Author's response to reviews

Title: The concept and definition of therapeutic inertia in hypertension in primary care: a qualitative systematic review

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Date: 22 June 2014

Author's response to reviews: see over
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Editor,
*BMC Family Practice*

Dear Editor,

On behalf of the authors, I have the pleasure of submitting the new version of our article: “The concept and definition of therapeutic inertia in hypertension in primary care: a qualitative systematic review” revised after the peer-review of the initial version.

In the document attached to this letter, we gave point-by-point response to all the reviewers remarks, comments and suggestions, and provided a modified version of the initial article, with all revision marks left visible. We also addressed your specific recommendations regarding the PRISMA guidelines, and filled in a PRISMA checklist.

The role of the funder was clarified, and all authors declared that they have no competing interests regarding the content of this article.

The former “Table 1” was too large for a table, with regards to your format requirements, and was changed to “Additional file 1”. The new Table 1 was elaborated after a reviewer’s suggestion.

The manuscript was checked again for English language by a native speaker with scientific research expertise.

I confirm that I will personally organize payment, should our article be accepted for publication.

Best regards

Pr. Jean-Pierre Lebeau
Therapeutic inertia in hypertension: answers to the reviewers and to the editorial comments

First of all, the authors would like to sincerely thank the reviewer for their thorough analysis of our article and their wise advices. Their comments and suggestions were very valuable, and helped us a lot in giving more relevance to our article. Most of these comments and suggestions have led to substantial modifications in the manuscript. In our answers, the line numbers refer to the modified version of the article.

Reviewer’s report
Title: The concept and definition of therapeutic inertia in hypertension in primary care: a systematic review
Version: 1 Date: 21 April 2014
Reviewer: Concepcion Carratala-Munuera
Reviewer’s report:
Major Compulsory Revisions
REVIEWER OPINION
Title: The concept and definition of therapeutic inertia in hypertension in primary care: a systematic review
Jean-Pierre Lebeau (corresponding author)

Is the question posed original, important and well defined?

The aim of the study is to search the literature for definitions and discussions on the concept of therapeutic inertia in hypertension in primary care, to try and form an operational definition.

The research question posed by the authors is easily identifiable and understood. But some questions regarding the term “clinical inertia” must be defined more clearly.

Line 89.- Clinical and Therapeutic Inertia.- LS Phillips was the author who defined clinical inertia. No other term is used in Phillips paper’s. Later, the term therapeutic
Inertia is used by Okonufa. The authors have defined the term “therapeutic inertia” in the title of the paper but the original term is clinical inertia. This means than the authors prefer the term "therapeutic inertia" than the original "clinical inertia" defined by Phillips. If so, it must be justified.

The Phillips' definition of clinical inertia is “failure of health care providers to initiate or intensify therapy when indicated” so therapy is included.

Thank you for raising this issue. In fact, it has been a debate between the authors since the beginning of this research, but we did not give much space to this debate in the manuscript. As you pointed out, LS Phillips et al. used the words “clinical inertia” in their paper. Nevertheless, not only did they include therapy in their definition, but they did not address any other aspect of the clinical process. We think this is the reason why a number of subsequent authors changed the wording to “therapeutic inertia”, though still referring to Phillips' definition. In fact, a few authors have suggested that “clinical inertia” should also include other aspects of care, such as the diagnostic process, hence assuming that the initial definition did not.

To make this clearer, we made the following changes in the manuscript:

- Lines 95-96: “(we chose to use the latter in this article)” was added;
- Line 98: “clinical (or therapeutic) inertia” was changed for "clinical inertia”;
- Line 106: “clinical or” was added.

Line104.- “Clinical (or therapeutic) inertia as defined by Phillips...LS Phillips was the author who defined clinical inertia. No other term is used in Phillips paper’s. The reference number 13 that is used to justify this affirmation is from Okonufa, no from LS Phillips.

Once the upper being stated, we have considered that “clinical inertia” and “therapeutic inertia” shared the same initial definition. Okonufa (“therapeutic inertia (TI), that is, failure of providers to begin new medications or increase dosages of existing medications when an abnormal clinical parameter is recorded », cited in Additional file 1) made the point a little bit clearer by speaking of “medications”, therefore excluding any other kind of what could be considered as therapeutics, such as lifestyle counselling.
We clarified this point in the manuscript by adding:
- Lines 93-94: “With the exact same definition, Okonufa et al. introduced the terms “therapeutic inertia” in 2006.” was added;
- Line 98: “clinical (or therapeutic) inertia” was changed for “clinical inertia”.

Are the data sound and well controlled?

Line 198.- In the coding section there are too many words and a table or figure that summarize the information could be more easy to understand for Readers. A meta-aggregation figure or table could be of help. Meta-aggregation is a method of systematic review that mirrors the processes of a quantitative review whilst holding to the traditions and requirements of qualitative research (it aggregates findings into a combined whole that is more than the sum of the individual findings in a way that is analogous with meta-analysis). Some examples of meta-aggregation figures or tables can be found in the literature.

Meta-aggregation, in our experience, is a (powerful) method of meta-synthesis of qualitative studies. Two of us had worked before with the QUARI software of the Joanna Briggs Institute to perform a systematic review and meta-aggregation of qualitative studies, so we had a chance to discuss the opportunity to use it for this research. Here, we did not review specifically qualitative research articles, and in fact, found only 5 qualitative studies (including a nominal group consensus study) in the final selection. It seemed to us that a meta-synthesis of the findings of these 5 studies did not make much sense with regards to our objective.

Our systematic review is really a qualitative analysis of written documents systematically retrieved, but not a meta-synthesis. This is why we used a classic constant comparative method according to grounded theory to collect and classify the data.

We added a sentence to the discussion to clarify this point.
- Lines 445-446: “Although relying on a systematic search of the literature, this research was not a meta-synthesis of qualitative research.” was added.
Line 203 Terms.- As it was said before, the original term is “clinical inertia” so this must be the first concept to initiate the comment.

The “terms and definition” section of the results actually starts with clinical inertia (Line 208).

Line 221.- Definitions.- Probably the category "semantic" must be an unique section without differentiating terms and definitions in different sections. For readers, is more clear to see the terms and its definitions together. A table including terms and definitions could be of help.

Thank you for this very valuable suggestion. While we initially felt that the two sections did not address the same problem, re-reading it in the light of your comment made it clear that there was no way to delineate clearly between terms and definition and furthermore no logical reason to do it. Apart from removing the titles, we did not make other rewriting than the following point (i.e. clinical myopia), but added a table of terms and definitions.
- Lines 204 and 207 (and in the abstract, Line 43): section title was changed to “Terms and definitions”;
- Line 228: section title “Definitions” was suppressed;
- “Table 1: terms and definition” was added to the manuscript.

Line 259.- A new term “clinical miopía” is defined in the “WHO” section. It could be more apropiate to include it in the “term” section.

We agreed with this judicious remark, and signalled first “clinical myopia” in the “terms and definitions” section. We nevertheless kept unchanged lines 264-268, as their content still relates to “Who”.
- Lines 225-227: “Discussing the synergy between patient non adherence and healthcare provider inertia, Reach proposed “Clinical myopia” for the common mechanism underlying these behaviors.” was added.
Definition and causes are not equivalent. The aim of the paper is to review the concept and definition of therapeutic inertia but not to analyze its causes, that will need a different strategy. So the results must focus on this aim.

This was a difficult issue. At first glance, it actually seemed that all we had to care for were terms and definition, regardless of causes or mechanism, so the “How and why” would be out of focus. At the same time, we wanted to get all possible elements of definition and conceptualization, relying as much as possible on empirical data, in order to produce inductive outcomes. When it comes to intimate mechanisms of human behaviours, causes and consequences exist first, and then possibly the concept arises. To say it in another, more ‘existentialist’ way: “existence precedes essences”. In fact, a number of authors in this review did think about the definition and the concept starting from observed or assumed causes, and so their contribution to the conceptualization was in terms of (possible) causes.

- Line 462-467: “When dealing with definitions and concepts, exploring the causes (“How and why”) might seem questionable, and even out of focus. But when it comes to intimate mechanisms of human behaviours, causes and consequences exist first, and then, possibly, the concept arises. A number of authors in this review did think about the definition and the concept starting from observed or assumed causes, and so their contribution to the conceptualization was in terms of (possible) causes, which justified the “How and why” section of the results.” was added to the discussion to clarify this point:

Another question to be answered is how to measure inertia in research. In table 1, could be of interest to describe how different authors have measured inertia.

This, in our opinion, mirrors the previous point. While many authors thought about inertia in terms of causes and mechanism, the few who tried to measure it started from an assumed definition. Therefore, the actual measurement of inertia, although questionable in itself, could not lead to any new element of conceptualization, and so we decided it was out of focus and should be ignored.
Is the interpretation (discussion and conclusion) well balanced and supported by the data?

Line 420.-Strengths and limitations.- Authors pointed that there is no standard method for this kind of research. There is a systematic qualitative review strategy from the literature that is well defined in Cochrane Library or Joanna Briggs Institute (http://joannabriggs.org/sumari.html) (Qualitative Assessment and Review Instrument, QARI) from the University of Adelaide. With this instruments the quality of the studies can be also described.

Prior to starting the review itself, we did search for tools adapted to the systematic review of opinion papers.

- We did not find anything from the Cochrane Collaboration at the time. The first review of qualitative evidence published by the CC came in November 2013, and the Cochrane standards for this kind of research are currently under construction (http://www.thecochranelibrary.com/details/editorial/5442531/Reviews-of-qualitative-evidence-a-new-milestone-for-Cochrane.html).

- As already stated, two authors had already worked with the Joanna Briggs institute set of tools, so we thought the strategy described in Chapter 11 of the Joanna Briggs Institute Reviewer’s Manual would be of help. Many of the methodological choices we had already made were indeed the same, particularly regarding critical appraisal of texts, data extraction, and results display. We did not use the JBI-NOTARI tool, as it is a “private” software tool dedicated to systematic reviews proposed or approved by the JBI, but not widely disseminated. Once again, the quality assessment tools are designed for systematic reviews and meta-synthesis of qualitative studies, which is not what we conducted.

- For quality assessment, we chose to stick to the PRISMA checklist. Although it was designed for quantitative research, a number of items regarding quality of the review can be transposed to qualitative reviews. Yet, the quality of the studies presented in the selected article was not a concern regarding the aim of our research, and we did not systematically assess it.
The manuscript was modified to clarify this point:
- Lines 449-450: “Although relying on a systematic search of the literature, this research was not a meta-synthesis of qualitative research” was added;
- Lines 453-455: “Because we were only looking for elements of definitions and concepts, quality assessment of the studies described in the selected articles was not justified.” was added.

Are the methods appropriate and well described, and are sufficient details provided to allow others to evaluate and/or replicate the work?

Methods are not appropriate but could be improved.

The systematic review process should be transparent and replicable. Nevertheless this is a qualitative review as it is not focused on quantitative results from intervention studies; this study is based on a qualitative analysis about definitions of therapeutic inertia in hypertension. So it could be more clear to use the term "qualitative systematic review" instead of "systematic review".

Thank you for this suggestion: we changed the title according to this.

Inertia is still not a Mesh in Medline as it is more difficult to find adequate information as no controlled language can be used, so this problem must be commented.

The fact that inertia is not a MeSH term was stated in the introduction (line 101).
We added a note of caution in the discussion regarding your comment:
- Lines 441-445: “As already stated, “inertia” is not a MeSH, which made the search a bit more difficult and “risky”, and it is possible that we missed articles discussing the concept using other terms. We tried to avoid this by elaborating a search algorithm as sensitive as possible to all aspects of the concept, and by paying a special attention to the publications cited in references in the selected articles.” was added.
The search is focused on primary care. But no Mesh related to primary care have been used in the Search strategy for identification of studies. Including this mesh (general practice, family medicine, primary health care) the results could be different.

Including a MeSH term related to primary care would have had two possible consequences:

- Added with an OR, it would have of course resulted in an overwhelming “background noise” and was not conceivable
- Added with an AND, it would have narrowed the search a little. We tried it out, and observed that the reduction in the number of abstract was not really significant (in terms of workload, that is), but that there was indeed a loss of articles of interest.

Considering this, and the fact that, even though our interest was in primary care, chances were that a concept could be discussed in other fields with relevant remarks and interesting outcomes, we decided not to include such terms in the search.

To clarify this point, we modified the manuscript:

- Lines 445-448: “Although our concern was general practice, we did not include any MeSH terms related to primary care. Narrowing the search with such terms would have resulted in a loss of a few articles of interest, which discussed theoretical aspects of guideline adherence or inertia regardless of the context of care.” was added.

Line 127.- Related to the data bases that have been used LILACS is not included. This database is International as Medline, and includes languages as spanish, portuguese and english. One objective of a systematic review is to include all international databases of interest as LILACS is. This database have many papers from America (northamerica, southamerica) and Spain and Portugal.

With regards to this suggestion, we did search LILACS. We used the algorithm constructed for PubMed, and “translated” it in LILACS language:

(MH:"guideline adherence" OR (MH:"practice guidelines as topic" AND (MH:"clinical audit" OR MH:"clinical competence" OR MH:"attitude of health personnel" OR MH:"delivery of health care" OR MH:"physician's practice...")))
patterns" OR MH:"nurse's practice patterns")) AND (MH:"hypertension" OR MH:"antihypertensive agents")) OR TW:"clinical inertia" OR TW:"therapeutic inertia"

This search returned 7 results:

References 6 and 7 were already selected in our review. References 3, 4 and 5 were retrieved in PubMed initial search, but were rejected. Reference 2 is an epidemiological study with no elements of definition or conceptualization. Reference 1 is an editorial that endorses, in Spanish language, Phillips original publication (with the author’s agreement), with no further reflection or new input. Finally, we did not find any new article to be included.

We discussed the appropriateness of including this search in the article. Since we had not tested the sensitivity of our algorithm with this specific database, and although a “quick checkout” lead us to think that this sensitivity was good, we decided that it would not be correct to include this search. Still, we are confident that the results would not have been significantly modified if we would have include it.

Additional searches. By the other hand google is used as a database. Google is a metasearcher or a web page but it do not have a systematic search. Google scholar could be of more useful to retrieve information of interest (unpublished papers in journals and doctoral thesis). Also the Digital Library of Theses and Dissertations. Or Open Gray for grey literature.
We did not, in fact, use Google as a database. We first search “systematically” Google scholar for “clinical inertia” and “therapeutic inertia”. We then “checked” Google with the same terms (respectively 162 and 142 results), and went through the various forums and blogs where the subject was discussed, looking for unknown references, but we did not find any.

- Lines 141-143 were changed according to your remark.
- Lines 185-188: “Systematic check of all the results retrieved in Google with the terms “clinical inertia” (162 results) and “therapeutic inertia” (142 results) did not lead to any new inclusion, and neither did personal databases of the authors and the experts we contacted.” was added.
- Lines 188-189: “A manual search of the unpublished literature, including general and personal databases” was suppressed

As for thesis, dissertations, and grey literature in general, this is a choice we made. It is stated in the “Strengths and limitations” section of the discussion, and we persist to think that “it is unlikely that such works would have dramatically modified the results”.

Line 143.- Personal databases from Experts can not be replicated in another research. More information is needed about this source of information in order to make it replicable.

Thank you for this remark: since we did not get any additional article or abstract from this source, we simply forgot to mention it! The 21 additional abstracts resulting from “manual search” in Figure 1 were all retrieved from the lists of references of the included articles.

- We added this specification to the figure 1.
- Lines 185-188: “Systematic check of all the results retrieved in Google with the terms “clinical inertia” (162 results) and “therapeutic inertia” (142 results) did not lead to any new inclusion, and neither did the personal databases of the authors and the experts we contacted.” was added.
Line 184.- In the results section a manual search of the unpublished literature is commented but in the method section this manual search is not mentioned. As we said before personal databases must be identified in order to make replicable the search by other researchers.

    The terms “manual search” were suppressed from the manuscript, and the search process was clarified as described above.

Some MESH as “patient non-adherence” or “medicatoin adherence” were not used in the search strategy. The term “treatment intensification” could also be of interest.

    Of course, clinical (or therapeutic...) inertia and patient adherence maintain a relation that could be a research theme in itself. Patient adherence was not our theme, but we still realised that we had to go as close as possible to the line between the two concepts.
    Defining the search strategy and writing down the appropriate algorithms for each database was a long process. The MeSH terms that you mention were all discussed, as well as others such as “Guidelines (As topic)” ; “Standard of care” ; “Peer review” ; “Disease management” and others. The decisions to use or not each of these various terms in the final search strategy resulted from the search results and were carefully balanced.
    More specifically, the terms you mention added a lot of background noise, but did not seem to give new results of interest for our topic. We therefore decided not to include them in the search strategy.

*What are the strengths and weaknesses of the methods?*

The aim of the study is of interest and the method (systematic review) is very appropriate.

The metodology of qualitative systematic review could be improved. Some data bases have not been reviewed as LILACS. Related to grey literature, the Digital Library of Theses and Dissertations or Open Gray could be of interest too.
Regarding manual search, to use personal databases from experts is not the concept of manual search. The access these personal databases must be specified in order to replicate by other authors.

Regarding definitions and terms, a new table or figure is needed in order to clarify it.

_Can the writing, organization, tables and figures be improved?_

Yes.

When revisions are requested.
Revision is recommend for the following reasons:
- data need to be added to support the authors' conclusions;
- better justification is needed for the arguments based on existing data;
- the clarity and/or coherence of the paper needs to be improved.

_Are there any ethical or competing interests issues you would like to raise?_

No. The Project received a Grant from Pierre Fabre and from the French College of GP Teachers.

_Are the included additional files (supplementary materials) appropriate?_

Yes

**Level of interest:** An article of importance in its field  
**Quality of written English:** Acceptable  
**Statistical review:** No, the manuscript does not need to be seen by a statistician.  
**Declaration of competing interests:**  
I declare that I have no competing interests
This survey of how the term ‘therapeutic inertia’ has been used since its inception to medical literature is valuable and carefully performed. You have conducted a thorough search and thoughtful analysis and have clearly delineated how vague and confusing ‘therapeutic inertia’ is as a term of art in medicine. It is then apparent that ‘therapeutic inertia’ be discontinued from use so that better terms are employed. For management of hypertension at the outset and during follow-up, decisions as reflected by the limited documentation of chart review, may be perceived as ‘appropriate’, ‘inappropriate’ or neither. In each case there is usually some degree of uncertainty. “Inertia” or “momentum” taken from physics indicating a fixed course and, in the medical context, is a pejorative term implying blame, as was used by Phillips et al. You have clearly described how the issues of complexity are now far better recognized in the extensive literature you have cited and analyzed. Why not be more bold in suggesting which terms are far better for examining the complicated process of decision making for treatment of the large populations of individual patients with raised arterial pressure, hypertension.

Thank you for these very supportive comments. As for your suggestion of proposing new terms, we actually started to do so in the “Further research” section of the discussion, suggesting “appropriate inaction” and “inappropriate inertia”. Yet, we tried to remain as factual as possible, and since no new terms to describe these behaviours emerged as such from the results, we decided to be cautious in our conclusions, and settle for a simple suggestion. As suggested in that same “further research” section, we think that new terms should now be adopted, clearly defined, and – hopefully - widely accepted. This is the aim of the subsequent works that we are now conducting.
Line 375 “Certainty” This is vague as ‘certainty’ may be high for knowledge (What does the guideline say?) compared to the uncertainty of prediction (What is the likelihood that this patient will benefit (risk ratio with confidence limits) from antihypertensive treatment in the next 10 years?)

We used “certainty” her as the opposite of “uncertainty”. “Clinical uncertainty” is the term dedicated to the situation where the physician is unsure about the reality of the hypertension, usually because of measurement issues. To clarify this, we used brackets for the term, and an explanation.

- Line 391: brackets were added;
- Lines 388-389: “defined as the feeling of the physician that the numbers might not be reliable and therefore the patient might not be hypertensive” was added.

Line 383, One never treats ‘hypertension’, only the patient except for population based interventions- eg reducing diet salt at the source)

We could not agree more, and this is exactly what we meant by writing: “Treating hypertension is a matter of number. Treating a hypertensive patient requires...”. We rephrased the sentence to make this point even clearer:

- Line 399: “in a patient” was added.

Lines 432-3 For precision, I suggest that you re-word this sentence to emphasize that “therapeutic inertia” is a made up, fuzzy, arbitrary term that blurs over important components of care.

Although we do agree with you on this point, we have tried, again, to remain factual, and keep away from adjectives that would more reflect our opinions than our findings (and hence to avoid the trap of “deductiveness” that the initial promoters of the concept might have fallen into!). Nevertheless, we feel that the reader might come to this kind of conclusion by himself…
Lines 436-9. In relation to a given situation, action/inaction may be appropriate, inappropriate and indeterminate. The ‘inertia’ term clearly stimulated many publications and some research, but is a fuzzy concept at best and useless at worst.

We understand that you mean that we should propose “appropriate inaction” and “inappropriate inaction” (instead of inappropriate inertia), as new terms to define these behaviours and to sort the wheat from the chaff. True, the word “inertia” can be (and is probably usually) heard as pejorative, and already including some kind of inappropriateness. Nevertheless, it is, after all, a term of physics, and, as such, should have no element of judgment attached to it. What’s more, we found it difficult to simply “wipe out” the whole term and concept, and perhaps more effective to try and move away smoothly from judgement to patient-centred care.

Maybe our subsequent works will allow us to go even further on empirical basis.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:** I declare that I have no competing interests.
Editorial comments

1) We consider systematic reviewers proper research studies and it is our policy to request that they are reported according to the PRISMA guidelines, this is to improve research reporting and reproducibility. We appreciate that this study is not a typical one and not all of the criteria in PRISMA can be fulfilled. Therefore, please follow the PRISMA guidelines as closely as possible, and clearly state if particular points are not applicable to your research.

http://www.prisma-statement.org/

From the beginning of this research, we had decided to follow the PRISMA guidelines whenever possible. Of course, these guidelines were made for quantitative reviews and meta-analysis, but we nevertheless tried to stick to as many items as possible.

We modified the manuscript to clarify this:

- Lines 38-39 and 55: we modified the abstract to get closer to the PRISMA guidelines for the abstract.
- Lines 115-117: “As much as possible, we have tried to report this review according to the PRISMA guidelines [14]. However, these guidelines were designed for the report of quantitative systematic reviews and meta-analysis, and a number of item could not be considered here.” was added as a preliminary note in the “Method” section
- Lines 438-440: “We followed the PRISMA guidelines as much as possible, provided that a number of items relate to quantitative systematic reviews and meta-analysis, and therefore could not be considered for this qualitative review [14].” was added to the “Strengths and limitations” section of the discussion.

Also, we filled the PRISMA checklist (again, whenever possible) and you will find the form below.

2) Authors are required to complete a declaration of competing interests. At the moment, this section only contain a statement of funding. Where an authors give no
competing interests, the listing will also read 'The author(s) declare that they have no competing interests'.

The statement: “All the authors declare that they have no competing interest regarding the content of this article” was added at the end of the manuscript (Lines 490-491)
In the meantime, we clarified the role of the funder in Lines 487-489.

3) Please include 'Acknowledgements' section in your manuscript.
We have no particular acknowledgement to include.
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<td><strong>Data items</strong></td>
<td>The coding method is described thoroughly on pages 7-8.</td>
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<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
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<td><strong>Risk of bias in individual studies</strong></td>
<td>Not applicable</td>
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<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
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<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>Not applicable</td>
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<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., ( I^2 )) for each meta-analysis.</td>
<td>Not applicable</td>
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<td>Risk of bias across studies</td>
<td>15</td>
<td>Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).</td>
<td>Not applicable</td>
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<tr>
<td>Additional analyses</td>
<td>16</td>
<td>Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.</td>
<td>Not applicable</td>
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**RESULTS**

<table>
<thead>
<tr>
<th>Study selection</th>
<th>17</th>
<th>Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.</th>
<th>Page 8 and Figure 1</th>
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<tbody>
<tr>
<td>Study characteristics</td>
<td>18</td>
<td>For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.</td>
<td>Not applicable as such, but table 1 provide the major quotes for each article included.</td>
</tr>
<tr>
<td>Risk of bias within studies</td>
<td>19</td>
<td>Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Results of individual studies</td>
<td>20</td>
<td>For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.</td>
<td>Not applicable</td>
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<tr>
<td>Synthesis of results</td>
<td>21</td>
<td>Present results of each meta-analysis done, including confidence intervals and measures of consistency.</td>
<td>Not applicable</td>
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<tr>
<td>Risk of bias across studies</td>
<td>22</td>
<td>Present results of any assessment of risk of bias across studies (see Item 15).</td>
<td>Not applicable</td>
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<tr>
<td>Additional analysis</td>
<td>23</td>
<td>Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).</td>
<td>Not applicable</td>
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**DISCUSSION**

<table>
<thead>
<tr>
<th>Summary of evidence</th>
<th>24</th>
<th>Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).</th>
<th>Pages 15-16: main findings are detailed, but levels of evidence are not applicable.</th>
</tr>
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<tbody>
<tr>
<td>Limitations</td>
<td>25</td>
<td>Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).</td>
<td>Detailed on pages 17-19, “Strengths and limitations” section</td>
</tr>
<tr>
<td>Conclusions</td>
<td>26</td>
<td>Provide a general interpretation of the results in the context of other evidence, and implications for future research.</td>
<td>General interpretation is provided in pages 16-17, at the end of the “Main findings” section and on page 19, in the conclusion.</td>
</tr>
</tbody>
</table>

**FUNDING**

| Funding                   | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | Detailed on page 19 (477-484) |
The concept and definition of therapeutic inertia in hypertension in primary care: a qualitative systematic review

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Running title: Therapeutic inertia in hypertension
Abstract

Background. Therapeutic inertia has been defined as the failure of health-care provider to initiate or intensify therapy when therapeutic goals are not reached. It is regarded as a major cause of uncontrolled hypertension. The exploration of its causes and the interventions to reduce it are plagued by unclear conceptualizations and hypothesized mechanisms. We therefore systematically searched the literature for definitions and discussions on the concept of therapeutic inertia in hypertension in primary care, to try and form an operational definition.

Methods. A systematic review of all types of publications related to clinical inertia in hypertension was performed. Medline, EMBase, PsycInfo, the Cochrane library and databases, BDSP, CRD and NGC were searched from the start of their databases to June 2013. Articles were selected independently by two authors on the basis of their conceptual content, without other eligibility criteria or formal quality appraisal. Qualitative data were extracted independently by two teams of authors. Data were analyzed using a constant comparative qualitative method.

Results. The final selection included 89 articles. 112 codes were grouped in 4 categories: semantics (terms and definitions), “who” (physician, patient or system), “how and why” (mechanisms and reasons), and “appropriateness”. Regarding each of these categories, a number of contradictory assertions were found, most of them relying on little or no empirical data. Overall, the limits of what should be considered as inertia were not clear. A number of authors insisted that what was considered deleterious inertia might in fact be appropriate care, depending on the situation.

Conclusions. Our data analysis revealed a major lack of conceptualization of therapeutic inertia in hypertension and important discrepancies regarding its possible causes, mechanisms and outcomes. The concept should be split in two parts: appropriate inaction and inappropriate inertia. The development of consensual and operational definitions relying on empirical data and the exploration of the intimate mechanisms that underlie these
behaviors are now needed.

Registration number: none.

Keywords: Hypertension, Primary care, Quality of health care, Systematic review, Therapeutic inertia

Introduction

The burden of uncontrolled hypertension

The burden of hypertension weighs heavily on public health in all industrialized countries [1]. Surveys in Europe and North America show prevalences of 40–80% in patients aged 35–64 years [2]. Hypertension leads to a major risk of stroke and acute myocardial infarction (AMI), with morbidity and mortality increasing linearly with increases in both systolic and diastolic blood pressure (BP) [3]. At the same time, there is strong evidence for the major benefits of treating hypertensive patients, resulting in a reduced risk of up to 15% for AMI, 40% for stroke, and 30% for cardiovascular mortality [4].

Considering this evidence, a number of guidelines have been published on the diagnosis, treatment, and follow-up of hypertensive adult patients, either by health authorities or by scientific colleges and societies [5-7]. The way drugs should be used and combined, the treatment targets, and elements of the patients' education and follow-up have been clearly and thoroughly expressed in these guidelines.

Despite this clearly codified and evidence-based assessment, real-life primary care shows quite disappointing results. The classical rule of halves still holds in most European countries: approximately half of the patients with a diagnosis of hypertension are not treated and half of those who are treated do not reach set targets [8]. Although the situation is somewhat better in the US, where two-thirds of the diagnosed patients reach the therapeutic goals, there is still room for improvement [9].
A number of reasons can be put forward to explain these poor results: many are related to the health system and to the patients (notably adherence to treatment). Other reasons are related to health-care providers, and particularly to clinical inertia.

**Clinical and therapeutic inertia**

Clinical inertia was initially defined in 2001 by Phillips [10]. According to this definition, clinical inertia applies only to the management of risk factors, when therapeutic targets are clearly defined and the benefits to reach those targets are well established. Effective therapies should be widely available, and practice guidelines disseminated extensively. Clinical inertia appears whenever the health-care provider does not initiate or intensify therapy appropriately when therapeutic goals are not reached: “recognition of the problem, but failure to act”.

Phillips described three main sets of reasons for therapeutic inertia: overestimation of care, soft reasons (i.e. “improving control”, “target almost reached”, etc.), and lack of training and organization in the practice at “treating to target”. Subsequent articles added clinical uncertainty [11] and competing demands [12] as other reasons for clinical inertia. This initial definition was Phillips’ own idea, and was produced on a deductive basis. With the exact same definition, Okonufa et al. introduced the terms “therapeutic inertia” in 2006 [13]. Since then, the terms “clinical inertia” and “therapeutic inertia” have been used indistinctly (we chose to use the latter in this article). Neither of them, nor “inertia” alone, is a Medical Subject Heading (MeSH) term.

Clinical (or therapeutic) inertia as defined by Phillips has become increasingly acknowledged as a major impediment to reaching both individual and public-health targets for a number of risk factors [13]. Hypertensive patients, in particular, experience therapeutic inertia from their physician in up to 85% of visits in some European countries [9]. On the other hand, Phillips et al. themselves gave a note of caution in their paper that exceptions occur and that appropriate care should allow individualization: “the uniform application of guidelines for patient management could result in overtreatment or inappropriate action”[10].
Since then, this major ambivalence nested in the core of the concept has plagued all research on mechanisms and outcomes of clinical or therapeutic inertia, and all experimental attempts to reduce it. Very few studies have tried to clarify the concept or to refine the definition of therapeutic inertia from empirical data, to make it operational on an inductive basis.

We have conducted a systematic review of the literature on therapeutic inertia in hypertension, and have looked for elements of its definition and conceptualization. Our aim was to come up with a clear concept and to form an operational definition upon which clinical trials could rely.

**Methods**

As much as possible, we have tried to report this review according to the PRISMA guidelines [14]. However, these guidelines were designed for the report of quantitative systematic reviews and met-analysis, and a number of item could not be considered here.

**Types of studies considered for the review**

Because we were looking for definitions of a recent concept, we considered that every type of paper could be eligible.

- Trials
- Surveys and epidemiological studies
- Qualitative research
- Reviews
- Opinion papers and editorials about the concept of inertia or about guideline-implementation issues

**Search strategy for identification of studies**

**Databases.** The following databases were searched from their beginnings until June 2013: Medline, EMBase, PsycInfo, the Cochrane library and databases, BDSP (French Public
The search algorithm for Medline (via PubMed) was: ("guideline adherence"[MeSH Terms] OR ("practice guidelines as topic"[MeSH Terms] AND ("clinical audit"[MeSH Terms] OR "clinical competence"[MeSH Terms] OR "attitude of health personnel"[MeSH Terms] OR "delivery of health care"[MeSH Terms] OR "physician's practice patterns"[MeSH Terms] OR "nurse's practice patterns"[MeSH Terms])) AND ("hypertension"[MeSH Terms] OR "antihypertensive agents"[MeSH Terms])) OR "clinical inertia"[All Fields] OR "therapeutic inertia"[All Fields]. The other databases were searched using the same algorithm adapted to their respective syntactic structures.

Languages were limited to English, French, Spanish, Portuguese, German, and Dutch.

Additional searches. Google Scholar was systematically searched for “clinical inertia” and “therapeutic inertia”. All results retrieved by searching Google with the same terms were explored. The reference list of each selected article was systematically screened for other relevant articles. Experts in the field were contacted and asked for their personal databases.

Methods of the review

Abstracts selection. Two researchers (JPL and TP) reviewed independently the titles, abstract sections, and keywords of every record retrieved, using a score list. The article was included if one of the following characteristics was present:

- The words “clinical inertia” or “therapeutic inertia” appeared
- Hypertension guidelines implementation was the main subject
- Design, assessment, or evaluation of any kind of intervention directed to the general practitioner for hypertension control was the main topic
- The general practitioners’ behaviors or barriers to change regarding hypertension treatment were the main topic.
Although these last topics were not part of the research question, chances were that the concept of therapeutic inertia would be discussed in such articles.

*Full-texts assessment.* The articles were rejected if they recorded no element of definition or conceptualization. Articles which only cited the words “therapeutic inertia” or “clinical inertia” with no further explanation, or which referred directly and explicitly to the initial publication by Phillips without any restriction or discussion about its content were rejected. Epidemiological surveys that measured the gap between actual care for hypertension and guidelines but did not discuss the mechanisms of poor implementation were also rejected, as they did not provide any criteria or element of a definition for therapeutic inertia.

Agreement between the researchers was calculated using Cohen's kappa. Differences in opinion were resolved by discussion that included a third researcher (JSC).

*Process of data collection.* A constant comparative qualitative method according to grounded theory was used to collect and classify emerging data from the full articles [15,16]. Units of text (words, sentences, paragraphs) were labeled through an open-coding process. A lexical analysis was carried out simultaneously, which focused on the words used to comment on inertia. Axial coding was then conducted, which consisted of comparing and grouping codes together into categories. Finally, through a selective coding process, all the categories were organized hierarchically according to their reliability and consistency, which led to an accurate description of the emerging concepts.

Data were independently analyzed from each article by the two teams of researchers (JPL/TP and IAA/AM), using a qualitative analytical software package (NVivo 9.2, QSR International Pty Ltd, Doncaster, Australia; 2011). Discrepancies were resolved by discussion, and any disagreement went to arbitration with a fifth researcher (JSC).

**Results**

*Search results*
The initial search of the databases resulted in a total of 2,946 abstracts: 1,061 from Medline, 1,732 from EMbase, 74 from PsycInfo, 77 from the Cochrane Library and database, and 2 from the other databases. After reviewing the abstracts, removing duplicates, and discussion to resolve differences in opinions, 145 abstracts were included: 84 from Medline, 51 from EMbase, 8 from PsycInfo, 2 from the Cochrane Library and database, and none from the other databases (duplicates were removed in this order).

Systematic check of all the results retrieved in Google with the terms “clinical inertia” (162 results) and “therapeutic inertia” (142 results) did not lead to any new inclusion, and neither did the personal databases of the authors and the experts we contacted. A manual search of the unpublished literature, including general and personal databases, and a systematic search of the reference lists of selected articles retrieved found 21 more abstracts. Inter reviewer agreement at this stage, expressed as the observed Cohen’s kappa was 0.84 (95%CI: 0.80–0.88).

The full texts of 165 articles were assessed and checked for relevant content independently by two researchers (JPL and TP): 76 did not contain any relevant information, and 1 article could not be found (no archive kept by the journal nor by the author). The final selection included 89 articles (Figure 1).

**Types of publications and their contents**

Of the 89 articles, 36 were clinical studies (8 trials, 16 cross-sectional studies, 7 cohort studies and 5 surveys), 5 were qualitative studies (including a nominal group consensus study), 15 were literature reviews – of which none matched the criteria of a systematic review -, 10 were editorials, and the other were experts opinion or position articles (including commentaries and 2 letters) (Table see Additional file 1).

**Coding**

Open coding of the relevant content of the articles resulted in 112 codes. These open codes were grouped for analyses into four categories: *semantics* (terms and definitions),...
Terms and definitions (Table 1)

Most authors considered that “clinical inertia”, “therapeutic inertia” and “physician inertia” were all synonymous. This was either explicit [17,18] or implicit when Phillips’ definition of clinical inertia was quoted to define therapeutic inertia [11] or physician inertia [19]. A few authors, however, insisted that different terms should mean different things: “the terms “clinical inertia” and “therapeutic inertia” have been used recently by authors, primarily to attribute to physicians the apparent failure of patients to attain therapeutic blood pressure goals. We think it would be helpful to define and differentiate these terms” [20]. Scheen made a clear distinction, stating that: “Therapeutic inertia is one of the components of clinical inertia”, but gave no further explanation [21]. Giugliano et al. made a distinction between the overall phenomenon of clinical inertia and the part that was attributable to the physician’s behavior: i.e., physician inertia [22], a term also used by Krakoff et al., but without any distinction from clinical inertia [19]. Gil-Guillén et al. separated “diagnostic inertia” from “therapeutic inertia”: “Diagnostic inertia was identified when a patient without known hypertension had high blood pressure (BP) but was labeled “normal” by the medical staff, and therapeutic inertia when treatment was not modified for a hypertensive patient on the presence of high BP values” [23]. Vinyoles proposed three kinds of inertia: “Three inertias are barriers to change: physician’s inertia, patient’s inertia, and health authorities inertia”, but the respective definitions remained implicit [24]. Discussing the synergy between patient nonadherence and healthcare provider inertia, Reach proposed “Clinical myopia” for the common mechanism underlying these behaviors [25].

Definitions

While the presumed causes of clinical inertia were widely discussed in a number of articles, considerations on the definition remained scarce. A few authors pointed out that there was a
need for an accurate definition: “While there is additional history behind the use of the terms “clinical inertia” and “therapeutic inertia,” much of the more recent usage is imprecise. We think that it is time to use these terms more carefully and more purposefully and to refer to models that have some basis in theory and evidence.”[20].

A few specific elements were not clear about Phillips’ definition. Ardery et al. considered that: “Infrequent documentation of lifestyle recommendations could reflect another type of clinical inertia—namely, missed opportunities to promote patient self-management” [26]. Gugliano et al. stated that: “Clinical inertia also may apply to the failure of physicians to stop or reduce therapy no longer needed” [22], a situation for which Rodrigo et al. proposed the specific term “therapeutic momentum” [27], although this term had already been defined as synonymous to clinical inertia by Faria et al. [17].

Scheen considered that the actual term “inertia” already meant “unjustified”: “therapeutic inertia can be defined as an unjustified delay in treatment initiation or intensification”, or “deleterious”: “a caregiver behavior resulting in a deleterious delay” [21]. The possible occurrence of a justified or beneficial delay was not discussed in this article. Looking for an operational definition, O’Connor concluded that: “Flexibility in how clinical inertia is defined could be seen by some as a limitation. However, from the point of view of care improvement, this sort of flexibility may often be an advantage because it allows local tailoring of initiative and interventions.” [28].

Who

All authors agreed that the practitioner had the principal role in the phenomenon. Nevertheless, many insisted on the imbrication of the various stakeholders leading to inertia, and on the patient and health system responsibilities. O’Connor et al. proposed a conceptual model that combined physician, patient, and office and system factors [28]. The same type of classification emerged from the qualitative study of Howe et al., with some overlapping of the categories [29].
Although Phillips, in his initial article, considered that: "Patient nonadherence cannot explain the failure of providers to initiate or advance therapy appropriately", he also admitted that: "Clinical inertia may also reflect patients' lack of enthusiasm for management of asymptomatic problem" [10]. The actual complexity of the relation between the caregiver's inertia and the patient's adherence or preferences was often discussed: "the inability to achieve adequate BP control likely arises through a complex interaction of patient and provider behaviors" [30]. In their attempt to provide a conceptual model for clinical inertia, O'Connor et al. hypothesized that the various patient factors involved accounted for 30% of the whole phenomenon [28]. These factors would include denial of disease, low health literacy, number, cost and side effects of medications, and doctor-patient relationship issues.

Lin et al. found that patient's non-adherence was cited by the physician as the barrier to intensifying therapy in 19% of the visits, and "other patient factors" in 49% [31]. Reach proposed a common mechanism leading to physician's inertia and patient nonadherence [25]. He defined "clinical myopia" as giving preference to the immediate and tangible benefits of nonadherence or inertia, instead of long-term benefits, and hypothesized that these behaviors, sharing the same psychological structure, enter into resonance. However, the large retrospective cohort study of Heisler et al. found that patient adherence had little effect on provider's decision about intensifying therapy [32].

Office and system factors accounted for 20% of clinical inertia according to O'Connor et al. [28]. In the qualitative studies, time was an issue raised by many participants, and systematically related to competing demands [29,33]. Some authors agreed with O'Connor to regard this time issue as being a part of clinical inertia and include it in the "Physician factors": "Providers often have competing interests, including lack of time, more urgent requests made by the patient, and practice habits that can prohibit the escalation of care when such a modification is clinically indicated. This behavior (or lack thereof) is known as clinical inertia" [34]. Others considered it as being out of the reach of the practitioner, and therefore not a part of clinical inertia: "...health system issues such as lack of time in
consultations.” [35]; “The impact of the medical environment should also be underscored (…) providers need to have adequate time and resources to be able to adhere to guidelines and to provide the necessary patient education and counseling” [36].

How and Why

Clinical uncertainty regarding BP measurements was considered in very different ways. Repeated measurement could be regarded as a need, as stated by general practitioners in a qualitative study: “To monitor therapy more accurately, more automated machines for home monitoring and greater access to ambulatory BP monitoring were considered of need” [29], or as a pure waste of time, according to Phillips and Twombly answering to criticism on their editorial: “Our understanding of the basis for clinical inertia has been advanced by the demonstration of contributions from “clinical uncertainty” and “competing demands”, but it’s been almost 7 years since the concept was promulgated. We believe that rather than doing further studies on mechanisms, it’s time to focus on overcoming clinical inertia” [37,38].

Acceptable control seemed to have two different acceptations. The first one was to consider that a BP close enough to the recommended target was satisfying, and the other that the actual target for a given patient would be dictated by the baseline BP [39-42]. Although most authors considered this behavior as inappropriate and unjustified, some had slightly different views. Banegas et al. pointed out that: “In fact, the trial-based differences in achieved cardiovascular protection within this range of BP values seem to be small at best” [43]. Discussing their empirically derived model of “clinical inaction” Safford et al. noted that: “best level of control may appropriately differ from patient to patient as patients increase in complexity, especially in the geriatric population” [44]. Others clearly stated that this behavior was not inertia. Crowley et al. conclude their work on hypertension telemanagement with: “However, when physicians did not intensify treatment, it was because blood pressure was closer to an acceptable threshold, and repeat blood pressure elevations occurred less frequently. Failure to intensify treatment when home blood pressure is elevated may, at times, represent good clinical judgment, not clinical inertia” [41], and Kennedy and Mac Lean
stated: “It is important to distinguish clinical inertia from modified therapeutic goals” [45].

Competing demands have proven to contribute consistently to clinical inertia [11,46,47]. In terms of concepts, a controversy between authors summarizes the problem. Phillips and Twombly proposed in an editorial to overcome the problem by recommending that physicians “run the numbers first and deal with blood pressure and glucose before asking about other problems” [37]. This editorial led to a number of answers. Among them, Boyd and Leff stated that “this is the wrong way to frame the issue because it does not adequately acknowledge a patient-centered perspective of chronic illness care, in which all of the patient’s conditions are considered in terms of the relative benefit of treating each condition in the presence of the other conditions, the cumulative effect of all the recommended treatments, and the individual’s treatment priorities” [38]. Vijan et al. added that: “If primary care physicians focused on the numbers first, they would end up imposing their own priorities onto patients, rather than letting patients help set the agenda. Consider a visit with a patient who has depression or chronic pain. Until a physician addresses such issues, there is little chance of managing chronic conditions well” [38].

Guidelines skepticism has been widely discussed in a number of conditions, including hypertension, since Cabana et al. founding article [48]. This skepticism includes distrust of the evidence underpinning the guidelines, discrepancies between the various guidelines, unrealistic treatment targets and inappropriateness for primary care. Each of these factors is controversial: "clinical inertia may be a clinical safeguard through which physicians acknowledge the uncertainty in some current practice guidelines” [22]; “realistic expectations about the results of adherence to clinical practice guidelines are also called for when considering the subject of possible clinical inertia.” [20]; “clinical inertia or inaction may actually act as a safeguard for some patients when overzealous guidelines require treatment before definitive trials are available” [49]; “in most guidelines, the full versions make clear that evidence on targets is limited and their recommendations are unattainable in many patients” [50]. Borzecki et al. separated guidelines skepticism from clinical inertia: "The most important
Provider-related barriers to adherence to best practice include clinical inertia and lack of provider agreement with guidelines [36].

Overestimation of care is a well-known phenomenon. All authors agreed to consider its results as “pure inertia” that should be specifically and systematically addressed [51,52].

Perceived patient attitude, and notably perceived non-adherence or unwillingness to take more medications or to follow counseling, relates to both non-adherence and doctor-patient relationship. Although cited in many articles as a cause of inertia, it was very rarely explored, and even less commented. Campbell made this remark in an editorial about hypertension guidelines: “Individual patients vary widely in their perception of acceptable risk and side effects. (…) Surprisingly, the patient’s role in deciding his or her own blood pressure target receives scant attention in guidelines for hypertension” [50].

Appropriateness

A number of authors insisted that the lack of treatment intensification for a patient who did not reach the target BP could actually reflect appropriate care. Various specific situations involving this issue were already highlighted in the previous sections. The gap between guidelines and actual care could be regarded as an appropriate translation of trials results in real-life: “Sometimes the inertia may be appropriate. There might be a difference between effects in controlled trials and effectiveness in primary care patients. The GP has to take into account all circumstances for each patient, e.g. other risk factors, concurrent disease, medications, and function of different organs” [53]; “It is possible that the guidelines may be correct, but there is also the possibility that the care by the physicians is appropriate since BP 130/80 mmHg is hard to achieve, and recent reviews suggest there is insufficient evidence to support such a low BP target” [43]. Hicks et al. conducted a prospective survey on the point of care in hypertensive diabetic patients. They found that: “26% of patients are ‘near goal’, and action in this group is infrequent. This phenomenon has been referred to as ‘clinical inertia’ (…). The reasons given by providers for no action may reflect an
individualized approach to patient care, rather than an unquestioned adherence to guidelines. (…)We did not find evidence for a pattern of a poor quality of care. On the contrary, providers seemed willing to consider the needs of their patients and the specific clinical circumstances” [47].

With a nominal group approach, Safford et al. were able to provide some qualitative evidence on the possible appropriateness of inaction. Experts voted and agreed on a number of situations where inaction would be appropriate and others on when it would not. After giving useful clues for further research on the topic, the authors emphasized the need to make the appropriate decision "to not intensify treatment" as clear as possible: “Distinguishing potential clinical inertia from appropriate inaction is an important initial step for interventionists seeking to identify strategies to improve care and for policy makers seeking to measure quality of health care.” [44].

Discussion

Main findings

This review retrieved major discrepancies between the authors regarding definition and conceptualization of therapeutic inertia. Opinions differed widely on every issue, from semantics to the inner quality of inertia regarding therapeutic decisions. Whereas some claimed that the practitioner’s decision should rely on numbers and numbers only, others regarded inertia as a choice that could sometimes be reasonable and adequate. On a more factual level, some suggestions for interventions to reduce clinical inertia went against the principles of evidence-based medicine and patient-centered practice, and some studies highlighted behaviors that matched the definition of therapeutic inertia but were nevertheless appropriate.

The reliability of BP measurement is crucial. Nested in therapeutic inertia as one of its factors, “clinical uncertainty”, defined as the feeling of the physician that the numbers might
not be reliable and therefore the patient might not be hypertensive, appears to be a concept in itself. The diagnosis of hypertension means a lifelong treatment. The decision to initiate or intensify a treatment requires “certainty”, and emergency is exceptional. Whether a reasonable delay to secure a diagnosis with ambulatory measurement is acceptable is not addressed by the initial definition. In some trials and surveys, such a delay was regarded as pure inertia. Recent guidelines have advocated the systematic use of home or ambulatory blood pressure monitoring before any treatment initiation or modification [6]. On the other hand, a delay in confirmation should remain reasonable, and measurements should not be repeated indefinitely.

Above all, evidence-based practice in primary care should always remain patient-centered. Treating hypertension in a patient is a matter of numbers. Treating a hypertensive patient requires a thorough analysis of the patient’s global health and comorbidities, including psychological and social issues, and shared decision making on the patient’s expectations as well as the biomedical data [4,54,55]. Still, there is a risk of abusive reference to the informal frames of evidence-based practice and shared decision making to mask unjustified delays.

Our findings suggest that the definition of therapeutic inertia should take into account the inherent complexity of primary care situations. Health care system realities on one side, patients’ values and attitudes on the other, both interact with the GPs’ behaviours to generate a complex system, not accounted for by the initial definition. What is more, this definition did not take into account the consequences, deleterious, neutral or useful of inaction.

A definition that merges an unacceptable loss caused by lack of knowledge, conviction, or time with a legitimate demand for reliable data and an appropriate decision is definitely not an operational definition. There is no sense in trying to reduce a complex phenomenon without knowing the precise conditions of its occurrence and to what extent it can be deleterious or useful. This issue has become increasingly acknowledged in the most recent
articles, with a number of authors trying to differentiate “pure” inertia from “appropriate” inaction.

Finally, our main conclusion is that it all comes down to appropriateness, with regards to both the various mechanisms of inertia and the patient-centered model of care (Figure 2).

**Further research**

Semantics should now reflect these findings as clearly as possible. The words appropriate and inappropriate refer to neutrality and objectivity, without any judgment quality or manichaeism attached to them, and reflect a genuinely factual approach. We therefore suggest that two different definitions, one for “appropriate inaction” and the other for “inappropriate inertia”, should now be developed. Of course, we realize that a number of items in this review could be part of either of these two definitions. For example, clinical uncertainty can lead to appropriate inaction when blood pressure has been measured only in the office, and the practitioner claims for a home or ambulatory measurement, or to inappropriate inertia when this has been already done twice and yet a third time is scheduled. Further research is needed to clarify and precisely define to what extent each of these items should be accounted for, and achieve a consensus that should rely as much as possible on an inductive basis and empirical data.

The intimate causes and reasons leading to such behaviors should also be explored thoroughly. There is a major lack of qualitative data in this field. There is no way behaviors can be changed without prior exploration of their ins and outs.

On these new bases, interventions could be designed and assessed to either encourage appropriate inaction or reduce inappropriate inertia.

**Strengths and limitations**
We followed the PRISMA guidelines as much as possible, provided that a number of items relate to quantitative systematic reviews and meta-analysis, and therefore could not be considered for this qualitative review [14].

As already stated, “inertia” is not a MeSH, which made the search a bit more difficult and “risky”, and it is possible that we missed articles discussing the concept using other terms.

We tried to avoid this by elaborating a search algorithm as sensitive as possible to all aspects of the concept, and by paying a special attention to the publications cited in references in the selected articles. Although our concern was general practice, we did not include any MeSH terms related to primary care. Narrowing the search with such terms would have resulted in a loss of a few articles of interest, which discussed theoretical aspects of guideline adherence or inertia regardless of the context of care.

Although relying on a systematic search of the literature, this research was not a meta-synthesis of qualitative research. This was because we conducted a qualitative analysis of original articles that could be qualitative research, quantitative research or opinion papers. There is no standard method for this kind of research, and the choice of a constant comparison qualitative method can be questionable. Because we were only looking for elements of definitions and concepts, quality assessment of the studies described in the selected articles was not justified. Therefore, the selection of the relevant articles very much depended on the researchers’ opinions. We tried to minimize this bias with a systematic blinded selection process.

We did not systematically search for “grey” literature. Considering the lack of qualitative research in this review and the wide use of qualitative methods in theses and dissertations, we might have missed some interesting works. However, it is unlikely that such works would have dramatically modified the results.

When dealing with definitions and concepts, exploring the causes (“How and why”) might seem questionable, and even out of focus. But when it comes to intimate mechanisms of
human behaviours, causes and consequences exist first, and then, possibly, the concept arises. A number of authors in this review did think about the definition and the concept starting from observed or assumed causes, and so their contribution to the conceptualization was in terms of (possible) causes, which justified the “How and why” section of the results.

Finally, the extraction of data and their coding is always, to some extent, affected by the personal understanding of the researcher. However, the two teams coded separately and a fifth researcher adjudicated any discrepancies, in order to minimize this bias.

Conclusion

This systematic review of the literature revealed important discrepancies, and sometimes antagonisms, regarding the possible causes, inner mechanisms and outcomes of therapeutic inertia in hypertension. The initial definition proposed by Phillips, and referred to by most authors, does not take into account the inner complexity of doctor-patient relationship and shared decision making in primary care.

Our data analysis led us to conclude that the concept of therapeutic inertia should be split into two separate concepts, namely appropriate inaction and inappropriate therapeutic inertia. The development of consensual and operational definitions and the exploration of intimate mechanisms that underlie these behaviors are now needed.

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Authors’ contributions

All authors participated in the conception and initial design of the project. JPL, JSC and TP searched the databases and other sources. JPL, JSC, IAA, AM and TP assessed the articles, extracted the data, and performed the initial coding. ER, KH and EV reviewed the initial coding. All authors participated in definition and organization of the categories. JPL, KH and EV drafted the manuscript. All authors revised the draft and approved the final manuscript.

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**Figures**

Figure 1. Systematic research flow chart

Figure 2. Model of shared decision-making leading to either appropriate inaction or inappropriate inertia

**Tables**

Table 1. Terms and definitions

**Additional files**

Additional file 1 – Results

(Therapeutic_inertia_in_hypertension_Additional_1_Results.pdf)