

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Late myocardial reperfusion in ST-elevation myocardial infarction: protocol for a systematic review and meta-analysis
<b>AUTHORS</b>	Vargas-Fernández, Rodrigo; Chacón-Díaz, Manuel; Basualdo-Meléndez, Gianfranco W.; Barón-Lozada, Francisco A.; Visconti-Lopez, Fabriccio J.; Comandé, Daniel; Hernández-Vásquez, Akram

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Diego Araiza Universidad Nacional Autónoma de México, Cardiology
<b>REVIEW RETURNED</b>	06-Feb-2022

<b>GENERAL COMMENTS</b>	Thank you for the opportunity to review the present study protocol. My opinion is that the topic is relevant for clinical practice in low to middle income countries; that the protocol presents a clear guideline for the elaboration of the systematic review and meta analysis, and that results may be relevant for
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<b>REVIEWER</b>	Jussielly Cunha Oliveira Universidade Federal de Sergipe
<b>REVIEW RETURNED</b>	17-Feb-2022

<b>GENERAL COMMENTS</b>	I suggest that two important points be reviewed and reflected upon, in the light of the most recent guidelines and publications on the subject, to support the objective and expected result of this research: it is given that late revascularization (12 hours after the onset of symptoms) by itself only affects cardiovascular mortality indicators and is an unfavorable prognostic indicator for patients with STEMI. Therefore, what is the point of suggesting a study to address as a positive result possible benefits of delayed revascularization in patients with STEMI in different contexts, especially in low and middle-income countries, given that the entire world struggles against health systems and their resources? limited in order to understand the harms of late revascularization and the benefits of thrombolytic therapies and primary angioplasty for these same patients?
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<b>REVIEWER</b>	Arun Kanmanthareddy Creighton University School of Medicine
<b>REVIEW RETURNED</b>	27-May-2022

<b>GENERAL COMMENTS</b>	The paper is well written and the methods and discussion are well written. You might as well complete the entire research paper and publish it. What is the need for publishing the protocol methods paper separately?
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## VERSION 1 – AUTHOR RESPONSE

**Reviewer 1: Dr. Diego Araiza, Universidad Nacional Autónoma de México**

### Comments to the Author:

1. Thank you for the opportunity to review the present study protocol. My opinion is that the topic is relevant for clinical practice in low to middle income countries; that the protocol presents a clear guideline for the elaboration of the systematic review and meta analysis, and that results may be relevant for

**Response:** Thank you for the commentary. Indeed, the issue of our protocol is relevant so that health personnel can identify the risk of this population in the hospital environment, especially when low- and middle-income countries have economic (lack of medical and drug supplies and healthcare infrastructure) and human resource limitations<sup>1</sup> that could have a negative impact on the management of these patients due to an increase in cardiovascular complications, hospital stay and mortality.

1. Mills A. Health care systems in low- and middle-income countries. *N Engl J Med*. 2014 Feb 6;370(6):552-7. doi: 10.1056/NEJMra1110897. PMID: 24499213.

**Reviewer 2: Dr. Jussielly Cunha Oliveira, Universidade Federal de Sergipe**

### Comments to the Author:

1. I suggest that two important points be reviewed and reflected upon, in the light of the most recent guidelines and publications on the subject, to support the objective and expected result of this research: it is given that late revascularization (12 hours after the onset of symptoms) by itself only affects cardiovascular mortality indicators and is an unfavorable prognostic indicator for no patients with STEMI. Therefore, what is the point of suggesting a study to address as a positive result possible benefits of delayed revascularization in patients with STEMI in different contexts, especially in low and middle-income countries, given that the entire world struggles against health systems and their resources? limited in order to understand the harms of late revascularization and the benefits of thrombolytic therapies and primary angioplasty for these same patients?

**Response:** We appreciate the comment. The reality in developing countries is far from what is specified in the clinical practice guidelines. Whether due to lack of access to health services in a timely manner or ignorance of the disease, many patients access a health service with more than 12 hours after the onset of symptoms, or if they arrive at a hospital at time, it does not have reperfusion capacity, so it is not uncommon to find STEMI patients with more than 12 hours of evolution. Several studies, mostly observational, have tried to answer the question of whether there is any benefit of late myocardial reperfusion, and precisely the aim of this systematic review is to collect all the available data in an adequate way to be able to answer that question. The aim is not to promote delayed reperfusion, but rather to promote

timely reperfusion, without neglecting those patients who for extraneous reasons do not benefit from reperfusion in the period of time suggested by the guidelines (which also suggest mechanical reperfusion between 12 and 24 hours with a lower level of evidence).

### Reviewer 3: Arun Kanmanthareddy, Creighton University School of Medicine

#### Comments to the Author:

1. The paper is well written and the methods and discussion are well written. You might as well complete the entire research paper and publish it. What is the need for publishing the protocol methods paper separately?

**Response:** Thanks for the advice. There are many reasons to publish a protocol before publishing a systematic review. First of all, the BMJ Open journal has a specific section for the publication of systematic review protocols (Registered Reports and Protocols - BMJ Open Science). Second, many types of bias can occur in research studies, in which systematic, rather than random, error in the results can occur. One of the most basic strategies to reduce bias is to establish the hypotheses to be tested and the methodological approaches to be used in a research study before starting it, even if the data are not yet known. Research protocols fulfill this role by providing a roadmap for planned research. Finally, it allows the scientific community to assess whether the final analysis and results are in line with the initial intentions of the researcher. In addition, the scientific community is also informed about what studies are being done, which helps avoid duplication and better coordinate research efforts.

On the other hand, we have carried out a search for systematic review protocols of intervention studies (bmj open[ta] AND protocol[ti] AND systematic[ti]), where we have selected the first ten results to demonstrate that publication of systematic review protocols is routine practice in BMJ Open:

Fulton JI, Singh H, Pakkal O, Uleryk EM, Nelson M. Community-based culturally tailored education programmes for black adults with cardiovascular disease, diabetes, hypertension and stroke: a systematic review protocol of primary empirical studies. BMJ Open. 2022 Jun 10;12(6):e059883. doi: 10.1136/bmjopen-2021-059883. PMID: 35688600.

Lyons J, Campese S, Learmonth YC, Metse A, Kermode AG, Karahalios A, Marck CH. Comparing the effectiveness, safety and tolerability of interventions for depressive symptoms in people with multiple sclerosis: a systematic review and network meta-analysis protocol. BMJ Open. 2022 Jun 9;12(6):e055796. doi: 10.1136/bmjopen-2021-055796. PMID: 35680262.

Beasant B, Lee G, Vaughan V, Lotfaliany M, Hosking S. Health literacy and cardiovascular disease prevention: a systematic scoping review protocol. BMJ Open. 2022 Jun 8;12(6):e054977. doi: 10.1136/bmjopen-2021-054977. PMID: 35676010.

Yang H, Xiao YQ, Liu JJ, Xu GX, Li J, Xiao ZY, Zhou J, Zheng XY, Liu LY, Yu Z, Yang J, Liang FR. Effect of non-pharmacological interventions for overweight/obese women with polycystic ovary syndrome on ovulation and pregnancy outcomes: a protocol for a systematic review and network meta-analysis. *BMJ Open*. 2022 Jun 8;12(6):e059090. doi: 10.1136/bmjopen-2021-059090. PMID: 35676007.

Brewer KM, Grey C, Paynter J, Winter-Smith J, Hanchard S, Selak V, Ameratunga S, Harwood M. What are the gaps in cardiovascular risk assessment and management in primary care for Māori and Pacific people in Aotearoa New Zealand? Protocol for a systematic review. *BMJ Open*. 2022 Jun 8;12(6):e060145. doi: 10.1136/bmjopen-2021-060145. PMID: 35676004.

McCann P, Kruoch Z, Qureshi R, Li T. Effectiveness of interventions for dry eye: a protocol for an overview of systematic reviews. *BMJ Open*. 2022 Jun 7;12(6):e058708. doi: 10.1136/bmjopen-2021-058708. PMID: 35672062.

Kowalski KL, Lukacs MJ, Mistry J, Goodman M, Rushton AB. Physical functioning outcome measures in the lumbar spinal surgery population and measurement properties of the physical outcome measures: protocol for a systematic review. *BMJ Open*. 2022 Jun 6;12(6):e060950. doi: 10.1136/bmjopen-2022-060950. PMID: 35667717.

Lunghi C, Dugas M, Leclerc J, Poluzzi E, Martineau C, Carnovale V, Stéfan T, Blouin P, Lépine J, Jalbert L, Espinoza Suarez NR, Svyntozelska O, Dery MP, Ekanmian G, Nogueira DM, Akinola PS, Turcotte S, Skidmore B, LeBlanc A. Global prevalence of antidepressant drug utilization in the community: protocol for a systematic review. *BMJ Open*. 2022 May 31;12(5):e062197. doi: 10.1136/bmjopen-2022-062197. PMID: 35641008.

Pondofe K, Marcelino AA, Ribeiro TS, Torres-Castro R, Vera-Urbe R, Fregonezi GA, Resqueti VR. Effects of respiratory physiotherapy in patients with amyotrophic lateral sclerosis: protocol for a systematic review of randomised controlled trials. *BMJ Open*. 2022 May 30;12(5):e061624. doi: 10.1136/bmjopen-2022-061624. PMID: 35636801.

Lathlean TJH, Wassie MM, Winter JM, Goyal R, Young GP, Symonds EL. Accuracy of blood-based biomarkers for screening precancerous colorectal lesions: a protocol for systematic review and meta-analysis. *BMJ Open*. 2022 May 30;12(5):e060712. doi: 10.1136/bmjopen-2021-060712. PMID: 35636795.

#### Other changes:

Assessment of certainty of the evidence by GRADE was included. Assessment of risk of bias of the studies included will be assessed using the Cochrane 'risk of bias' tool or ROBINS-I tool.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Jussielly Cunha Oliveira Universidade Federal de Sergipe
<b>REVIEW RETURNED</b>	30-Jun-2022
<b>GENERAL COMMENTS</b>	O artigo é bem escrito e os métodos e discussões estão bem escritos.