PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Proposed Minimum Information Guideline for Kidney Disease: Research and Clinical Data Reporting – A Cross Sectional Study
AUTHORS	Kumuthini, Judit; van Woerden, Christiaan; Mallett, Andrew; Zass, Lyndon; Chaouch, Melek; Thompson, Michael; Johnston, Katherine; Mbiyavanga, Mamana; Baichoo, Shakuntala; Mungloo-Dilmohamud, Zahra; Patel, Chirag; Mulder, Nicola

VERSION 1 – REVIEW

REVIEWER	Shuchi Anand Assistant Professor, Stanford University, US
REVIEW RETURNED	03-Apr-2019

GENERAL COMMENTS	I commend the authors on a major attempt to provide a standardization instrument for kidney disease related data collection. The authors' rationale as presented in the introduction is strong. I have following concerns regarding methods: 1) While the authors title their instrument, "Minimum Information Required Guideline: Kidney Disease Research and Clinical Data Reporting", the survey sent to field specialists (as attached as a RedCap document) seems to have evaluated "Genetic Kidney Disease Research and Clinical Data Reporting Standardization survey", which may have influenced the responses of the participants. 2. The authors don't spell out the numbers of field specialists the survey was sent, how they were selected (was there an objective threshold to be selected?), and the overall response rate. Clearly there was less representation from Asia and North America, but I am not sure if this was due to the sampling frame or due to the response. --A minor point here but the # of responses in the abstract versus results are different 3. How did the authors use the responses? Was there a cut off of % used to deem an element as essential or optional or not necessary? I find it also odd that in urinary markers 24 hour collections are deemed essential, since these are so difficult to obtain and urine protein to creatinine ratios are not asked for. Further serum assessments are also placed in the 'urine related test index' category, but I am happy with the elements assessed in the serum. 4. Similarly the histopathology field seems sparse, and may be related to a genetic lens rather than a broader kidney disease lens, since most researchers would want to abstract much higher level details of pathology if available.

	5. Other demographic features that would be likely worth consideration for inclusion include occupation and education (as a marker of income an/do health literacy) . On the other 'tribal affiliation' may be very specific to Africa and not relevant to large portions of Asia for example. 6. Sections on kidney disease related are clearly not meant to be filled out by patients (whereas other questions in this section could be directly filled out by patients), but rather a very highly trained health care worker or physician--> in the example survey some one filled in 'chronic hematuria'; most health care workers I have worked with would not be able to identify this as a symptom or sign based on review of medical records. 7. I liked the study elements and experimental design sections very much especially since they ask for DOI which can assist with creation of an observatory/registry and facilitate collaboration with secondary data analyses; given that it would be important to ascertain sample storage and storage conditions In the presentation of the results the authors should note that inclusion of the redcap survey led to several additional (meaningless) pages attached. The figures are important but somewhat hard to read legends due to font size and color. In the discussion, I would like the author to clarify two possible uses of their instrument: 1) data abstraction from existing or ongoing studies for reporting to a larger database (as implied by the 'big data' rationale) versus 2) use for primary data collection in studies to launch. I don't believe the authors have to pick one, but it would be important to clarify which one was their primary intent and how they would envision the instrument would be used in the alternate scenario (thus deeper discussion on operationalizing this instrument).

REVIEWER	Allyson Lister OERC, University of Oxford, UK
REVIEW RETURNED	17-Apr-2019

GENERAL COMMENTS	The authors have described how there are no previous reporting guidelines for kidney disease, and have created such a guideline based on 1) survey results, and 2) pre-existing guidelines. Specifically, the manuscript states that a number of pre-existing guidelines were ‘proposed’ as part of the first draft of their own reporting guideline, which was then further refined based on a survey of experts in the field. The pre-existing guidelines initially used in the creation of the survey were: PhenX collection measures, CKDO, MIAPE and MIDE. What makes these particular guidelines the best choice? There are currently 161 Reporting Guideline standards in FAIRsharing (https://fairsharing.org/standards/?q=&selected_facets=type_exact:reporting%20guideline). What made the proteomics and Drug Metabolism Enzymes and Transporters standards the preferred choices in the initial requirements-gathering phase? This is relevant to this manuscript and should be included, especially as some, such as MIAPE, have no direct relevance to kidney disease. Others, such as PhenX, seem to have broken URLs (https://original-phenxtoolkit.rti.org/index.php isn’t working, and I don’t see how what is visible at https://www.phenxtoolkit.org/protocols is relevant to the manuscript - this needs to be explained more). The relationship between the

	chosen pre-existing guidelines and the research area of interest (kidney disease) should be explained. Many of the elements of the guideline have been linked to external ontologies. How do the authors see these ontologies being used in future? Will they be linked to the XML Schema / XML files? As the manuscript stands now, the ontologies are mentioned but not contextualized - though I know they are used, I would like to know how and why they are used. While the guideline name itself as well as the manuscript reference the more general “clinical data” part of this standard, the relevance to clinical data beyond kidney disease data is not fully described. I would appreciate more explanatory text as to how the more generic aspects of this guideline relate to / enhance available clinical data standards or CRFs (such as CDISC, if relevant)? While the manuscript is clear in how the guidelines are novel with respect to kidney disease research, I would appreciate having an explanation of how this guideline provides a novel services for clinical data standards generally. Line 46 of page 8 references “XML schemas”, but earlier in the manuscript only one schema was described. How many are there? A short explanation of why REDcap was used in preference to other publicly-available survey applications such as Google Forms or SurveyMonkey would be helpful, as the survey itself did not contain any sensitive information. An XML schema associated with the guidelines is useful, but no use cases have been provided to show readers how the authors expect the XML files to be used. Will the ontology terms linked to the guideline elements be used within the XML file? Will the XML files that validate against this schema then be accepted into a publicly-available database? What is the intended use of such XML files? Additionally, the authors state the following: “An associated XML schema was developed for REDCap implementation, consisting of 3 sections - the participant-, experiment and study-level information, and can be found in Supplementary File 5.“ This reads like an XML scheme specifically for REDCap - if this is indeed the same schema as that which has been implemented for the guideline, this needs to be stated. Page 6, line 12 - should read “XML” Line 8, page 5: “principals” should be “principles” The columns labelled “Ontology ID”, “Concordant Ontologies”, and “Concordant Standards” are unexplained in the text. Please can the intent and meaning behind these parts of the guideline be included. I found it difficult to read the full reporting guidelines, as the PDF formatting has truncated the majority of the table to just the first 3 columns, and then after those are shown, the next three columns. I would appreciate having an alternative format for the guidelines to have a better look at them please. I tried to look at the URL provided (https://www.h3abionet.org/data-standards/datastds) but there were no clickable links for the guidelines on that page.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:

1. While the authors title their instrument, "Minimum Information Required Guideline: Kidney Disease Research and Clinical Data Reporting", the survey sent to field specialists (as attached as a RedCap document) seems to have evaluated "Genetic Kidney Disease Research and Clinical Data Reporting Standardization survey", which may have influenced the responses of the participants.

We would like to thank the reviewer for the constructive feedback. To address the feedback, we have added an additional section to the draft development section of the Methods, on pg. 5, line 128, highlighted in green. To elaborate, surveys were constructed specifically to gain the opinions on elements which may veer more towards acquired or inherited kidney disorders. Some elements will only be applicable to one type, this is why the Essential and Optional classification is so important, highlighting the adaptability between disease type application.

2. The authors don't spell out the numbers of field specialists the survey was sent, how they were selected (was there an objective threshold to be selected?), and the overall response rate. Clearly there was less representation from Asia and North America, but I am not sure if this was due to the sampling frame or due to the response.

--A minor point here but the # of responses in the abstract versus results are different

3. How did the authors use the responses? Was there a cut off % used to deem an element as essential or optional or not necessary? I find it also odd that in urinary markers 24-hour collections are deemed essential, since these are so difficult to obtain and urine protein to creatinine ratios are not asked for. Further serum assessments are also placed in the 'urine related test index' category, but I am happy with the elements assessed in the serum.

4. Similarly, the histopathology field seems sparse, and may be related to a genetic lens rather than a broader kidney disease lens, since most researchers would want to abstract much higher-level details of pathology if available.

We would like to thank the reviewer for the constructive feedback given from points 2 through 4. To address the feedback, we have added additional sections in the Online Survey section under Methods, to further clarify how the survey was setup, and how the survey feedback framed the final output. Further detail with regards to how participants were selected is provided on pg. 5, line 136, highlighted in yellow, and pg.6, line 147, highlighted in green. Additional detail on how the response framed the final output is provided on pg. 6, line 142, highlighted in yellow. To clarify, surveys were not sent to a limited number of participants, they were open, and could be forwarded to varying professionals within the research field with the requesting level of expertise. The surveys were sent to members within established kidney disease research networks for broad uptake and feedback. Additionally, survey response influenced the final output in the following way, “Elements were classified as either E or O based on the E% percentage of E votes received. This percentage was calculated by dividing the total number of E votes by the number of votes made for a given element. Elements with lower than 50% were classified as O, while elements higher than 70% were classified as E, and elements within the 50 – 70 E% were classified with discretion based on correlations with the previously developed reporting guidelines and standard collection measures. Additional suggestions, not included in the draft, made by respondents were similarly classified.” However, here, we would like to highlight again, the adaptability of the reporting guideline based on the E/O optionality. As the reviewer highlighted, histopathology may specifically applicable to genetic/inherited kidney diseases. This is why the element is classified as Optional – not necessarily essential for acquired to diseases, but likely very relevant to genetic diseases. Similarly, with regards to the Urine Test Index, these were defined based on survey feedback and alignment to existing standards. Importantly, to highlight serum tests, the 'urine related test index' was renamed Urine and Serum Test Index in the reporting guideline. Additionally, the numbers variance was corrected in the abstract.

5. Other demographic features that would be likely worth consideration for inclusion include occupation and education (as a marker of income an/do health literacy). On the other 'tribal affiliation' may be very specific to Africa and not relevant to large portions of Asia for example.
We would like to thank the reviewer for the constructive feedback. To address the feedback, we added an additional section, as previously highlighted, on pg. 6, line 142, highlighted in yellow. The primary aim of the reporting guideline is to provide African researchers the tools to enhance their own data management, therefore the tribal affiliation, is more applicable to African populations, but this is also why the element is classified as optional. The additional elements suggested by the reviewer are useful to incorporate in a future update of the reporting guideline. Similar suggestions under investigation for inclusion are albumin:creatinine and protein:creatinin ratios. We're still investigating the best methods to garner consensus with regards to future adaptions to the guideline.

6. Sections on kidney disease related are clearly not meant to be filled out by patients (whereas other questions in this section could be directly filled out by patients), but rather a very highly trained health care worker or physician--> in the example survey someone filled in 'chronic hematuria'; most health care workers I have worked with would not be able to identify this as a symptom or sign based on review of medical records.
We would like to thank the reviewer for the constructive feedback. To address the feedback, we have added a section in the Discussion, to clarify the difference between the case report form and the reporting guideline, detailing who should be employing/completing the reporting guideline. The addition is made on pg. 9, line 219, highlighted in green. The reporting guideline was not developed to replace the case report form but rather to provide a set of data reporting rules for researchers to adhere too. Therefore, it is not to be used/completed by patients but rather trained healthcare professionals and researchers.

In the discussion, I would like the author to clarify two possible uses of their instrument: 1) data abstraction from existing or ongoing studies for reporting to a larger database (as implied by the 'big data' rationale) versus 2) use for primary data collection in studies to launch. I don't believe the authors have to pick one, but it would be important to clarify which one was their primary intent and how they would envision the instrument would be used in the alternate scenario (thus deeper discussion on operationalizing this instrument).
We would like to thank the reviewer for the constructive feedback. To address the feedback, a detailed discussion on the intent of the reporting guideline was added on pg. 8, line 212, highlighted in yellow. The primary intent of the reporting guideline is to encourage harmonized data collection when launching new projects within the kidney disease research field. Ultimately, this will enhance the overall research community's capacity for conducting high-quality, interoperable, and reusable research, adding long-term value to the collected clinical data and generated research data and encouraging more collaborative efforts worldwide. Similarly, the reporting guideline can also be employed retrospectively for data abstraction from existing or ongoing studies when reporting to a larger database, enabling the previously mentioned efforts. Although, in this approach it may be more difficult to adhere to the guideline due to missing information. In the future, we aim to write a guideline, outlining how these can be managed.

Reviewer #2:
The authors have described how there are no previous reporting guidelines for kidney disease and have created such a guideline based on 1) survey results, and 2) pre-existing guidelines. Specifically, the manuscript states that a number of pre-existing guidelines were 'proposed' as part of the first draft of their own reporting guideline, which was then further refined based on a survey of experts in the field. The pre-existing guidelines initially used in the creation of the survey were: PhenX collection measures, CKDO, MIAPE and MIDE. What makes these particular guidelines the best choice? There are currently 161 Reporting Guideline standards in FAIRsharing. What made the proteomics and Drug

Metabolism Enzymes and Transporters standards the preferred choices in the initial requirements-gathering phase? This is relevant to this manuscript and should be included, especially as some, such as MIAPE, have no direct relevance to kidney disease. Others, such as PhenX, seem to have broken URLs (https://original-phenxtoolkit.rti.org/index.php isn't working, and I don't see how what is visible at https://www.phenxtoolkit.org/protocols is relevant to the manuscript - this needs to be explained more). The relationship between the chosen pre-existing guidelines and the research area of interest (kidney disease) should be explained.
We would like to thank the reviewer for the constructive feedback. To address the feedback and clarify how pre-existing guidelines shaped the creation of the current reporting guideline, we expanded on the Draft Development section in the Methods. See pg. 5, line 117, highlighted in yellow. The PhenX collection measures, H3Africa Standard CRF and CKDO were primarily used to inform kidney-specific clinical data, while the experimental standards were primarily used to inform study- and experiment data specifically. Many of the experimental standards have overlapping study- and experiment-fields, which were used to develop the draft. Notably, once a dedicated site has been developed for our developed reporting guidelines, we will also be submitting them to FAIRsharing, to be added to the collection.

Many of the elements of the guideline have been linked to external ontologies. How do the authors see these ontologies being used in future? Will they be linked to the XML Schema / XML files? As the manuscript stands now, the ontologies are mentioned but not contextualized - though I know they are used, I would like to know how and why they are used.
We would like to thank the reviewer for the constructive feedback. To address the feedback, we have added an additional section on pg. 10, line 240, highlighted in yellow, detailing the purpose of the ontologies. Currently, the ontologies cannot be intrinsically linked to the guideline elements, within the REDCap XML. In the future we aim to provide base XML schemas, adaptable for broad implementation on various data capturing platforms. This will allow us to link the guideline elements to the mapped ontologies. Ultimately, the ontologies serve to promote FAIR reporting by adding an underlying layer of metadata and understanding to the overall dataset.

While the guideline name itself as well as the manuscript reference the more general "clinical data" part of this standard, the relevance to clinical data beyond kidney disease data is not fully described. I would appreciate more explanatory text as to how the more generic aspects of this guideline relate to / enhance available clinical data standards or CRFs (such as CDISC, if relevant)? While the manuscript is clear in how the guidelines are novel with respect to kidney disease research, I would appreciate having an explanation of how this guideline provides a novel services for clinical data standards generally.
We would like to thank the reviewer for the constructive feedback. To address the feedback, we have altered the title to make clear that both the research and clinical data within the reporting guideline are aimed to be kidney-specific. We also added an additional line explaining this on pg. 4, line 108, highlighted in green. Therefore, the clinical data as referenced in the current reporting guideline are not separated from kidney specificity. Additionally, it is not meant to replace general CRF, as explained on pg. 9, line 219, highlighted in green.

Line 46 of page 8 references "XML schemas", but earlier in the manuscript only one schema was described. How many are there?
Page 6, line 12 - should read "XML"
Line 8, page 5: "principals" should be "principles"
We would like to thank the reviewer for the constructive feedback. All the corrections for these have been made in the revised version. Thank you kindly.

A short explanation of why REDcap was used in preference to other publicly-available survey applications such as Google Forms or SurveyMonkey would be helpful, as the survey itself did not contain any sensitive information.
We thank the reviewer for the feedback. The REDCap sentence has since been shortened on pg. 6 (line 151) in the methods section, highlighted in green. REDCap was used because it is our standard survey capturing tool within our institution, due to its inherent security features. REDCap allows complicated and nested questions to be set up and is free for academic use. It also allows implementation in your local environment giving users appropriate control and space to store data. Though REDCap provides the aforementioned features with security features, we shortened this description so that it does not draw unnecessary focus.

An XML schema associated with the guidelines is useful, but no use cases have been provided to show readers how the authors expect the XML files to be used. Will the ontology terms linked to the guideline elements be used within the XML file? Will the XML files that validate against this schema then be accepted into a publicly-available database? What is the intended use of such XML files? Additionally, the authors state the following: “An associated XML schema was developed for REDCap implementation, consisting of 3 sections - the participant-, experiment and study-level information, and can be found in Supplementary File 5.“ This reads like an XML scheme specifically for REDCap - if this is indeed the same schema as that which has been implemented for the guideline, this needs to be stated.
We would like to thank the reviewer for the constructive feedback. To address the feedback, we have added an additional section on pg. 10, line 240, highlighted in yellow, detailing the purpose of the ontologies. We have also added a section on pg. 8, line 212, highlighted in yellow, highlighting the primary use cases for these XMLs and added an additional supplementary file, titled “Recommendations For Use Guideline” which details how the XML should be used. The XML discussed in the article, is specific for implementation in REDCap, we also made/are developing additional technical XMLs which can be adapted for various platforms. These are to be released at a later stage.

The columns labelled “Ontology ID”, “Concordant Ontologies”, and “Concordant Standards” are unexplained in the text. Please can the intent and meaning behind these parts of the guideline be included.
I found it difficult to read the full reporting guidelines, as the PDF formatting has truncated the majority of the table to just the first 3 columns, and then after those are shown, the next three columns. I would appreciate having an alternative format for the guidelines to have a better look at them please. I tried to look at the URL provided (https://www.h3abionet.org/data-standards/datastds) but there were no clickable links for the guidelines on that page.
We would like to thank the reviewer for the constructive feedback. To address the feedback, all columns were explained on pg. 8, line 196, highlighted in yellow. Additionally, the supplementary file with the full guideline has been removed, and the URL link has been fixed. Therefore, the URL can be referred when investigating the complete guideline.

VERSION 2 – REVIEW

REVIEWER	Allyson Lister FAIRsharing, OeRC, University of Oxford, UK
REVIEW RETURNED	19-Jun-2019

GENERAL COMMENTS	Thank you for providing a second manuscript - the changes have created a much clearer manuscript. Thank you also for your letter outlining the differences in audience and in results between the kidney disease and stroke guidelines, as it is a useful clarification. The authors' thorough responses to the reviewers' comments have been most appreciated, and very helpful when reading the second proof. Thank you for the detail of the reply. I had 9 questions about the first draft. 6/9 of those questions have been resolved to my satisfaction. I have listed all 9 below, with comments as to why or why not the issues have been resolved. I finish with some additional notes. 1.Original comment: The pre-existing guidelines initially used in the creation of the survey were: PhenX collection measures, CKDO, MIAPE and MIDE. What makes these particular guidelines the best choice? Comments on 2nd proof: The authors have added more explanatory text that resolves this comment: “The standards relevant to clinical data collection included the H3Africa Standard Case Report Form (CRF) (www.h3abionet.org/data-standards/datastds), the CKDO and various collection measures hosted on PhenX. The standards relevant to research data reporting included various experimental reporting guidelines hosted on FAIRsharing, such as MIAPE, MIDE, MIRAGE, MINSEQE, MIAME and more, from which common study- and experiment-specific elements were derived.” 2. Original comment: PhenX seems to have broken URLs (https://original-phenxtoolkit.rti.org/index.php isn’t working, and I don’t understand how PhenX is related). The relationship between the chosen pre-existing guidelines and the research area of interest (kidney disease) should be explained. **Comments on 2nd proof: This URL (https://original-phenxtoolkit.rti.org/index.php) remains broken and shouldn’t be used in the manuscript. It should be replaced with a correct URL. Modifications in the new text, however, make it clear that PhenX is a hosting platform that the authors searched to find appropriate elements / recommendations to incorporate into their guidelines. Therefore other than the broken URL, this question has also been resolved. 3. Original comment: Many of the elements of the guideline have been linked to external ontologies. How do the authors see these ontologies being used in future? Will they be linked to the XML Schema / XML files?

	**Comments on 2nd proof: This has been resolved through greater description of the ontologies as well as the statements in the paragraph at the top of page 12. 4. Original comment: While the guideline name itself as well as the manuscript reference the more general “clinical data” part of this standard, the relevance to clinical data beyond kidney disease data is not fully described. I would appreciate more explanatory text as to how the more generic aspects of this guideline relate to / enhance available clinical data standards or CRFs (such as CDISC, if relevant)? **Comments on 2nd proof: The changes they made in response to my accidentally thinking that "clinical data" and "kidney disease research" were two separate subjects is fantastic. In page 6 line 107 there is the text “the project drew from the experience of previous standardization initiatives and aimed to develop a multi-purpose reporting guideline, which focuses on the reporting of both clinical and research data within the kidney disease field”. This provides much-needed context for the scope of the guidelines. Thanks for making this clearer - the colon (“:”) in the title of the reporting guidelines clarifies things for me. Therefore I suggest that, in keeping with the new title of the paper, line 109 on page 6 (where the title of the guidelines is listed) should also read “The Minimum Information Required Guideline for Kidney Disease: Research and Clinical Data Reporting”. In addition, the paragraph starting at line 221 on page 11 clearly outlines the reporting guideline’s relationship to CRFs. As such, this question has been resolved. 5. Original comment: Line 46 of page 8 references “XML schemas”, but earlier in the manuscript only one schema was described. How many are there? **Comments on 2nd proof: It seems from https://www.h3abionet.org/data-standards/datastds that, even though it is often referred to in the plural, there is in fact only one XSD for the kidney disease reporting guideline. What has happened, I believe, is that the plural has been used in the manuscript to refer (accidentally) to both the kidney disease xsd and the stroke xsd. However, as this manuscript only refers to the kidney disease guidelines, for clarity please modify the manuscript to use the singular "schema". The “XML Schemas” section beginning on page 66 (“Recommendations for Use”) and the associated FAQ after it are a very useful section of the manuscript. It clearly explains how the schema is to be used and its association with REDcap. It appears clear from the “Recommendations for Use” section that it is appropriate to refer to both guidelines and XML schemas in the plural form, as I presume that this “how-to” document is both for the kidney disease and the stroke reporting guidelines. However, in the manuscript itself, it should be XML schema (singular). Therefore this comment is not resolved yet. 6. Original comment: A short explanation of why REDcap was used in preference to other publicly-available survey applications

	such as Google Forms or SurveyMonkey would be helpful, as the survey itself did not contain any sensitive information. **Comments on 2nd proof: A sentence has been simplified in page 8 line 153 that provides the reasons for using REDcap. This resolves this comment. 7. Original comment: An XML schema associated with the guidelines is useful, but no use cases have been provided to show readers how the authors expect the XML files to be used. Will the ontology terms linked to the guideline elements be used within the XML file? **Comments for 2nd proof: There is a bit more of an explanation of this, in the paragraph starting at line 156 page 8. A summary of why XML / XML schemas are useful is available in this paragraph, and I am happy with this summary. However, I am still confused as to why this XML schema, which "was designed to carry all the data and metadata within the reporting guideline" was *also* "specifically for REDCap implementation". Why is the Reporting Guideline XSD specifically for implementation within REDcap? Some explanation is given in the "XML Schemas" section beginning on page 66 ("Recommendations for Use") and the associated FAQ after it in the supplementary material. These are very useful sections of the manuscript. It clearly explains how the schema is to be used and its association with REDcap. Here, it is clear to see that the user-friendliness aspect comes *not* from the xsd, but from the fact that the xsd can be uploaded in REDcap to create a project that can then have data / metadata added to it. However, this information should also be summarised in the main text in one of the sections described above, for clarity, as it is currently only in the supplementary material. Also, even if the XSD was developed to be used with the REDcap software, is it possible to use it without REDcap? If the xsd is software independent, this would be beneficial and should be stated. In page 12 from line 243 it is stated that "In the future we aim to provide base XML schemas, adaptable for broad implementation on various data capturing platforms". It appears the xsd is only applicable for REDcap, and if so this should be stated earlier, when the XSDs are first introduced in the main body of the document. Therefore this question has not yet been resolved. 8. Original comment: The columns labelled "Ontology ID", "Concordant Ontologies", and "Concordant Standards" are unexplained in the text. Please can the intent and meaning behind these parts of the guideline be included. **Comments on 2nd proof: This has been addressed, both via the "Recommendations for Use" supplementary file and in page 10 in the paragraph starting at 195. This comment is now resolved. 9. Original comment: I found it difficult to read the full reporting guidelines, as the PDF formatting has truncated the majority of the table to just the first 3 columns, and then after those are shown, the next three columns. I tried to look at the URL provided (https://www.h3abionet.org/data-standards/datastds) but there were no clickable links for the guidelines on that page.

	This has been resolved, as you can use the website to look at the standards. Additional notes * I am not an expert in kidney disease or in clinical data reporting, and therefore this review comes from the context of the informatics and data standards aspects only. I am not qualified to comment on the medicial/clinical/research relevance to kidney research. * Line 192 page 10 - should “Instrumentation employed” be “Instrumentation Employed”? * Line 209 page 10 - why do you need the and(or) here? Is it a collection or a reporting guideline, or both? * The questionnaire and its raw responses are difficult to read (from page 27). Is there any way to present the responses in a better way, while still preserving the fact that it is primary data? This isn’t a required change. * While the PhenX toolkit correctly has its citation, the FAIRsharing citation is missing (although the FAIR principles publication is correctly referenced). For FAIRsharing, please use https://doi.org/10.1038/s41587-019-0080-8

VERSION 2 – AUTHOR RESPONSE

Reviewer #1:

**Comments on 2nd proof: This URL (https://original-phenxtoolkit.rti.org/index.php) remains broken and shouldn’t be used in the manuscript. It should be replaced with a correct URL. Modifications in the new text, however, make it clear that PhenX is a hosting platform that the authors searched to find appropriate elements / recommendations to incorporate into their guidelines. Therefore other than the broken URL, this question has also been resolved.

We would like to thank the reviewer for the constructive feedback. There may have been some confusion during the review, as we changed the link our previous revision. However, we’ve checked this again to ensure that the correct link is used. These changes are highlighted on pg. 5 as indicated below, “The consensus measures for Phenotypes and eXposures (PhenX) Toolkit (www.phenxtoolkit.org), has proposed...”

**Comments on 2nd proof: It seems from https://www.h3abionet.org/data-standards/datastds that, even though it is often referred to in the plural, there is in fact only one XSD for the kidney disease reporting guideline. What has happened, I believe, is that the plural has been used in the manuscript to refer (accidentally) to both the kidney disease xsd and the stroke xsd. However, as this manuscript only refers to the kidney disease guidelines, for clarity please modify the manuscript to use the singular "schema".

The “XML Schemas” section beginning on page 66 (“Recommendations for Use”) and the associated FAQ after it are a very useful section of the manuscript. It clearly explains how the schema is to be used and its association with REDcap. It appears clear from the “Recommendations for Use” section that it is appropriate to refer to both guidelines and XML schemas in the plural form, as I presume that this “how-to” document is both for the kidney disease and the stroke reporting guidelines. However, in the manuscript itself, it should be XML schema (singular).

Therefore this comment is not resolved yet.

We would like to thank the reviewer for the constructive feedback given. We have taken great care to refer to a singular schema throughout the document, there should no longer be confusion regarding this matter – the only referral to multiple schemas remains in the discussion, where we discuss the development of multi-platform/adaptable schemas.

**Comments for 2nd proof: There is a bit more of an explanation of this, in the paragraph starting at line 156 page 8. A summary of why XML / XML schemas are useful is available in this paragraph, and I am happy with this summary. However, I am still confused as to why this XML schema, which "was designed to carry all the data and metadata within the reporting guideline" was *also* "specifically for REDCap implementation". Why is the Reporting Guideline XSD specifically for implementation within REDcap?

Some explanation is given in the "XML Schemas" section beginning on page 66 ("Recommendations for Use") and the associated FAQ after it in the supplementary material. These are very useful sections of the manuscript. It clearly explains how the schema is to be used and its association with REDcap. Here, it is clear to see that the user-friendliness aspect comes *not* from the xsd, but from the fact that the xsd can be uploaded in REDcap to create a project that can then have data / metadata added to it. However, this information should also be summarised in the main text in one of the sections described above, for clarity, as it is currently only in the supplementary material. Also, even if the XSD was developed to be used with the REDcap software, is it possible to use it without REDcap? If the xsd is software independent, this would be beneficial and should be stated. In page 12 from line 243 it is stated that "In the future we aim to provide base XML schemas, adaptable for broad implementation on various data capturing platforms". It appears the xsd is only applicable for REDcap, and if so this should be stated earlier, when the XSDs are first introduced in the main body of the document. Therefore this question has not yet been resolved.

We would like to thank the reviewer for the constructive feedback. To address the feedback, we have made additions on pg. 8 and pg. 10, clarifying why the reasons for developing an XML for REDCap implementation, due to its ease-of-use and wide availibility, and more clearly referring to the additional documentation which explains how it can be implemented locally.

VERSION 3 – REVIEW

REVIEWER	Allyson Lister Knowledge Engineer, Oxford e-Research Centre, University of Oxford, UK
REVIEW RETURNED	23-Sep-2019

GENERAL COMMENTS	Thank you for providing a third manuscript - the provided changes have resolved all of my outstanding comments. Thank you also for your letter outlining the changes you've made. The authors' thorough responses to the reviewers' comments have been most appreciated, and very helpful when reading the third proof. Thank you for the detail in your reply. The 3 outstanding questions are listed below, with updated comments . After that I have a few additional notes. 1. Original comment: PhenX seems to have broken URLs (https://original-phenxtoolkit.rti.org/index.php isn't working, and I don't understand how PhenX is related). The relationship between the chosen pre-existing guidelines and the research area of interest (kidney disease) should be explained.

	**Comments on 2nd proof: This URL (https://original-phenxtoolkit.rti.org/index.php) remains broken and shouldn't be used in the manuscript. It should be replaced with a correct URL. Modifications in the new text, however, make it clear that PhenX is a hosting platform that the authors searched to find appropriate elements / recommendations to incorporate into their guidelines. Therefore other than the broken URL, this question has also been resolved. **Comments on 3rd proof: Thanks for pointing out that you had the correct URL, this question has been resolved. 2. Original comment: Line 46 of page 8 references "XML schemas", but earlier in the manuscript only one schema was described. How many are there? **Comments on 2nd proof: It seems from https://www.h3abionet.org/data-standards/datastds that, even though it is often referred to in the plural, there is in fact only one XSD for the kidney disease reporting guideline. What has happened, I believe, is that the plural has been used in the manuscript to refer (accidentally) to both the kidney disease xsd and the stroke xsd. However, as this manuscript only refers to the kidney disease guidelines, for clarity please modify the manuscript to use the singular "schema". The "XML Schemas" section beginning on page 66 ("Recommendations for Use") and the associated FAQ after it are a very useful section of the manuscript. It clearly explains how the schema is to be used and its association with REDcap. It appears clear from the "Recommendations for Use" section that it is appropriate to refer to both guidelines and XML schemas in the plural form, as I presume that this "how-to" document is both for the kidney disease and the stroke reporting guidelines. However, in the manuscript itself, it should be XML schema (singular). Therefore this comment is not resolved yet. **Comments on the 3rd proof: Thank you for ensuring that the XSD schema is referred to in the singular throughout the document other than when purposefully referring to the related schemas. This is now resolved. 3. Original comment: An XML schema associated with the guidelines is useful, but no use cases have been provided to show readers how the authors expect the XML files to be used. Will the ontology terms linked to the guideline elements be used within the XML file? **Comments for 2nd proof: There is a bit more of an explanation of this, in the paragraph starting at line 156 page 8. A summary of why XML / XML schemas are useful is available in this paragraph, and I am happy with this summary. However, I am still confused as to why this XML schema, which "was designed to carry all the data and metadata within the reporting guideline" was *also* "specifically for REDCap implementation". Why is the Reporting Guideline XSD specifically for implementation within REDcap?

	Some explanation is given in the “XML Schemas” section beginning on page 66 (“Recommendations for Use”) and the associated FAQ after it in the supplementary material. These are very useful sections of the manuscript. It clearly explains how the schema is to be used and its association with REDcap. Here, it is clear to see that the user-friendliness aspect comes *not* from the xsd, but from the fact that the xsd can be uploaded in REDcap to create a project that can then have data / metadata added to it. However, this information should also be summarised in the main text in one of the sections described above, for clarity, as it is currently only in the supplementary material. Also, even if the XSD was developed to be used with the REDcap software, is it possible to use it without REDcap? If the xsd is software independent, this would be beneficial and should be stated. In page 12 from line 243 it is stated that “In the future we aim to provide base XML schemas, adaptable for broad implementation on various data capturing platforms“. It appears the xsd is only applicable for REDcap, and if so this should be stated earlier, when the XSDs are first introduced in the main body of the document. Therefore this question has not yet been resolved. **Comments for 3rd proof: The additions the authors have made have addressed my comments. Additional notes * Line 39: “Additionally, an associated XML schema was created for REDCap implementation to increase user friendliness and adoption.” should read ““Additionally, an associated XML schema was created for the REDCap implementation to increase user friendliness and adoption.” (added “the”) * Line 91: “...are being driven, by FAIRsharing[],…” should be “...are being driven by FAIRsharing[],…” (remove first comma) * Line 192: “which describes where the date will be saved” should be “which describes where the data will be saved” (“date” changed to “data”) * Line 234: “The XML has been used extensively” should probably read “XML has been used extensively” (remove “The”) if I’m reading the sentence correctly. * Line 239: “linked to the guideline elements, within the REDCap XML” should perhaps be ““linked to the guideline elements within the REDCap XML” (removed comma) * Line 194 and 256: when checking that the URL was valid, I noticed that your FAIRsharing record now has a DOI, so you could use https://doi.org/10.25504/FAIRsharing.fCAD2Z as the link to your record instead of https://fairsharing.org/bsg-s001385 * I am not an expert in kidney disease or in clinical data reporting, and therefore this review comes from the context of the informatics and data standards aspects only. I am not qualified to comment on the medicial/clinical/research relevance to kidney research.