerity measures and the economic crisis might have affected LOS. There is a large literature to be referred, not only for Portugal but also for other countries, about the implications of this context on hospital practice.

We improved the introduction with further references.

3. Theoretically, LOS might be reduced because of financial constraints. However, some papers mention that the crisis might have reduced access to primary care and increased the
severity of diseases, so that an increase in LOS may also be expected. This alternative hypothesis must be mentioned and supported by the literature.

We have discussed that issue with more detail in the Discussion section.

4. A reduction in LOS can be viewed as an efficiency improvement but also as a decrease in the quality of care. Authors should present this issue with more caution.

We have discussed that issue with more detail in the Discussion section.

5. The econometric considerations should be removed from the Introduction to the Methods section.

We moved that paragraph to the Methods section.

Methods

1. The data source must be more detailed, giving some information about how data are collected, from which institutions, and detailing which information is collected. Remember this paper will be read by an international audience that is not familiar with these data.

We improved the Methods section.

2. It is unclear whether the database permitted follow patients across hospitalizations at different settings, in particular when transfers occurred across different years. In case of transfer, was the total LOS considered across admissions?

No, we considered episodes of hospitalization instead of patients. If one patient was hospitalized 2 days in Hospital A, was transferred to Hospital B for 5 days and come back to Hospital A for 3 days before being discharged, we would have to attribute the total 10 days to one hospital and introduce a bias in the database. However, we mentioned this in the Methods. Overall, we are dealing with 507 transfers in the study period (2.5% of the total number of episodes).

3. What about short-term readmissions, were they considered as part of the same hospitalization? I.e., hospitals may have shortened LOS but readmitted the patient shortly thereafter, so that complete LOS over admission could be considered.
As we wanted to capture the dynamics of hospitalizations, we did not merge any short term readmissions, unless the readmission was made on the same day of the discharge. This methodology might “decrease” artificially LOS, but allows a better analysis of this variable. We mentioned this issue in the Discussion section.

4. It is ESSENTIAL to present the "period" or year variables, which are the explanatory variable, i.e., the variable of interest, which allows answer the research question. All other variables are merely covariates or potential confounders. In the results, it is unclear whether the "period" variable was a linear trend, a dummy for a specific period, or a dummy referring to a specific sub-period. In case it is a period variable, it is a loss of information, so that I suggest substitute by year dummies.

We estimate another model with one dummy for each year and we choose year 2009 as the reference class, as it is presented in the Results.

5. LOS is presented as proxy of efficiency; again, this is a very subjective view, which may be challenged. I suggest mentioning only that LOS was the outcome, without further referral to efficiency.

We followed the reviewer’s advice and corrected the sentence accordingly.

6. It is unclear why random effects were used instead of fixed effects. Hospital fixed effects allow control for all unmeasured hospital characteristics that are potentially strong driver of LOS, namely its location, financial situation, professionals' experience and training, type of practice, etc.

In our specification we have a so-called multilevel model with two levels: individual and hospital level. Because of this characteristic we know that observations within each hospital are correlated, violating one of the classical hypothesis; not taking into account this correlation will have consequences in estimator’s properties: they will be inefficient (in general). One way to deal with this problem is to specify the model with random effects at the hospital level: this means that the variance-covariance of the estimators will be corrected to take into account these the correlations within hospitals; it can be shown that in general, random effects models estimators are more efficient than fixed effects. Moreover, the hospital residuals (estimated random effects) represent unmeasured hospital characteristics that affect the LOS; it is these unobserved characteristics that lead to correlation between outcomes for

With fixed effect models the estimators will, in general, be less efficient. Because of this we keep the random effect specification.

7. I suggest extending the analysis by including a variable on the hospitals' financial situation. I would expect a larger LOS among more indebted hospitals. This would allow measure to what extent LOS was reduced due to austerity measures and financial incentives. Alternatively, other hospital characteristics.

We agree with the reviewer and we included an additional variable: Current ratio.

8. The choice of a Poisson distribution must be justified. In particular, overdispersion must be tested.

We agree with the reviewer, although this is a complex model where it is very hard to test the overdispersion since it is not developed in most softwares. Prior research (mentioned in the paper) have performed tests for overdispersion.

Results

1. It would be important to include values, for the reader to know the magnitude of the effects. E.g., by how much does the number of diagnoses increase LOS? This is relevant also to inform how coefficients must be interpreted. I suppose it is in percentage terms (e.g., each diagnosis increases LOS by 4.3%) but I am not sure.

The Poisson Model:

Let Y be the dependent variable (a count variable) and X1, X2, ….Xk the k covariates. For each observation i=1, …n, the Poisson model is specified as following:

\[ E(Y_{(i)}/X_i) = \exp(\beta_1 + \beta_2 X_{2i} + \beta_3 X_{3i} + \ldots + \beta_k X_{ki}) \]

Taking the logs the model is sometimes also called log-linear:
\[
\ln E(Y_{i}/X_{i}) = \beta_1 + \beta_2 X_{2i} + \beta_3 X_{3i} + \ldots + \beta_k X_{ki}
\]

Interpretation of the coefficients:

It can be shown that a one unit change in the jth covariate leads to a change in the conditional mean of Y by the amount \(\ln E(Y_{i}/X_{i})\beta_j\) (whereas in the linear model it is simply \(\beta_j\)). Another way of saying this is that a one unit change in the jth covariate leads to a proportionate (or percentage) change in \(\ln E(Y_{i}/X_{i})\) of \(\beta_j\). Sometimes it is called a semi-elasticity.

If the covariate is in logarithms the coefficient is the elasticity. (Further details can be found in the book by A. Cameron, Regression Analysis of Count Data)

For this particular case, we can say, for example, that one additional number of diagnosis increases the estimated LOS by 0.043%. In the manuscript, we included a simple explanation of the Poisson coefficients.

Discussion

1. The decreasing trend followed by an increase in 2014 was only supported by descriptive results, but not by the multivariate analysis. I suggest testing this by including year dummies instead of a period effect.

We agree with the reviewer and estimates another model with one dummy for each year, choosing the year 2009 as the reference class.

2. The effect of HAART is expected to decrease the risk of hospitalization, by preventing the occurrence of opportunistic diseases. It is unclear why HAART would decrease LOS for those who are hospitalized. A good explanation must be found for the increase in 2014, although it may not be confirmed by year dummies in the multivariate analysis (to be checked).

We absolutely agree with the comment and we eliminated that silly reference to HAART. Of course HAART does not have influence in decreasing LOS of people that are already hospitalized unless we analysed AIDS-related conditions specifically, which was not the aim of this paper.
3. I am not surprised that hospital mergers increased LOS. The mergers in Portugal were merely cosmetic, that is, grouping hospitals from different areas under a common administration, but generally keeping the previous practices and duplication of services. Anecdotal evidence suggests mergers reduced efficiency because a single administration had to deal with hospitals situated in different places, increasing the difficulties in monitoring practices. The literature refers economies of scale up to a certain number of beds; when hospitals become too large, efficiency decreases.

We reformulated the sentence in the manuscript. In fact, as mergers were presented, the main expected effect would be increasing efficiency, but that did not happen for the reasons the reviewer mentioned. Actually, hospitals centers are also very different: some hospitals are very geographically dispersed and still work as if they have never been merged (eg Trás-os-Montes) and others are geographically very close to each other (eg North Lisbon).

4. The random hospital effects are difficult to interpret, and authors use hypothetical explanations. I suggest substituting these effects by explicit hospital characteristics, in particular the hospital financial situation, and test the interaction between these characteristics and period variables, to examine what type of hospitals have more reduced their LOS.

As already mentioned before, in our specification we have a so-called multilevel model with two levels: individual and hospital level. Because of this characteristic we know that observations within each hospital are correlated, violating one of the classical hypothesis; not taking into account this correlation will have consequences in estimator’s properties: they will be inefficient (in general). One way to deal with this problem is to specify the model with random effects at the hospital level: this means that the variance-covariance of the estimators will be corrected to take into account these the correlations within hospitals; it can be shown that in general, random effects models estimators are more efficient than fixed effects. Moreover, the hospital residuals (estimated random effects) represent unmeasured hospital characteristics that affect the LOS; it is these unobserved characteristics that lead to correlation between outcomes for individuals/hospitalizations from the same hospital [Goldstein, H. (2003). Multilevel Statistical Methods, 3rd ed. London: Edward Arnold.]

However, we agree that we could have included other hospital characteristics: we re-estimate the model with an additional variable to reflect hospital financial situation.

5. A major limitation must be mentioned, i.e., that a longer period was not considered. The economic crisis started officially in 2009 (two consecutive trimes of recession), so that to measure its impact data should have been included for the pre-crisis period. This would have allowed distinguish the crisis/austerity effect from long-term trends in LOS.
We have included that limitation in the Disussion section. We agree that the economic crisis started before 2012 and we added that limitation in the manuscript. However, the main focus of our analysis is the EFAP, which lasts from May 2011 until May 2014. We have reviewed every sentence of the manuscript to make it clear. As the first set of measures targeting the health sector only took effect in the 2012 State Budget, we considered 2012, 2013 and 2014 as the “EFAP years” in our analysis.

6. Beyond long-term care, other reforms have been adopted over the period that might have a confounding effect, namely the continuation of the primary care reform, the increase in co-payments, the decrease in hospital beds and hospitals human resources, etc.

We improved the Discussion section with these interesting issues.

Conclusion

1. The last paragraph mentions policy implications that are not supported by the data, namely the possibility to benchmark hospitals, which was not assessed nor an objective of the paper. Some recommendations are also too vague and of little interest, "Appropriate policies can be developed to manage hospital resources". It is necessary for the paper to develop policy implications that are not well supported, making the reader less confident or confused about the real findings, which are strong enough by themselves.

We improved the Discussion and the Conclusion sections.

Alberto Freitas (Reviewer 2):

This paper aims to analyse factors associated with HIV/AIDS length of stay (LOS) among Portuguese mainland public hospitals, and the possible effect of the economic and financial adjustment programme (EFAP) on LOS.

This paper may increment the knowledge about factors possibly affecting LOS on HIV/AIDS related hospitalizations, but it needs improvements and additional discussion. Some limitations
are discussed, but several other might also be discussed (for instance the use of data only from public hospitals).

Other comments:

Why only study data from HIV/AIDS hospitalizations?

The scope of the current analysis is a PhD thesis on how HIV/AIDS policy was shaped by the economic and financial adjustment programme. Therefore, only HIV/AIDS hospitalization were included in the analysis.

Why was the selection performed with MDC 24 and not using the ICD diagnosis codes? What are the potential differences between this and the used approaches?

We did use ICD-9 codes as explained in the Methods sections. We have improved that section with further details.

Authors refer that they analysed data from 41 public hospitals (among how many hospitals? And private hospitals?). Please include additional information to better understand the magnitude / scope of the used data.

We have improved the Methods section with further details.

The data used in the analysis was collected from the national database of diagnosis related groups (DRG). There are different types of DRG definitions (AP, APR, MS, among other). Please clarify.

We have improved the Methods section with further details.

Typically, the DRG data in Portugal includes both inpatient and outpatient data. In this study it is not clear if outpatient data was also included.

Outpatient data were not included. We clarified that in the manuscript.
Authors say that they did not exclude hospital transfers. They also say that "hospitals were coded as to simulate the current Hospital Centre they are part of". As so, why not also merge data from transfers within hospitals of the same centre, including the merge of possible LOS in these within-group transfers?

Transfers within hospital centre were not recorded at the database as only the code of the hospital centre was registred.

An increased number of hospital centres may imply less transfers (with the majority of them within hospitals of the centre, and thus not being reflected in the database), and possibly an increased LOS (because it is not split among hospitals). Is this plausible?

We noticed that transfers increased until 2012 and decreased after that.

2009 – 80
2010 – 75
2011 – 105
2012 – 115
2013 – 88
2014 – 44

So it is plausible that patients were being transferred within hospitals centres.

How were readmissions within 30 days of discharges defined and calculated? Please clarify.

We identified episodes from the same patient by the fictional number. We analysed episode by episode to establish the flow. The variable “readmission within 30 days of discharge” was calculated as any admission from the same patient 30 days or less after the discharge (from the prior episode). Therefore, it took weeks to analyse all admissions, date by date, to understand if they were readmitted less than 30 days after discharged or if they were transferred to another hospital.

How where the selected co-infections / diseases (e.g. Pneumocystis pneumonia, Hepatitis B, Hepatitis C, and Tuberculosis, HIV) identified? Which conditions and/or ICD codes where used?

We have improved the Methods section with further details.
The number of secondary diagnosis was included in the analysis. Why not a comorbidity measure/score?

We adopted a similar methodology as other studies.

The number of procedures were also included in the analysis. What does this measure? There are many differences between procedures, e.g. between medical and surgical procedures.

We do agree. The number of procedures, also used in other studies, was used as variable to measure severe hospitalizations.

"Setting covariates included whether the hospital was merged into a Hospital Centre or not". Why not use additional variables for complexity / casemix of hospitals?

We included several covariates that are highly correlated with case-mix of hospitals, such as urgent, mortality, no. of procedures, no. of diagnosis and readmissions; and this is why we decided not to include case mix. However, we mentioned that issue in the limitations.

Due to the nature of the LOS distribution, why present the average LOS, and not the median (and IQR)?

We agree with the comment and we present the median and IQR in Table 2.

p.7, "The number of secondary diagnoses and the number of procedures both increase estimated HIV/AIDS LOS". How can we be sure of the direction of the association?

The estimated coefficients related to these covariates are positive and significantly different from zero.

p.8, "It was interesting to find that the merger of hospitals into hospital centres increased HIV/AIDS LOS". As pointed previously, additional analysis, with the merge of episodes form hospitals of the same centre (and also LOS), are needed to reach such a conclusion.

The discussion was reformulated. That variable was no longer significant.
Additionally, estimated HIV/AIDS LOS was shorter in hospitalizations occurred between 2012 and 2014, compared to hospitalizations taking place between 2009 and 2011”. In the 6-year period, the 2nd higher yearly LOS average occurs in 2014...

That finding is very interesting because in fact, analysing mean LOS year by year, we find a decreasing trend until 2012 and an increasing trend after that year. So, in 2014, mean LOS was almost as high as 2009, which suggests that pressure for efficiency was somehow relaxed once the EFAP ended in May 2014. We mentioned that in the manuscript.

Hospitals 39, 40 and 41 are the least efficient in terms of risk-adjusted LOS for HIV/AIDS patients”. If possible, provide additional analysis comparing these hospitals with the others.

We have included more details on those (40 and 41, according to the new analysis) hospitals, but it was not possible to extend the analysis.