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Clinical practice guideline for the integrated management of major trauma by the Italian National Institute of Health: process and methods

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Abstract

Background. Major trauma describes serious injuries requiring lifesaving interventions or resulting in long-term disability; it represents about 8% of all deaths worldwide. Specific guidelines can help reduce deaths and disabilities, provided they adhere to high quality and trustworthiness standards. This article aims at introducing the development process of the Istituto Superiore di Sanità, ISS (Italian National Institute of Health) guideline for major trauma integrated management.

Methods. We applied the ISS methodological standards including the GRADE-ADOLOPMENT approach for adoption, adaptation, and *de novo* development of trustworthy guidelines.

Results. The scope was formulated by the multidisciplinary panel with stakeholders' involvement; two guidelines were identified as appropriate sources for adolopment. Forty questions from the two source guidelines were prioritised and five new ones formulated. New systematic reviews or updates were conducted for each clinical question, Evidence to Decision frameworks developed or re-assessed and the recommendations formulated after public consultations and external review. The policy on conflicts of interest was applied throughout the process.

Conclusions. Through a broad expertise representation, the early and wide stakeholders' participation, a continual process for disclosure and management of conflict of interests and the transparency of the process, ISS standards are proving to be an efficient model for developing trustworthy clinical guidance.

Key words

- major trauma
- Italian National Guidelines System
- GRADE approach
- Clinical Practice Guidelines
- healthcare decision-making

INTRODUCTION

Clinical Practice Guidelines (CPGs) are "statements that include recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options" [1]. They represent the healthcare benchmark for health workers and patients and an essential tool for making health policy decisions [2].

In Italy, the Law n. 24/2017 [3] confers CPGs an important role in the field of medical liability and identifies

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the Istituto Superiore di Sanità (ISS, Italian National Institute of Health) as methodological guarantor of the CPGs produced. CPGs have to be released by the National Guidelines System (Sistema Nazionale Linee Guida - SNLG) after a thorough review of their methodological quality, according to ISS standards based on internationally recognized CPGs development process benchmarks [4-10].

Major trauma is defined as "an injury or a combination of injuries that are life-threatening and could be life changing because it may result in long-term disability" [11]. In 2019, more than 4 million people died as a result of injuries, representing about 8% of all deaths, and 11% of YLLs worldwide [12].

Globally, according to the Global Burden of Disease [13] road injuries ranked first in the 25-49-year age group in percentage of DALY (6.6, 5.6 to 7.7). Overall, major trauma will be the third leading cause of disability by 2030 [14]. In Italy, in 2017, falls and road injuries are among the top 25 causes of DALYs [15].

The Italian Integrated System for Major Trauma Assistance established in 2015 [16] is coherent with the international evidence on the best clinical organizational models; however, there are still many critical issues, such as (i) regional variability in mortality outcomes; (ii) regional availability of Trauma Centers and Trauma Units; (iii) lack of integration between the pre-hospital and hospital emergency system; (iv) inappropriate organizational management model for major trauma in many hospitals.

To overcome these challenges, since October 2019, the ISS has been developing a guideline on major trauma, on mandate of the Ministry of Health [17].

The goal of this article is to discuss the application of the methodological standards set by the ISS for developing CPG for the integrated management of major trauma. As the guideline development is still ongoing, we focus here on how the process was applied, from the establishment of guideline development group to recommendations' formulation. The final aim is to highlight the challenges and strengths of this guideline development process, with special reference to the application of the GRADE-ADOLOPMENT approach that allows for adopting or adapting existing high-quality guidelines. This is particularly important for the Italian context where there is an urgent need of an appropriate body of trustworthy clinical guidelines in the SNLG on priority health issues, given the role of CPGs in the field of medical liability.

We will report and discuss the specific recommendations after completion of the whole guideline, in a separate paper.

METHODS

The ISS guideline on major trauma is developed according to the SNLG standards, which include GRADE-ADOLOPMENT approach for adoption, adaptation, and *de novo* development of trustworthy guidelines [18-21]. *Figure 1* summarizes the main steps of the development process as defined by the ISS methodological manual [10], while a narrative description follows below.

The establishment of guideline development group

The guideline development group is composed by several teams who work collaboratively, supported by the scientific and technical-organizational secretariat, as well as the stakeholders participating in the process. Their roles and tasks are described below.

The *ISS Steering Committee* leads and oversees the whole guideline development process, from panel members' selection to Conflict of Interest (CoI) management and strategies for patient and public participation.

The involvement of the *expert of ethics* within the guideline development group ensures that the guideline recommendations are ethical and draw upon the principles outlined by the ISS Ethics Committee.

The *expert panel* contributes to the scope and clinical questions' formulation, critically evaluates the evidence, makes judgements on the Evidence-to-Decision (EtD) framework criteria, formulates recommendations, appraises stakeholders' and external referees' comments. The *chair* and *methodological co-chair* lead the works and guide the application of the GRADE EtD framework, from the critical assessment of the evidence to the formulation of recommendations.

After literature searching by documentalists, the *Evidence Review Team* (ERT) selects, summarizes and rates the certainty of evidence and prepares the EtD framework.

The *developers* are methodologists who act as a bridge between the panellists and the ERT.

The *External Reviewers* assess the draft recommendations content and methodology.

The Quality Assurance (QA) team ensures that the guideline development process complies with the ISS methodological standards.

Scoping

Scoping aims at defining the target population, the application context, thematic areas and the economic perspective.

For this guideline, scoping was conducted through different steps, from context analysis to target population and key topics' identification and stakeholders' involvement. Unlike other ISS guidelines [22], stakeholders' opinion was collected prior to drafting the scope through a scoping workshop aimed at discussing the main thematic areas; it followed the public consultation on the draft scope through the SNLG web platform (https://piattaformasnlg.iss.it) and the guideline scope finalization by the panel.

Patient and public participation

We ensured patient and public involvement through the inclusion of a lay member in the panel, the public consultations on the draft scope and draft recommendations, and through specific searches on patients' values and preferences.

Unlike the lay member, stakeholders represent interests common to a category or organization; individuals are encouraged to participate to the public consultation through stakeholders' organizations classified as scientific societies and health professions associations, associations of citizens, patients and caregivers, industry,

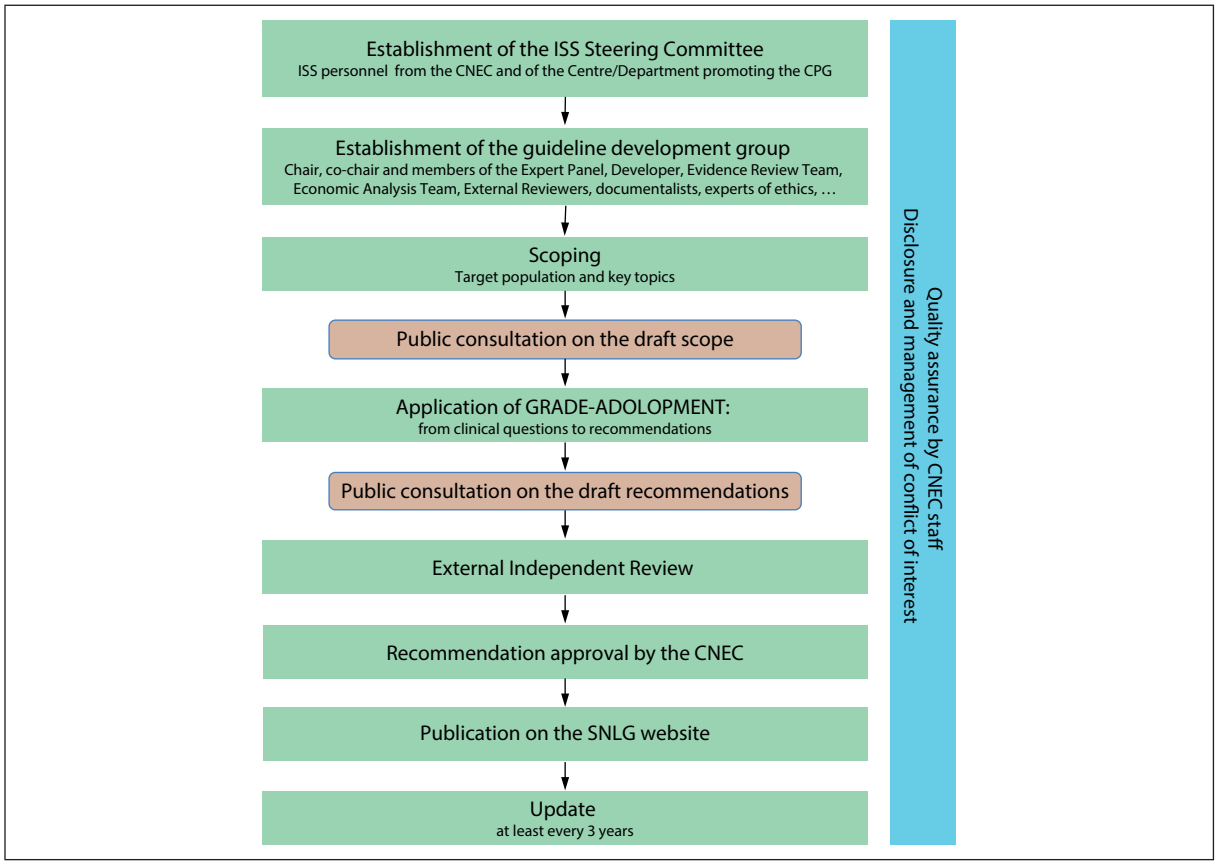

Figure 1
Guideline development process set by the Istituto Superiore di Sanità (ISS) (adapted from the methodological manual for ISS guidelines development).

national and regional public institutions, universities, public and private research institutes.

The ad hoc questionnaires used for the public consultations are reported in *Table 1*.

The GRADE-ADOLOPMENT approach

This approach combines advantages of adoption, adaptation and *de novo* guideline development and consist of the following main steps [21]:

1. identify trustworthy existing guidelines or evidence synthesis on the topic, while setting the guideline priorities, involving relevant stakeholders;
2. evaluate and complete GRADE EtD Frameworks for each recommendation by updating the systematic reviews as needed and by either developing new EtDs or reassessing existing EtD;
3. deciding on a final adoption, adaptation or *de novo* development of recommendations based on the extent of changes made or the availability of the recommendation itself in the source guideline.

Table 1
Questionnaires used for the public consultations on the draft scope and on draft recommendations

Public consultation on the draft scope
Open questions:
Does the draft scope consider aspects that are relevant to the target population of the guideline?
Does the draft scope consider key clinical topics?
Are the outcomes relevant and in adequate numbers?
Other comments on the scope
Public consultation on draft recommendations
Stakeholders were asked to express their degree of agreement/disagreement for each of the 5 statements, using a scale of 1 to 5 in which each response indicates respectively: (1) "in complete disagreement", (2) "disagreeing", (3) "uncertain", (4) "agree", (5) "completely agreed".
The recommendation is formulated in an understandable manner with regard to the intervention recommended to be used.
The recommendation is formulated in such a way that adherence to the recommendation is easy to document and measure.
The rating of the strength of recommendation is consistent with my knowledge and judgement of the supporting evidence
The rating of the certainty of evidence is consistent with my knowledge and judgement of the supporting evidence
Additional remarks provide useful information on how to implement the recommendation (if applicable).
Optional open question: "Please insert any comments here and include bibliographical references, where possible"

External review

Each draft recommendation and process documentation is submitted to two independent experts. By using the AGREE reporting checklist [23] and AGREE II [24, 25], they critically review the draft recommendations, suggest improvements, point out challenges for implementing recommendations, thus informing the guideline development and recommendations formulation.

Management of conflict of interest

Based on international standards [26, 27], the ISS policy on the management of CoI requires that all the subjects participating in the process have to declare all financial, non-financial, personal and institutional interests related to the guideline by completing a standardized CoI form (https://snlg.iss.it/wp-content/uploads/2021/02/Modulo-CdI-compilabile_feb2019.docx.), adapted from the WHO form [28]. Each declared interest is examined by the Steering Committee on the basis of its nature, type, specificity, financial value, period and duration, and then assigned a level of potential conflict, from minimal/trivial to relevant, and related actions to be taken from full participation, with public disclosure of the interest in the guideline document to a total exclusion.

RESULTS

The expert panel and external reviewers

ISS Steering Committee selected 14 panel experts, including a lay member, and two external reviewers, on the basis of their expertise, ensuring a balanced representation of relevant disciplines and health professions, as well as geographical provenience and healthcare setting *(Table 2)*.

During the inception meeting, panellists were trained on GRADE-ADOLOPMENT approach [18, 19, 21] for guideline development. Clear instructions about the disclosure and management of CoI were also given.

The guideline scope

Key-topics and target population were first identified by evaluating the evidence from existing guidelines or evidence synthesis. The international CPGs were identified through a search via PubMed using "multiple trauma" and "trauma centers" as Mesh terms and the terms "trauma", "polytrauma", "multiple trauma", and "major trauma" as text words and using the filter "Guideline" as publication type.

In addition, the ECRI repository (https://guidelines.ecri.org/) for clinical guidelines was searched. CPGs were considered eligible if they were published after 2016 in English language, dealt with major/severe trauma, and met the guideline definition proposed by the IOM [1]. We excluded consensus conference, position statement, and any secondary publication of the guidelines. The searching process led to the identification of 6 potential CPGs *(see Supplementary Materials available online)*, among them the National Institute for Clinical Excellence (NICE) guidelines, NG39 [11] and NG40 [29] were selected as the highest quality guidelines, with an AGREE II score of 7 out of 7 [24, 25]. Moreover, the NICE guidelines allowed for covering both the clinical and organizational aspects of major trauma management in pre-hospital and hospital settings and had a detailed publicly available material (e.g., identifiable PICO elements, presence of full systematic reviews, accessible search strategy, and analysis method and evidence tables/summaries) for updating and GRADE ADOLOPMENT application.

A preliminary document with the main thematic areas thus identified, was discussed during a panel meeting and a subsequent scoping workshop with invited stakeholders. The draft scope was then finalized and ultimately commented through a public consultation on the SNLG web platform.

Trauma is a disease which starts at the time of accident, requires a support of vital functions, a timely diagnostic process, an emergency treatment of life-threatening conditions, a definitive correction of injuries and finally ends with rehabilitation process to restore function; thus, the final scope of the guideline, available at the SNLG website [17] and summarized by the infographic in *Figure 2*, is the integrated management of the condition, from the point of injury to definitive care, covering the clinical and organisational aspects of major trauma services in the Italian pre-hospital and hospital settings.

Table 2
Expertise of the expert panel and of the external reviewers

Role	Expertise	N.
Chair	Trauma surgeon	1
Co-chair	Emergency physician	1
Panel member	Anaesthetist	3
Panel member	Emergency physician	2
Panel member	Chief medical officer	1
Panel member	Orthopaedic traumatologist	2
Panel member	Trauma surgeon	1
Panel member	Interventional radiologist	1
Panel member	Clinical nurse	1
Panel member	Lay member	1
External reviewer	Orthopaedic traumatologist	1
External reviewer	Emergency physician	1

Stakeholders' involvement on the scoping phase

Nineteen out of 39 (55.8%) invited relevant stakeholders participated to the scoping workshop for discussing the main guideline thematic areas.

The draft scope formulated thereafter, was posted on the SNLG web platform for two weeks for public consultation. Fourteen scientific societies and health professions associations, registered on the web platform, submitted their comments using the standardized form shown in *Table 1*.

A total of 21 stakeholders participated both in the scoping workshop and public consultation, representing many scientific societies and health profession associations in different specialties: intensive care (n = 5); general and specialist surgery (n = 4); radiology (n = 3); forensic medicine (n=2) orthopaedics and traumatol-

ogy (n = 2); emergency medicine (n = 2) physiotherapy and rehabilitation (n=2); transfusion medicine and immunohematology (n = 1).

All the comments were discussed and responses included in a consultation report published on the SNLG website for transparency [17]. No comments were made on the target population; the key topics and relevant outcomes, instead, were revised according to the comments received.

Application of GRADE-ADOLOPMENT: from clinical questions to recommendations

The panel used a formal process to prioritise review questions from the two source guidelines NG39 [11] and NG40 [29] rating the priority of questions on a 9-point Likert scale, as follows: 7 to 9: high priority; 4 to 6: priority; 1 to 3: not a priority. As a result, 40 questions had a median value between 7 and 9 and were all included. Therefore, the panel selected the most urgent questions and those to be addressed afterwards, on the basis of considerations on uncertainty or variation in the clinical practice and new published evidence.

Following the ADOLOPMENT approach, the panel identified possibly matching recommendations of the prioritised questions on the basis of their credibility, update, acceptability and applicability to the national context and discussed whether those recommendations could be adapted, modified or developed *de novo*. Finally, the panel formulated five questions to be developed *de novo* for topics not addressed by the source guidelines.

The final list of 45 clinical questions approved by the panel addresses the following key-topics: pre-hospital triage, airway management, chest trauma assessment and management, haemorrhage assessment and management, monitoring, pain, heat loss, service organization, information, and support. These were grouped into five macro areas, following the concept of the continuity of care for major trauma patients, from the scene to the hospital: pre-hospital triage, assessment and early management, assessment and definitive management, service organization, information, and support. The final list of the clinical questions is reported in the *Supplementary Materials* available online.

As for the outcomes to be addressed in the evidence synthesis, we maintained those considered in the PICOs (Population, Intervention, Comparison and Outcomes) of the source guidelines; for the new PICOs, the panellists listed and rated the relative importance of the outcomes on a 1 to 9 scale (7 to 9: critical for decision-making; 4 to 6: important; 1 to 3: low importance).

Since then, the ERT is updating the original systematic reviews or conducting new ones for each PICO and preparing draft EtD frameworks. Supplementary searches for evidence on acceptability, patients' values and preferences and economic analysis are being conducted to complete and contextualize the EtD frameworks. During a one-day panel meeting, on the basis of the EtDs judgements, the panel formulates recommendations through consensus or voting, when needed.

By January 2021, the experts' panel has adoloped 20 recommendations related to 10 clinical questions and published them on the SNLG website.

Stakeholders' involvement on the draft recommendations

Through public consultations, stakeholders were invited to provide their feedback on the draft recommendations by expressing their degree of agreement on 1 to 5 Likert scale, on five statements regarding recommendations' formulation, strength, rating of the certainty of evidence and implementation, through a

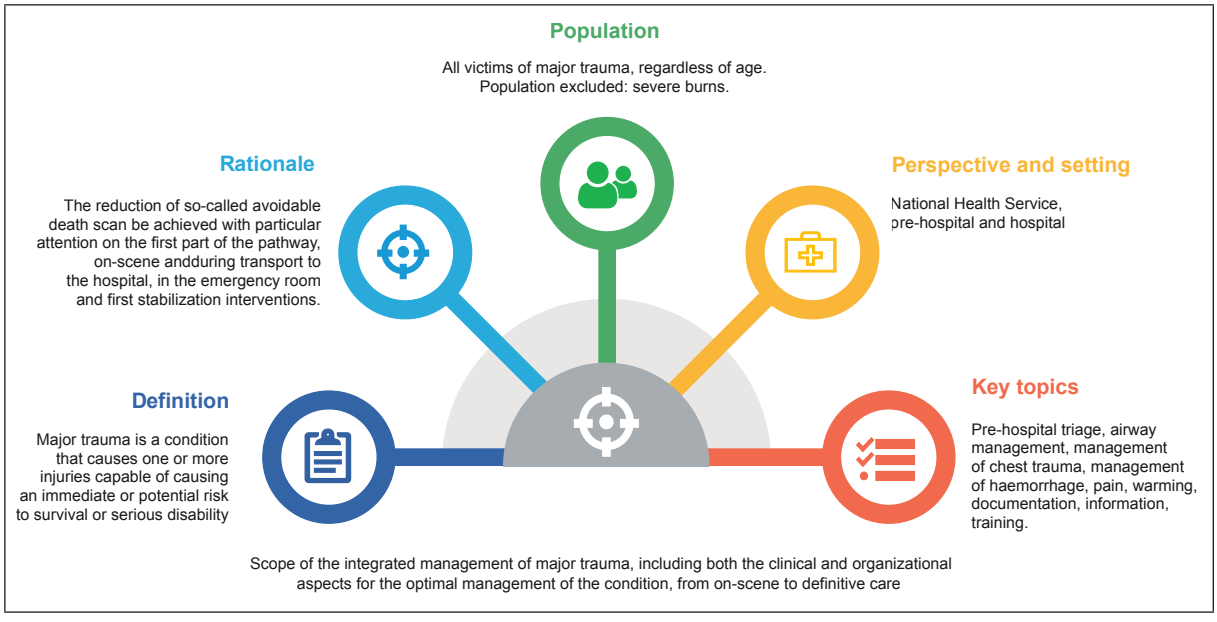

Figure 2
Scope of integrated management for major trauma clinical practice guideline by the Istituto Superiore di Sanità.

standardized form available on the SNLG web platform for two-weeks *(Table 1)*. For the 9 public consultations on draft recommendations carried out so far, the average agreement score was 4, with a mean response rate of 44% (range 34-57) as reported on the SNLG website [17].

External review

The 20 draft recommendations were sent to the independent experts for the external review. The final recommendations are published on the SNLG website [17].

Management of conflict of interest

None of the declared interests deemed to represent a potentially relevant or relevant conflict related to the guideline scope, so all the candidate members participated to the panel's work. Similarly, no relevant CoIs related to specific PICOs were identified, so no experts were excluded during the recommendations' formulation. All disclosures of CoI will be publicly reported with the final guideline document.

DISCUSSION

The application of ISS standards for developing this guideline aimed at facing several challenges for ensuring a broad representation of expertise, the widest involvement and participation of all stakeholders and the maximum transparency of the process.

The panel composition sought to reflect the multidisciplinary approach that characterizes the trauma team which should include physicians expert in intensive care, emergency and trauma surgery, specially trained nurses and radiologists; in addition, it must provide for the possibility of having immediately available figures such as orthopaedist, neurosurgeon, radiology technician [30].

The SNLG web platform facilitates a transparent participative process by allowing the engagement of stakeholders at crucial stages. Their involvement through both the scoping workshop and public consultations is the very novel aspect of this guideline. This strategy was considered useful for drafting a well-focused scope and ensuring that guideline development is straightforward, easy to manage and relevant to end users [31]. The relatively low response rate to the public consultations may be due to stakeholders' limited knowledge on the guideline's highly specific topics; it nevertheless suggests that more efforts should be done to improve ISS strategies for patient and public involvement, though limited research is available for identifying strategies for successful engagement [31, 32]. Stakeholders' consultation complements the contribution of the lay panel member, and so does the external independent review that provides a further opportunity to obtain relevant and reliable inputs on both content and methodology [33, 34]. In this case, stakeholders and experts' involvement is particularly useful for ensuring that questions, evidence and recommendations are contextualised to the local needs, since specific searches for patients' values and preferences and cost effectiveness and resources use produced limited data [21].

Transparency is also guaranteed by the publication on the SNLG website of public notices on public consultations, of draft and final recommendations and attached documentation, and of consultation reports, as well as by the application of a comprehensive and continual process for the disclosure and management of CoI, which is a hallmark of a trustworthy clinical guidance [26, 27].

ISS policy on CoI conceptualizes disclosure of interest as distinct from identification and management of a CoI [35]. Indeed, the determination of a conflict is the result of a case-by-case assessment that considers the characteristics of the interest itself; only a complete and careful disclosure of all the interests allows this assessment and the adoption of appropriate measures to manage CoI in a transparent, proportional and consistent way.

The application of ISS policy on CoI is a major challenge since it requires a skill change to acknowledge that an interest does not necessarily represent a CoI and to recognize as interests to be declared professional activities or scientific production related to the guideline topic. Hence, experts need to be supported in identifying and declaring interests and encouraged to regularly review and update their declarations, as disclosure of interests is a continual process throughout the guideline development.

Last, the adoption of GRADE-ADOLOPMENT [18, 19, 21] provides panel members with a transparent and systematic approach for decision making by ensuring that all recommendations are based on the best available evidence and that all potentially important criteria are considered ; this makes guideline users aware of the rationale behind each judgment and recommendation, including the contextual factors that influence any modifications to the original recommendations. In our guideline, contextual issues such as needs, values and resources are considered as important elements for the applicability and transferability of the original recommendations.

Guideline adaptation provides an important alternative to *de novo* development by making the process more efficient, allowing to save resources and time and avoiding duplication [36]. We completed adolopment of 20 recommendations within less than one year, considering that the process has suffered a brief setback due to the Covid-19 pandemic. This is a relatively short time, compared to the time estimates of up to three years made by the NICE [9] or WHO [2] for a *de novo* guideline development. Finally, the adaptation of CPGs to the local setting is expected to improve their uptake and implementation [37].

Despite the advantage of saving resources, still the GRADE-ADOLOPMENT approach requires advanced methodological skills and further investment on methodological training [18, 21].

Preventing the participation of individuals to the public consultation, due to the lack of human resources to cope with huge amounts of comments, may be also considered a limitation, though balanced by the possibility for any individual to convey a point of view through any of the broad stakeholders' categories.

CONCLUSIONS

The development of the ISS guideline for major trauma integrated management follows a rigorous, systematic, and transparent process that allows for the application of the GRADE-methodology for adoption, adaptation and de novo development of trustworthy guidelines.

The possibility of adoloping existing high-quality guidelines is particularly important for the Italian context where there is an urgent need of trustworthy guidelines, given the role of CPGs in the field of medical liability, for reducing regional variability, providing the basis for the definition of local clinical pathways and optimizing citizens' health outcomes.

By considering this guideline development experience, the next steps for guideline development are to invest on advanced methodological training on the GRADE-ADOLOPMENT approach, to develop strategies for a major patient and public involvement and to support the experts in identifying and declaring interests, thus facilitating that key cultural change needed for developing trustworthy guidelines.

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Availability of data and materials

All the material is available at: https://piattaformasn-lg.iss.it

Authors' contribution

AJF, DC, AN: conceptualization, methodology, writing - original draft; validation. AJF, DC, AN, DD, GC, SG: writing, review and editing. GC, SG, GP, AB: investigation; formal analysis. LI, RL, KS: data curation; visualization. PI, OC: writing, review and editing, supervision.

Conflict of interest statements

The Authors declare that they have no competing interests.

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