European Journal of Physical and Rehabilitation Medicine
EDIZIONI MINERVA MEDICA

Robot-assisted Arm Therapy in Neurological Health Conditions: Rationale and Methodology for the Evidence Synthesis in the CICERONE Italian Consensus Conference

Francesca GIMIGLIANO, Angela PALOMBA, Chiara ARIENTI, Giovanni MORONE, Luca PERRERO, Michela AGOSTINI, Irene Giovanna APRILE, Matteo PACI, Emanuela CASANOVA, Dario MARINO, Giuseppe LA ROSA, Federica BRESSI, Silvia STERZI, Daniele GIANSANTI, Alberto BATTISTINI, Sandra MICCINILLI, Serena FILONI, MONICA SICARI, Salvatore PETROZZINO, Claudio SOLARO, Stefano GARGANO, Paolo BENANTI, Paolo BOLDRINI, Donatella BONAIUTI, Enrico CASTELLI, Francesco DRAICCHIO, Vincenzo FALABELLA, Silvia GALERI, Mauro GRIGIONI, Stefano MAZZOLENI, Stefano MAZZON , Franco MOLTENI, Maurizio PETRARCA, Alessandro PICELLI, Federico POSTERARO, Michele SENATORE, Giuseppe TURCHETTI, Sofia STRAUDI, Italian Consensus Conference on Robotics in Neurorehabilitation (CICERONE)

European Journal of Physical and Rehabilitation Medicine 2021 Jun 15
DOI: 10.23736/S1973-9087.21.07011-8

Article type: Original Article

Supplementary material available online at http://www.minervamedica.it
Article first published online: June 15, 2021
Manuscript accepted: June 14, 2021
Manuscript revised: June 7, 2021
Manuscript received: April 15, 2021

Robot-assisted Arm Therapy in Neurological Health Conditions: Rationale and Methodology for the Evidence Synthesis in the CICERONE Italian Consensus Conference

Robot-assisted Arm Therapy in Neurological Health Conditions

Francesca Gimigliano[1], Angela Palomba[2]*, Chiara Arienti[3], Giovanni Morone[4], Luca Perrero[5], Michela Agostini[6], Irene Aprile[7], Matteo Paci [8], Emanuela Casanova[9], Dario Marino[10], Giuseppe La Rosa[11], Federica Bressi[12], Silvia Sterzi[12], Daniele Giansanti[13], Alberto Battistini[8], Sandra Miccinilli[12], Serena Filoni[14], Monica Sicari[15], Salvatore Petrozzino[15], Claudio Marcello Solaro[16], Stefano Gargano[17], Paolo Benanti[18], Paolo Boldrini[19], Donatella Bonaiuti[20], Enrico Castelli[21], Francesco Draicchio[22], Vincenzo Falabella[23], Silvia Galeri[3], Mauro Grigioni[13], Stefano Mazzoleni[24], Stefano Mazzon[25], Franco Molteni[26], Maurizio Petrarca[27], Alessandro Picelli[28], Federico Posteraro[29], Michele Senatore[30], Giuseppe Turchetti[31], Sofia Straudi[32], Italian Consensus Conference on Robotics in Neurorehabilitation (CICERONE)

Collaborators:
Ludovica Baluardo (Ferrara University Hospital, Neuroscience and Rehabilitation Department, Ferrara, Italy), Alex Martino Cinnera (Santa Lucia Foundation, IRCCS, Rome, Italy), Manuela Desilvestri (Neurorehabilitation Unit, Azienda Ospedaliera SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy, EU), Marco Bravi (Campus Bio-Medico University Hospital, Italy), Diletta Bruno (Campus Bio-Medico University Hospital, Italy), Fabio Santacaterina (Campus Bio-Medico University Hospital, Italy), Cristiano Pecchioli (Department of Neuroscience and Neurorehabilitation, IRCCS San Raffaele Pisana, 00167, Rome), Gandolfi Marialuisa (Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy), Emanuele Francesco Russo (Padre Pio Foundation and Rehabilitation Centers, San Giovanni Rotondo, Italy), Valentina Boetto (Università degli studi di Torino)

1- Department of Mental and Physical Health and Preventive Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy
2- Multidisciplinary Department of Medicine for Surgery and Orthodontics, University of Campania "Luigi Vanvitelli", Naples, Italy
3-IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
4- Santa Lucia Foundation, IRCCS, Rome, Italy
5- Neurorehabilitation Unit, Azienda Ospedaliera SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy, EU
6-San Camillo IRCCS, Venice, Italy
7-IRCCS Fondazione Don Carlo Gnocchi, Florence –Italy
8-AUSL (Unique Sanitary Local Company) District of Central Tuscany, Florence, Italy
9-IRCCS Istituto delle Scienze Neurologiche di Bologna, UOC Medicina Riabilitativa e Neuroriabilitazione, Bologna, Italia
10-IRCCS Neurolysis Center "Bonino Pulejo", Messina, Italy
11- C.S.R. - Consorzio Siciliano di Riabilitazione, Catania, Italy
12- Campus Bio-Medico University Hospital, Italy
13- National Center for Innovative Technologies in Public Health, Italian National Institute of Health, Rome, Italy

14 - Padre Pio Foundation and Rehabilitation Centers, San Giovanni Rotondo, Italy
15 - A.O.U. Città della Salute e della Scienza di Torino
16 - CRRF “Mons. Luigi Novarese” Moncrivello, VC, Italy
17- Fondazione Don Carlo Gnocchi - Torino
18- Pontifical Gregorian University, Rome, Italy
19- Società Italiana di Medicina Fisica e Riabilitativa (SIMFER)
20 - Istituto Geriatrico Piero Redaelli, Milan, Italy
21 -Paediatric Neurorehabilitation, Bambino Gesù Children's Hospital, Rome, Italy
22 - Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, INAIL, Monte Porzio Catone, 00185 Rome, Italy.
23 -President Italian Federation of Persons with Spinal Cord Injuries (Faip Onlus), Rome, Italy
24- Department of Electrical and Information Engineering, Politecnico di Bari, Italy
25- AULSS6 (Unique Sanitary Local Company) Euganea Padova - Rehabilitation Department
26- Villa Beretta, Costa Masnaga, Italy
27- “Bambino Gesù” Children's Hospital – IRCCS, Movement Analysis and Robotics Laboratory MARlab, Rome, Italy
28 - Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
29 - Versilia Hospital AUSL Toscana Nord Ovest, Italy
30 - Presidente AITO (Associazione Italiana Terapisti Occupazionali)
31- Management Institute, Sant'Anna School of Advanced Studies, Pisa, Italy
32- Ferrara University Hospital, Neuroscience and Rehabilitation Department, Ferrara, Italy

Corresponding author:

Palomba Angela, MD

Multidisciplinary Department of Medicine for Surgery and Orthodontics, University of Campania "Luigi Vanvitelli", Naples, Italy

E-mail: angela.palomba@unicampania.it

BACKGROUND:
Robot-assisted Arm Therapy (RAT) has been increasingly applied in the last years for promoting functional recovery in patients with disabilities related to neurological health conditions. Evidence of a knowledge-to-action gap for applying robot-assisted technologies in the rehabilitation of patients with neurological health conditions and the difficulty to apply and tailor the knowledge to the local contexts solicited the need for a national consensus conference on these interventions.

AIM:
This paper aims to explain the methodology used by the working group dedicated to synthesize evidence on the effectiveness of RAT in neurological health conditions in the context of the CICERONE Italian Consensus Conference.

DESIGN:
The methodological approach of the working group.

SETTING:
All rehabilitation settings.

POPULATION:
Patients with disability following a neurological health condition.

METHODS:
Following the indications proposed by the Methodological Manual published by the Italian National Institute of Health, a Promoting Committee and a Technical Scientific Committee have been set up. Six working groups (WGs) have been composed to collect evidence on different questions, among which WG2.2 was focused on the effectiveness of RAT in neurological health conditions.

RESULTS:
WG2.2 started its work defining the specific research questions. It was decided to adopt the ICF as the reference framework for the reporting of all outcomes. Literature search, data extraction and qualitative assessment, evidence analysis and synthesis have been performed.

CONCLUSIONS:
This paper summarizes the methodological approaches used by the WG2.2 of the CICERONE Italian Consensus Conference to define the effectiveness of RAT in the management of patients with neurological health conditions.

CLINICAL REHABILITATION IMPACT:
WG2.2 synthesis might help clinicians, researchers, and all rehabilitation stakeholders to address the use of RAT in the Individualized Rehabilitation Plan, to guide the allocation of resources and define clinical protocols and indications for the management of patients with different neurological health conditions.

Key words: rehabilitation, robot, upper limb, electromechanical devices, neurological health conditions, consensus conference

Introduction

The recovery of upper limb functioning is one of the main goals and probably the most critical of patients' rehabilitation with neurological health conditions.[1] Technology-assisted rehabilitation, and in particular Robot-assisted Arm Therapy (RAT), has been increasingly applied in the last years for promoting the repetitive execution of motor tasks and functional recovery in patients with disabilities related to neurological health conditions, including stroke traumatic brain injuries and neurodegenerative disorders.[2-4] Indeed, RAT is becoming part of the rehabilitative plan, and it is often proposed as an add-on to conventional therapy. In Italy, such technologies have been included in the latest Essential Levels of Health Care Plan (2018) provided and refunded by the Italian National Health System as official rehabilitation tools.[5]

However, evaluating RAT's effectiveness on upper limb functioning is often difficult due to upper limb complexity, mainly involving shoulder and elbow for reaching tasks, wrist and hand for grasping. Even though robotic devices have been designed to train reaching or grasping activities, there is still a lack of specific assessment tools able to detect the beneficial effects of implementing the Individualized Rehabilitation Plan (IRP) with RAT.[6] These tools should be based on the International Classification of Functioning, Disability and Health (ICF).[7] Other critical issues are understanding each robot's specificity and the ideal dosage and frequency in different health conditions and phases of the rehabilitation.

The translation of research findings (when available) into practice is often a slow and challenging process. There is growing interest in finding ways to minimize the so-called knowledge-to-action gap.[8] If ideally a knowledge-to-action process should include two concepts, i.e. knowledge creation and translation into action, that are distinct and consecutive, in reality, they represent dynamic concepts that are fluidly connected. Indeed, action may occur even simultaneously to knowledge creation, particularly in fields where the regulatory process is not well defined, such as applying new technologies in rehabilitation medicine.[9] The spread of robot-assisted arm devices into clinical practice was anticipated mainly by small promising pilot studies primarily conducted in the chronic phase after stroke when patients typically do not receive rehabilitation. On the other hand, the lack of translational research that builds a bridge between basic science and clinical practice contributes to generating uncertainty on RAT mechanisms, biomarkers of recovery, and potential responders' identification.[10]

Similarly to other fields, evidence of a knowledge-to-action gap for applying robot-assisted technologies in the rehabilitation of patients with neurological health conditions and the difficulty to apply and tailor the knowledge to the local contexts solicited the need for a national consensus conference on these interventions. The Italian Society of Physical and Rehabilitation Medicine (SIMFER), the Italian Society of Neurorehabilitation (SIRN) and the Italian National Institute of Health have launched a Consensus Conference named CICERONE,[5] to promote knowledge about the above-mentioned open issues based on the synthesis of available evidence and the contribution of a panel of experts including clinicians and researchers.

This paper aims to explain the methodology used by the working group dedicated to synthesize evidence on the effectiveness of RAT in neurological health conditions in the context of the CICERONE Italian Consensus Conference.

Materials and methods

CICERONE Italian Consensus Conference: leadership, committees and working groups

The CICERONE Italian Consensus Conference was promoted by SIMFER, SIRN and the Italian National Institute of Health.

The reference methodology for the Consensus Conference's development is based on the criteria proposed by the Methodological Manual published by the Italian National Institute of Health in 2013.[11] Following the indications presented by the manual, a Promoting Committee and a Technical Scientific Committee have been set up.

The Technical Scientific Committee includes exponents of health care institutions; representatives of Medical Scientific Societies and Associations of Professionals in the rehabilitation area, representatives of the Bioengineering area, exponents of Associations of Persons with Disabilities, representatives of the business world in the sector, economic, bioethical and Health Technology Assessment experts.

Six working groups (WGs) have been set up: WG1 classification of technologies; WG2 clinical indications in different health conditions and functioning spectra (WG2.1 health conditions in children and youth, WG2.2 upper limb functioning, WG2.3 lower limb functioning and ambulation, and WG2.4 balance); WG3 theoretical reference models, future perspectives, development and research; WG4 organizational contexts; WG5 training paths/skills for operators; WG6 aspects of a regulatory nature (e.g. risk management, off-label use, etc.), ethical, legal and social aspects. Each WG aimed to collect scientific evidence and prepare a summary of the available information, providing it to the Jury.

The Jury was selected based on the principles of authority, competence, multi-disciplinarity and multi-professionalism, as indicated in the manual.

Upper Limb Functioning Working Group

WG2.2 is focused on the effectiveness of RAT in neurological health conditions. In particular, the group was asked to provide knowledge translation about RAT's clinical application for neurological health conditions, answering the following questions: *In the light of the existing knowledge, which recommendations can be given about the use of RAT in everyday clinical practice? Which are the recommended outcomes to be used to assess their effectiveness?*

Results

Description of methodology

Coordinators of the WG2.2 were GM and SS. All other WG2.2 members were selected among those who replied to a call sent through the two National Scientific Societies. WG2.2 activities started in March 2019 and can be summarized into four main actions. See Figure 1.

INSERT FIGURE 1 ABOUT HERE

Action 1: Research questions definition: which are the main determinants of recovery after RAT?

The first activity was a brainstorming meeting aimed to define the specific research questions considering the different health conditions (i.e. stroke, others), the stage of recovery (subacute/chronic) and the type of robotic devices (end-effector, exoskeleton, hand-device). See Table I.

INSERT TABLE I ABOUT HERE

Subgroups were determined to address each specific question. In particular, three subgroups were dedicated to stroke (assessing randomized controlled trials - RCTs, systematic reviews, clinical practice guidelines, respectively). Another subgroup was dedicated to all the other neurological health conditions. Subgroups organization and composition can be found in the supplementary material (Table S1).

Action 2: Adoption of ICF as the reference framework for reporting upper limb robotic rehabilitation outcomes

The second action was the adoption of ICF as the reference framework for reporting RAT primary outcomes.[7] We defined how to apply it to upper limb RAT outcomes starting from previous works proposing ICF codes for neurorehabilitation[12] and upper limb robotic outcomes.[13]

Goal definition of RAT was expressed according to the ICF framework, with all outcomes categorized and described as body functions, activities and participation and linked, with the respective assessing scale(s), to one or more ICF codes, as shown in Figure 2.[13-14]

INSERT FIGURE 2 ABOUT HERE

Action 3: Literature search & data extraction

Literature search and data extraction started in November 2019. A literature search was performed, primarily using the following databases: PubMed (MEDLINE, PMC, NCBI Bookshelf), PEDro, Embase, Epistemonikos, Web of Science, Scopus, Cinahl and Cochrane Library. Separate and repeated searches were conducted to intercept different types of documents. The PICOS of the search was the following:

- Population: people with neurological health conditions including stroke, multiple sclerosis (MS), Parkinson’s disease (PD), and spinal cord injury (SCI);
- Intervention: RAT;
- Comparisons: other rehabilitation interventions;
- Outcomes: all upper limb functioning outcomes (see Action 2);
- Study designs: clinical trials (only RCTs were included for stroke), systematic reviews, and clinical practice guidelines.

The search was limited to the English language.

To focus on the effectiveness of RAT versus other interventions, we excluded a study that compared different RAT protocols or evaluated the effects of an additional technology (i.e. non-invasive brain stimulation).

Papers were screened by two independent reviewers (SS and GM) to check for duplicates and identify publications matching with the WG2.2 goals. For each document, the following data were extracted and tabulated into worksheets: a) authors; b) year; c) type of study; d) the number of patients; e) intervention; f) control; g) dose (sessions, duration, frequency); h) outcomes; i) results.

For data extraction, the different subgroups were asked to classify studies according to: their focus on hand rehabilitation (grasping tasks) or shoulder/elbow rehabilitation (reaching tasks); disease phase subacute or chronic (less or more than three months); type of robot (exoskeleton, end-effector or hand device); and a distinction has been done when RAT was used as an add-on to conventional therapy or not.

Action 4: Qualitative assessment, evidence analysis and synthesis

Different methodological quality assessment tools were used: PEDro for clinical studies,[15] AMSTAR2 for systematic reviews[16,] and AGREE II for guidelines.[17] Moreover, the level of evidence for each study was assessed according to 2011 Oxford CEBM Levels of Evidence.[18]

Results were expressed as positive (+) if there was a between-group difference with p <0.05 in favor of the experimental group, negative (-) if there was a between-group difference with p <0.05 in favor of the control group, neutral (=) if there was no statistically significant difference between groups.

Finally, the answers to each specific question addressed by WG2.2 were formulated on the available positive studies and considering their quality and evidence level. WG2.2 prepared the final report with the defined search questions and their answers, presented as evidence synthesis and submitted to the expert panel in November 2020. The report included the main conclusions summarized for health conditions, disease phase, type of robotic device, and outcomes. The format of the report was: introduction, search method, results, synthesis of recommendations, clinical practice implications, future developments, and references. The report was evaluated by the Jury and reviewed for achieving the final version.

Preliminary literature results description

The literature research resulted in 1,160 total papers, in particular including: a) 792 papers on MEDLINE (673 about stroke, 20 on MS, 13 on traumatic brain injuries - TBI, five on PD, 70 on SCI, 11 on ataxia); b) 260 papers in Cochrane Library (236 on stroke, 18 on SCI; 6 on MS); c) 108 papers on PEDro database (97 on stroke, four on MS, one on PD, six on SCI). After screening, a total number of 82 manuscripts were analyzed: 70 studies on stroke (8 clinical practice guidelines, 44 RCTs, 18 systematic reviews), six studies on MS (two RCTs, one case-control, two case series, one crossover trial), one study on PD (case series), five studies on SCI (two systematic reviews, two RCTs, one case series). Apart from stroke, the available evidence resulted in being inadequate, with few studies of low/moderate quality, despite the great diffusion of RAT in the rehabilitation of people with all neurological health conditions.

Discussion

This paper summarizes the methodological approaches used by the WG2.2 of the CICERONE Italian Consensus Conference to define the effectiveness of RAT in the management of patients with neurological health conditions. Specifically, methods for determining research questions, literature search, data extraction, qualitative assessment of evidence and synthesis are described. The Consensus Conference might represent the best way to fill the existing knowledge-to-action gap.

Subgroups' multi-disciplinarity helped reducing possible biases related to different backgrounds of their members. The adoption of the ICF as the reference framework for reporting upper limb robotic rehabilitation outcomes helped extracting patients centered functional aspects when dealing with the effectiveness of RAT following a bio-psycho-social approach.[19]

The choice to include literature from different sources has provided the members of the consensus and the Jury of a comprehensive picture of the available evidence. The non-homogeneity in terms of quantity and quality of the existing literature across different neurological health conditions led to different ways of approaching RAT evidence: in the case of stroke we could rely on RCTs and synthesis products such as systematic reviews and clinical practice guidelines, in the case of all other neurological health conditions we had to take into account studies with a broader range of levels of evidence, including RCTs, case series, case reports, and crossover trials. The inclusion of both primary and secondary studies introduced the issue of evidence overlapping, which could amplify the results of primary older studies; a way to overcome this issue is to weigh single studies (considering their effect and sample sizes).

We are confident that the synthesis produced might help clinicians, researchers, and all rehabilitation stakeholders to address the better use of RAT in the context of the IRP, to guide the allocation of resources and define clinical protocols and indications for managing patients with different neurological health conditions.[20-23]

Conclusions

We synthetized available evidence on the effectiveness of RAT in neurological health conditions with the purpose to guide experts' decisions during the Consensus Conference. The methodological approach used had the scope to be as much inclusive as possible without neglecting the quality assessment of available evidence and pointing out literature gaps. This approach might represent a good example in all those cases where there is a discrepancy between the diffusion of the intervention and available literature supporting its use. The results of our literature search are[23] or will be published as well as the final results of the Consensus Conference to assist the different stakeholders to answer the still open questions on the effectiveness of robotics in neurological health conditions.

REFERENCES

1. Morris JH, van Wijck F, Joice S, Donaghy M. Predicting health related quality of life 6 months after stroke: the role of anxiety and upper limb dysfunction. Disabil Rehabil. 2013 Feb;35(4):291-9.
2. Kwakkel G. Impact of intensity of practice after stroke: issues for consideration. Disabil Rehabil. 2006 Jul 15-30;28(13-14):823-30.
3. Hesse S, Heß A, Werner C C, Kabbert N, Buschfort R. Effect on arm function and cost of robot-assisted group therapy in subacute patients with stroke and a moderately to severely affected arm: a randomized controlled trial. Clin Rehabil. 2014 Jul;28(7):637-47.
4. Poli P, Morone G, Rosati G, Masiero S. Robotic technologies and rehabilitation: new tools for stroke patients' therapy. Biomed Res Int. 2013;2013:153872.
5. Boldrini P, Bonaiuti D, Mazzoleni S, Posteraro F. Rehabilitation assisted by robotic and electromechanical devices for persons with neurological disabilities: an Italian consensus conference. Funct Neurol. 2019 Apr/Jun;34(2):123-124.
6. Morone G, Cocchi I, Paolucci S, Iosa M. Robot-assisted therapy for arm recovery for stroke patients: state of the art and clinical implication. Expert Rev Med Devices. 2020 Mar;17(3):223-233.
7. World Health Organization. International classification of functioning, disability and health: ICF. World Health Organization, 2001. https://apps.who.int/iris/handle/10665/42407 [accessed on March 25, 2021]
8. Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W, Robinson N. Lost in knowledge translation: time for a map? J Contin Educ Health Prof. 2006 Winter;26(1):13-24.
9. Burridge JH, Hughes AM. Potential for new technologies in clinical practice. Curr Opin Neurol. 2010 Dec;23(6):671-7.

10. Butler D. Translational research: crossing the valley of death. Nature News, 2008, 453.7197: 840-842.

11. Candiani, G., Colombo, C., Daghini, R., Magrini, N., Mosconi, P., Nonino, F., Satolli, R. Come organizzare una conferenza di consenso. Manuale metodologico, 2009.

12. Lexell J, Brogårdh C. The use of ICF in the neurorehabilitation process. NeuroRehabilitation. 2015;36(1):5-9.

13. Sivan M, ’O’Connor RJ, Makower S, Levesley M, Bhakta B. Systematic review of outcome measures used in the evaluation of robot-assisted upper limb exercise in stroke. J Rehabil Med. 2011 Feb;43(3):181-9.

14. Stucki G, Kostanjsek N, Ustün B, Cieza A. ICF-based classification and measurement of functioning. Eur J Phys Rehabil Med. 2008;44(3):315-328.

15. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther. 2003 Aug;83(8):713-21.

16. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include zrandomized or non-zrandomized studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.

17. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE Next Steps Consortium. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ. 2010 Dec 14;182(18):E839-42.

18. OCEBM Levels of Evidence Working Group*. “The Oxford 2011 Levels of Evidence”. Oxford Centre for Evidence-Based Medicine. [Last accessed 2021 Mar 21]. Available from: http://www.cebm.net/index.aspx?o=5653

19. Zampolini M, Stucki G, Giustini A, Negrini S. The individual rehabilitation project: a model to strengthen clinical rehabilitation in health systems worldwide. Eur J Phys Rehabil Med. 2020 Feb;56(1):1-4.

20. Morone G, Masiero S, Coiro P, De Angelis D, Venturiero V, Paolucci S, Iosa M. Clinical features of patients who might benefit more from walking robotic training. Restor Neurol Neurosci. 2018;36(2):293-299.

21. Duret C, Hutin E, Lehenaff L, Gracies JM. Do all sub acute stroke patients benefit from robot-assisted therapy? A retrospective study. Restor Neurol Neurosci. 2015;33(1):57-65.

22. Padua L, Imbimbo I, Aprile I, Loreti C, Germanotta M, Coraci D, et al. FDG Robotic Rehabilitation Group†. Cognitive reserve as a useful variable to address robotic or conventional upper limb rehabilitation treatment after stroke: a multicentre study of the Fondazione Don Carlo Gnocchi. Eur J Neurol. 2020 Feb;27(2):392-398.

23. Morone G, Palomba A, Martino Cinnera A, Agostini M, Aprile I, Arienti C, et al. Systematic review of guidelines to identify recommendations for upper limb robotic rehabilitation after stroke. Eur J Phys Rehabil Med. 2021 Jan 25.

Acknowledgements.— The present study has been carried out within the framework of the Italian Consensus Conference on “Rehabilitation assisted by robotic and electromechanical devices for persons with disability of neurological origin” (CICERONE), promoted by the Italian Society of Physical and Rehabilitation Medicine (SIMFER, Società Italiana di Medicina Fisica e Riabilitativa) and Italian Society of Neurological Rehabilitation (SIRN, Società Italiana di Riabilitazione Neurologica) (2019-2021).

Conflicts of interest.— The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Funding.— The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

Authors' contributions.— Francesca Gimigliano, Chiara Arienti, Angela Palomba, Sofia Straudi, and Giovanni Morone conceptualized paper, performed and/or supervise research; Francesca Gimigliano, Angela Palomba, Sofia Straudi, and Giovanni Morone drafted manuscript; Paolo Benanti, Paolo Boldrini, Donatella Bonaiuti, Enrico Castelli, Francesco Draicchio, Vincenzo Falabella, Silvia Galeri, Mauro Grigioni, Stefano Mazzoleni, Stefano Mazzon, Franco Molteni, Maurizio Petrarca, Alessandro Picelli, Federico Posteraro, Michele Senatore, and Giuseppe Turchetti, as organization committee and scientific technical committee of the CICERONE consensus conference supervise research, read and correct manuscript; Luca Perrero, Michela Agostini, Irene Aprile, Matteo Paci, Emanuela Casanova, Dario Marino, Giuseppe La Rosa, Federica Bressi, Silvia Sterzi, Daniele Giansanti, Alberto Battistini, Sandra Miccinilli, Serena Filoni, Monica Sicari, Salvatore Petrozzino, Claudio Marcello Solaro, and Stefano Gargano read and correct manuscript. All authors read and approved the final version of the manuscript.

Group name— Upper limb working group within the "Italian Consensus Conference on rehabilitation assisted by robotic and electromechanical devices for persons with disability of neurological origin" (CICERONE): Michela AGOSTINI (San Camillo IRCCS, Venice, Italy); Irene APRILE (IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy); Ludovica BALUARDO (Ferrara University Hospital, Neuroscience and Rehabilitation Department, Ferrara, Italy); Alberto BATTISTINI (IRCCS Istituto delle Scienze Neurologiche di Bologna, UOC Medicina Riabilitativa e Neuroriabilitazione, Bologna, Italia); Paolo BENANTI (Pontifical Gregorian University, Rome, Italy); Valentina BOETTO (Università degli studi di Torino); Paolo BOLDRINI (Società Italiana di Medicina Fisica e Riabilitativa, SIMFER); Donatella BONAIUTI (Istituto Geriatrico Piero Redaelli, Milan, Italy); Marco BRAVI (Biomedical Campus University Foundation, Rome, Italy); Federica BRESSI (Biomedical Campus University Foundation, Rome, Italy); Diletta BRUNO (Biomedical Campus University Foundation, Rome, Italy); Emanuela CASANOVA (IRCCS Istituto delle Scienze Neurologiche di Bologna, UOC Medicina Riabilitativa e Neuroriabilitazione, Bologna, Italia); Enrico CASTELLI (Paediatric Neurorehabilitation, Bambino Gesù Children's Hospital, Rome, Italy); Manuela DESILVESTRI (Neurorehabilitation Unit, Azienda Ospedaliera SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy, EU); Francesco DRAICCHIO (Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, INAIL, Monte Porzio Catone, 00185 Rome, Italy); Vincenzo FALABELLA (President Italian Federation of Persons with Spinal Cord Injuries (Faip Onlus), Rome, Italy); Serena FILONI (Padre Pio Foundation and Rehabilitation Centers, San Giovanni Rotondo, Italy); Silvia GALERI (IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy); Marialuisa GANDOLFI (Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy); Stefano GARGANO (Fondazione Don Carlo Gnocchi - Torino); Daniele GIANSANTI (National Center for Innovative Technologies in Public Health, Italian National Institute of Health, Rome, Italy); Francesca GIMIGLIANO (Department of Mental and Physical Health and Preventive Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy); Mauro GRIGIONI (National Center for Innovative Technologies in Public Health, Italian National Institute of Health, Rome, Italy); Giuseppe LA ROSA (C.S.R. - Consorzio Siciliano di Riabilitazione, Catania, Italy); Dario MARINO (IRCCS Neurolysis Center "Bonino Pulejo", Messina, Italy); Alex MARTINO CINNERA (Santa Lucia Foundation, IRCCS, Rome, Italy); Stefano MAZZOLENI (Department of Electrical and Information Engineering, Politecnico di Bari, Italy); Stefano MAZZON (AULSS6 (Unique Sanitary Local Company) Euganea Padova - Rehabilitation

Department); Sandra MICCINILLI (Biomedical Campus University Foundation, Rome, Italy); Franco MOLTENI (Villa Beretta, Costa Masnaga, Italy); Giovanni MORONE (Santa Lucia Foundation, IRCCS, Rome, Italy); Matteo PACI (AUSL (Unique Sanitary Local Company) District of Central Tuscany, Florence, Italy); Angela PALOMBA (Multidisciplinary Department of Medicine for Surgery and Orthodontics, University of Campania "Luigi Vanvitelli", Naples, Italy); Cristiano PECCHIOLI (Fondazione Don Carlo Gnocchi, Roma); Luca PERRERO (Neurorehabilitation Unit, Azienda Ospedaliera SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy, EU); Maurizio PETRARCA ("Bambino Gesù" Children's Hospital – IRCCS, Movement Analysis and Robotics Laboratory MARlab, Rome, Italy); Salvatore PETROZZINO (A.O.U. Città della Salute e della Scienza di Torino); Alessandro PICELLI (Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy); Federico POSTERARO (Versilia Hospital AUSL Toscana Nord Ovest, Italy); Emanuele Francesco RUSSO (Padre Pio Foundation and Rehabilitation Centers, San Giovanni Rotondo, Italy); Fabio SANTACATERINA (Biomedical Campus University Foundation, Rome, Italy); Michele SENATORE (Presidente AITO (Associazione Italiana Terapisti Occupazionali)); Monica SICARI (A.O.U. Città della Salute e della Scienza di Torino); Claudio Marcello SOLARO (CRRF "Mons. Luigi Novarese" Moncrivello, VC, Italy); Silvia STERZI (Biomedical Campus University Foundation, Rome, Italy); Sofia STRAUDI (Ferrara University Hospital, Neuroscience and Rehabilitation Department, Ferrara, Italy); Giuseppe TURCHETTI (Management Institute, Sant'Anna School of Advanced Studies, Pisa, Italy).

TABLES

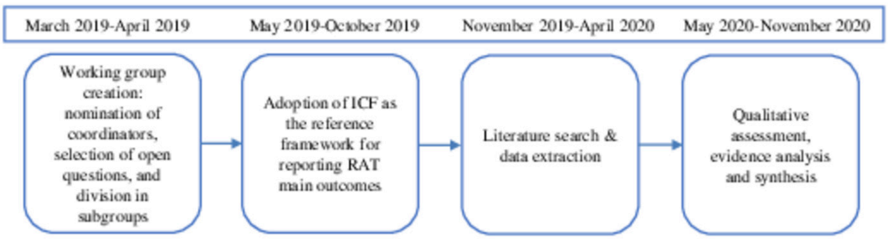
Table I.— *Box 1: Research questions*

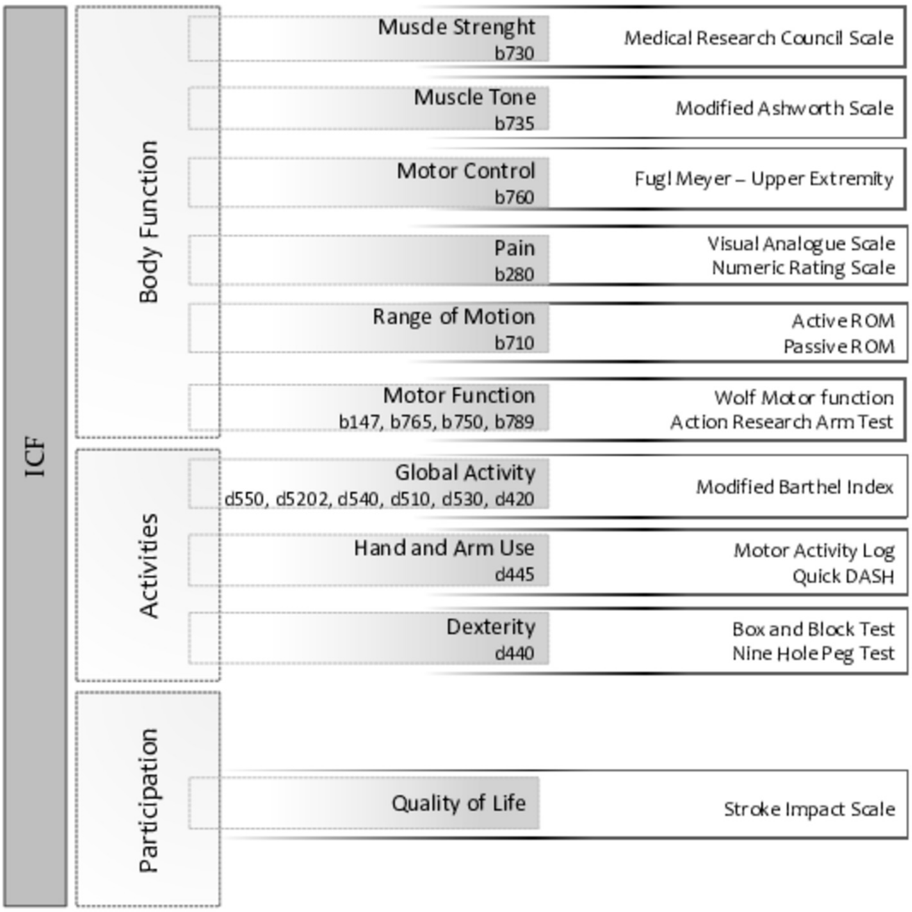
1. Which are the effects of upper limb robotic therapy in people with stroke?	*a. Considering different types of robotic devices (exoskeletons, end-effectors and hand devices)*
	b. Considering the use of robotic and electromechanical devices for upper limb in acute/subacute and chronic phase of stroke
2. Which are the effects of upper limb robotic therapy in people with neurological health conditions other than stroke?	

TITLES OF FIGURES

Figure 1.— *Upper Limb Functioning Working Group timeline*

Figure 2.— *Graphical categorization of clinical outcomes in robotic rehabilitation according to the International Classification of Functioning, Disability and Health (ICF)*


March 2019-April 2019
May 2019-October 2019
November 2019-April 2020
May 2020-November 2020
Working group creation: nomination of coordinators, selection of open questions, and division in subgroups
Adoption of ICF as the reference framework for reporting RAT main outcomes
Literature search & data extraction
Qualitative assessment, evidence analysis and synthesis


ICF
Body Function
Muscle Strenght
b730
Medical Research Council Scale
Muscle Tone
b735
Modified Ashworth Scale
Motor Control
b760
Fugl Meyer – Upper Extremity
Pain
b280
Visual Analogue Scale
Numeric Rating Scale
Range of Motion
b710
Active ROM
Passive ROM
Motor Function
b147, b765, b750, b789
Wolf Motor function
Action Research Arm Test
Activities
Global Activity
d550, d5202, d540, d510, d530, d420
Modified Barthel Index
Hand and Arm Use
d445
Motor Activity Log
Quick DASH
Dexterity
d440
Box and Block Test
Nine Hole Peg Test
Participation
Quality of Life
Stroke Impact Scale

Supplementary Digital Material

Download supplementary material file: Eur J Phys Rehabil Med-7011_Supplementary Digital Material1_V1_2021-04-15.docx