PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for a multicenter, multistage, prospective study in China using system-based approaches for consistent improvement in surgical safety
AUTHORS	Yu, Xiaochu; Jiang, Jingmei; Liu, Changwei; Shen, Keng; Wang, Zixing; Han, Wei; Liu, Xingrong; Lin, Guole; Zhang, Ye; Zhang, Ying; Ma, Yufen; Bo, Haixin; Zhao, Yupei

VERSION 1 - REVIEW

REVIEWER	Peter McCulloch University of Oxford UK
REVIEW RETURNED	29-Nov-2016

GENERAL COMMENTS	This protocol describes a hugely ambitious and very sophisticated patient safety intervention programme. There are a number of excellent features in the plan, including the creation os standard reporting measures, IT support and reminders for staff, developing interventions based on the analysis of very large datasets, anbd the integration of a safety reporting system with the intervention itself. Unusually for a protocol, the timetable indicates that the programme should already be half-completed, but it is nevertheless appropriate to publish details of the intervention and evaluation plans before any results are released, to avoid any susbequent impression of publication bias. The protocol is written in excellent English, but is nevertheless difficult to understand in some respects. I suspect that this represents differences in ways of thinking and conceptualising between Chinese and Western cultures rather than a true language difficulty. It would be very helpful to have some of these areas of uncertainty clarified, as this reader was left uncertain in some parts of the MS whether the approach taken was appropriate or not because of a lack of clarity about what was being said. There are some obvious weaknesses in the proposed intervention plan. However if we assume that the intervention is to be introduced into units which had not previously instigated any organised efforts to improve patient safety, one would expect it to produce a marked effect. AREAS OF UNCERTAINTY 1. I was not clear about the status of the stages 2 and 3 of the plan. It seemed to me that what was being described might be a sequential plan in which stage 2 represented the development and initial trialling of interventions, and stage 3 represented larger scale testing of a simplified and stable form of the intervention. This would be an approach similar to that recommended by the IDEAL

	Collaboration and would represent the Development and Exploration stages of IDEAL (McCulloch et al Lancet 2009). However the language did not make it clear whether the interventions used were modified and recycled until perfected in stage 2, nor how the final version for stage 3 was arrived at. It would be helpful to clarify further how stages 2 and 3 related to each other. 2. The claim is made that the IT system integrates the safety intervention and the collection of outcome data,but there is no detail to explain what this means in practice. 3. The data collection goes beyond process and outcome data to include patient characteristics, and these are explicitly included in the analysis to produce an evaluation of risk patterns and priority areas for intervention. Whilst I think this is perfectly reasonable, it does mean that the way in which the term patient safety intervention is used in this study differs from that in the literature generally, and this needs to be explained and justified. 4. I could not interpret Figure 4 AREAS OF POTENTIAL WEAKNESS It would be interesting to discover whether any of these apparent weaknesses are in fact due to misunderstandings. Where they are not,it could be valuable to see a reflective comment on them in the Discussion section. 1. There is no mention in the text of any strategy to engage the frontline staff whose efforts will be relied on to collect the data and implement the interventions. Many publications have emphasised the importance of this aspect of patient safety interventions, and it would be helpful to understand whether this aspect has truly been neglected or inadequately described. 2. It is also unclear whether the work of recording data and carrying out additional duties to implement interventions will be compensated by allocation of additional staff time or recreation time. Lack of time, and the imposition of additional workload on staff are recognised as powerful inhibitory factors for the success of intervention programmes. 3. Whilst the data recorded in high volumes will probably succeed in identifying areas of particular patient risk, they cannot necessarily explain the mechanisms of this risk, and solutions based on assumptions and reasoning rather than ergonomic analysis of process are often erroneous and ineffective. There is no discussion of any process analysis or ergonomic analysis to support the development of interventions. 4. The timelines for the phases of the project seem exceptionally ambitious particularly in view of its great scale and complexity

REVIEWER	Benjamin S. Brooke University of Utah School of Medicine Salt Lake City, Utah United States of America
REVIEW RETURNED	10-Feb-2017

GENERAL COMMENTS	The authors present the protocol for a multi-stage surgical safety project known as MSCP at four medical centers in China. This manuscript is well-written but lacks some details about the technology systems they plan to use and the specific methods they intend to use for implementation and evaluation of this project. I have several comments and recommendations as listed below.

	1. The MSCP is an ambitious program for improving perioperative surgical safety that is being implemented in four Chinese hospitals. On page 3, the authors state that “implementation quality is a key to the success of the project.” However, one of the limitations of this protocol is the lack of a validated implementation framework for evaluating implementation success or effectiveness of the project. I would recommend that the authors use a ‘hybrid’ implementation science model to provide a more scientifically appropriate framework for integrating the MSCP program, including barriers and limitations, as well as a model for evaluation the effectiveness of the project. The ‘RE-AIM’ model is an example of a hybrid implementation model but there are many others. A review of available implementation models can be found by reading: Tabak et al. Am J Prev Med. 2012 September; 43(3): 337–350 2. It’s unclear why the time frame for all 3 phases of this study protocol have already passed (2014-2016). Have the authors already implemented this study protocol or are they using these dates merely as a time frame estimate. If this project has been launched, have the authors analyzed any results to date? Please clarify. 3. On page 10, the authors state that methods for preventing various surgical complications will be generated by expert consensus in a pre-defined process. This appears to be a version of a Delphi method, although this is not directly stated. I would recommend that the authors use an established technique such as the Delphi method for selecting evidence-based interventions, and provide a clear explanation for how this was undertaken. 4. The authors refer to a ‘computerized safety intervention system’ and ‘information technology’, although these systems are not well-defined or described in the manuscript. Health IT can be used to mean a lot of different computerized systems and readers will want more information about the specific IT platform the MSCP is using. In particular, if the authors are intending to use electronic health record systems for patient safety, they need to explain how information be extracted and used by clinicians. 5. The specific outcomes the authors intend to measure need to be explicitly defined. In the ‘data analysis plan’ on page 12, the authors mention crude and adjusted mortality but do not state when it will be measured (i.e. 30-days, 1-year, etc.). If they intend to use survival models (i.e. Kaplan Meier) this needs to be described. In addition, ‘specialty-specific complication rates’ needs to be explicitly defined. For example, what specific complications or adverse event are they intending to measure following different specialty procedures.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1:
This protocol describes a hugely ambitious and very sophisticated patient safety intervention programme. There are a number of excellent features in the plan, including the creation os standard reporting measures, IT support and reminders for staff, developing interventions based on the analysis of very large datasets, anbd the integration of a safety reporting system with the intervention itself. Unusually for a protocol, the timetable indicates that the programme should already be half-

completed, but it is nevertheless appropriate to publish details of the intervention and evaluation plans before any results are released, to avoid any susbequent impression of publication bias. The protocol is written in excellent English, but is nevertheless difficult to understand in some respects. I suspect that this represents differences in ways of thinking and conceptualising between Chinese and Western cultures rather than a true language difficulty. It would be very helpful to have some of these areas of uncertainty clarified, as this reader was left uncertain in some parts of the MS whether the approach taken was appropriate or not because of a lack of clarity about what was being said.

There are some obvious weaknesses in the proposed intervention plan. However if we assume that the intervention is to be introduced into units which had not previously instigated any organised efforts to improve patient safety, one would expect it to produce a marked effect.

AREAS OF UNCERTAINTY

1. I was not clear about the status of the stages 2 and 3 of the plan. It seemed to me that what was being described might be a sequential plan in which stage 2 represented the development and initial trialling of interventions, and stage 3 represented larger scale testing of a simplified and stable form of the intervention. This would be an approach similar to that recommended by the IDEAL Collaboration and would represent the Development and Exploration stages of IDEAL (McCulloch et al Lancet 2009). However the language did not make it clear whether the interventions used were modified and recycled until perfected in stage 2, nor how the final version for stage 3 was arrived at. It would be helpful to clarify further how stages 2 and 3 related to each other.

Reply: We have made a few revisions to the description of the goals of the stage 2 and stage 3 in the METHODS AND ANALYSIS section (on Page 6), and further stressed the differences between these two sequential stages in second to the last paragraph of the Discussion section (on Pages 15-16). In brief, stage 2 is evidence-oriented and aims to carry out the intervention and demonstrate its effectiveness, while stage 3 is more practice-oriented and mainly aims to carry out approaches to enhance its implementation in the complex clinical context for further promotion. The latter focus is quite similar to the importance of context and implementation strategy you emphasized in BMJ Quality & Safety 2016;25(8):562-4, and the barriers and strategies for surgical quality improvement you described in the 3S Program. We appreciate that the IDEAL recommendations are a good framework to stage the process of innovations in surgical techniques and devices, but in the manuscript we did not directly map the staging of this project to the IDEAL (though much of the logical thinking is similar) as what we intend to do is integrating well-established approaches for preventing surgical complications into durable and efficient hospital systems, and to deliver them to patients in a target-sensitive and organized way.

2. The claim is made that the IT system integrates the safety intervention and the collection of outcome data,but there is no detail to explain what this means in practice.

Reply: Yes, clarifying this point is important. Please see the practical meanings of combining safety intervention with outcome data in the third paragraph of the Discussion section (on Page 15).

3. The data collection goes beyond process and outcome data to include patient characteristics, and these are explicitly included in the analysis to produce an evaluation of risk patterns and priority areas for intervention. Whilst I think this is perfectly reasonable, it does mean that the way in which the term patient safety intervention is used in this study differs from that in the literature generally, and this needs to be explained and justified.

Reply: As you mentioned, except for intervention and patient outcome data, we also collected a great number of clinical variables (such as patient characteristics) in the first stage, which forms a rich study

database for identifying risk patterns for various complications and areas for intervention. This is particularly important for China, where no such comprehensive databases were available before this project. To the unintended confusion, we did not mean that the way we used such data is a distinguishable feature of this study, but aim to stress the role of making full use of such data for patient safety studies, especially for providing an evidence base for developing target-sensitive and locally fitted interventions. We have revised relevant contents to make this intention clearer, please check the change on Page 15.

4. I could not interpret Figure 4

Reply: Figure 4 illustrates how the patients are stratified to receive different sets of interventions for prevention of different spectrums of complications. We have modified this figure and provided further explanations in the figure legend (on last page). We have also revised the description of the intervention strategy in the main text on Page 10.

AREAS OF POTENTIAL WEAKNESS
It would be interesting to discover whether any of these apparent weaknesses are in fact due to misunderstandings. Where they are not,it could be valuable to see a reflective comment on them in the Discussion section.

1. There is no mention in the text of any strategy to engage the frontline staff whose efforts will be relied on to collect the data and implement the interventions. Many publications have emphasised the importance of this aspect of patient safety interventions, and it would be helpful to understand whether this aspect has truly been neglected or inadequately described.

Reply: Actually a number of strategies to engage frontline staff were adopted in this project. We have added three major approaches on Pages 11-12 under an added subtitle “Strategies for clinical engagement”. Please also refer to one recently published article from this project (sub-study 1) for a more detailed description of these approaches: Yu X, Huang Y, Guo Q, et al. Clinical motivation and the surgical safety checklist. British Journal of Surgery, 2017, 104(4):472-479.

2. It is also unclear whether the work of recording data and carrying out additional duties to implement interventions will be compensated by allocation of additional staff time or recreation time. Lack of time, and the imposition of additional workload on staff are recognised as powerful inhibitory factors for the success of intervention programmes.

Reply: We agree with you on this important point. Actually, this is one of the starting points of this projects (the yellow mark in the Background section on Page 4), and a major focus in the current Stage 3. Please see the second to the last paragraph of the Discussion section (on Page 16) for a more detailed discussion. We have been and will be still working on reducing the workload (e.g. simplifying the items in the systems) while balancing it against patient safety needs.

3. Whilst the data recorded in high volumes will probably succeed in identifying areas of particular patient risk, they cannot necessarily explain the mechanisms of this risk, and solutions based on assumptions and reasoning rather than ergonomic analysis of process are often erroneous and ineffective. There is no discussion of any process analysis or ergonomic analysis to support the development of interventions.

Reply: We do appreciate that introducing ergonomic analysis and process analysis into the development of interventions can make the workflows of interventions more rationalized and standardized. There are actually no experts in that field in the current project. We have added it to the discussion of limitations (on Page 16), and will consider relevant work for further refinement.

4. The timelines for the phases of the project seem exceptionally ambitious particularly in view of its great scale and complexity

Reply: Though it seems very complex and labor-taking, we do have great faith in accomplishing the goals, as long as the project is elaborately designed, carefully and gradually implemented, and always remains open to great suggestions from both home and the international community. We take this opportunity to call for further comments and suggestions like yours on refining this project, and any opinions and cooperation for further research that will benefit the safety of surgical patients worldwide, especially in China.

Reviewer: 2
The authors present the protocol for a multi-stage surgical safety project known as MSCP at four medical centers in China. This manuscript is well-written but lacks some details about the technology systems they plan to use and the specific methods they intend to use for implementation and evaluation of this project. I have several comments and recommendations as listed below.

1. The MSCP is an ambitious program for improving perioperative surgical safety that is being implemented in four Chinese hospitals. On page 3, the authors state that “implementation quality is a key to the success of the project.” However, one of the limitations of this protocol is the lack of a validated implementation framework for evaluating implementation success or effectiveness of the project. I would recommend that the authors use a ‘hybrid’ implementation science model to provide a more scientifically appropriate framework for integrating the MSCP program, including barriers and limitations, as well as a model for evaluation the effectiveness of the project. The ‘RE-AIM’ model is an example of a hybrid implementation model but there are many others. A review of available implementation models can be found by reading: Tabak et al. Am J Prev Med. 2012 September; 43(3): 337–350

Reply: Thank you for your valuable suggestions. We have incorporated several strategies that we take to enhance clinical engagement (on Pages 11-12) into the available frameworks for improving implementation quality, and are planning to report the final results according to the five domains in the ‘RE-AIM’ model (on Page 13).

2. It’s unclear why the time frame for all 3 phases of this study protocol have already passed (2014-2016). Have the authors already implemented this study protocol or are they using these dates merely as a time frame estimate. If this project has been launched, have the authors analyzed any results to date? Please clarify.

Reply: The project has been carried out as is scheduled in the timeline. The third stage is being conducted and is anticipated to be finished at the end of 2017. Please see the added “Study status” statements in the revised manuscript.

3. On page 10, the authors state that methods for preventing various surgical complications will be generated by expert consensus in a pre-defined process. This appears to be a version of a Delphi method, although this is not directly stated. I would recommend that the authors use an established technique such as the Delphi method for selecting evidence-based interventions, and provide a clear explanation for how this was undertaken.

Reply: The development of this process was actually based on the basic ideas of Delphi method, but with an exception (anonymous mechanism is not used). Please see further explanation of this process on Pages 9-10.

4. The authors refer to a ‘computerized safety intervention system’ and ‘information technology’, although these systems are not well-defined or described in the manuscript. Health IT can be used to mean a lot of different computerized systems and readers will want more information about the specific IT platform the MSCP is using. In particular, if the authors are intending to use electronic health record systems for patient safety, they need to explain how information be extracted and used by clinicians.

Reply: We have specified the IT platforms used in this study, and provided other details of the system construction process in the revised manuscript. Please see the revisions on Pages 10-11.

5. The specific outcomes the authors intend to measure need to be explicitly defined. In the ‘data analysis plan’ on page 12, the authors mention crude and adjusted mortality but do not state when it will be measured (i.e. 30-days, 1-year, etc.). If they intend to use survival models (i.e. Kaplan Meier) this needs to be described. In addition, ‘specialty-specific complication rates’ needs to be explicitly defined. For example, what specific complications or adverse event are they intending to measure following different specialty procedures.

Reply: We have added such definitions in the revised manuscript. Please find them on Page 8. There is a planned process of narrowing down the items of complications for reporting, and more detailed information for this will be available in one manuscript on the sub-study 2 that we are currently drafting.

VERSION 2 – REVIEW

REVIEWER	Peter McCulloch University of Oxford UK
REVIEW RETURNED	21-Apr-2017

GENERAL COMMENTS	I think this study is very important not only because of its vast scale and careful organisation but because it makes an important conceptual leap. Safety in surgery has always been difficult to study because we have made a distinction between harm caused by error or imperfection in the treatment process and "normal complications". This is a false distinction and the authors are to be congratulated for formulating an intervention and study process which deals with the entire problem of failure to deliver the desired results holistically. The implications of taking this approach are very wide ranging and I believe will make a major impact on the field of research. The other reason why this study should be published now is time. The study is already nearing completion (if the timetable has not slipped in the final third) and the transparency benefits of prior publication of the protocol will be lost if this is not expedited. There remain a number of difficulties with the MS, in particular it remains rather difficult to envisage exactly what the intervention will comprise. Complications are a major endpoint, but these are notoriously difficult to define. As a minimum, I would urge the authors to require classification of complication severity using the widely accepted Dindo-Clavien scale. However I don’t think either of these criticisms should hold up publication.

REVIEWER	Benjamin S. Brooke, MD, PhD Department of Surgery University of Utah School of Medicine Salt Lake City, Utah

	United Stated of America
REVIEW RETURNED	02-Apr-2017

GENERAL COMMENTS	The authors have revised adequately addressed all comments raised in my previous review and have successfully revised their manuscript to address these concerns. I have read through the revised manuscript and feel that it is suitable for acceptance and publication.