Ann Ist Super Sanità 2025 | Vol. 61, No. 3

Annali
dell'Istituto Superiore di Sanità
A SCIENCE JOURNAL FOR PUBLIC HEALTH

Publication
Annali dell'Istituto Superiore di Sanità is published quarterly and in special issues.
Freely available online at www.iss.it/annali - https://annali.iss.it

Annali dell'Istituto Superiore di Sanità is indexed in
- CAB
- CHEMABS
- EMBASE/Excerpta Medica
- FSTA
- MEDLINE
- ProQuest
- SCOPUS
- WEB OF SCIENCE

The Journal Impact Factor is 1.7

Annali Editorial Office
Scientific Communication Service
Istituto Superiore di Sanità
Viale Regina Elena 299, 00161 Rome, Italy
Tel.: +39 06 49902945 Fax: +39 06 49902253
E-mail: annali@iss.it
www.iss.it/annali - https://annali.iss.it

Papers to be presented for publication should be submitted online to https://annali.iss.it

Instructions to Authors are available online at https://annali.iss.it

Publishing support
Il Pensiero Scientifico Editore, Rome
Via San Giovanni Valdarno 8, 00138 Rome, Italy
www.pensiero.it

Subscription information & terms
The journal is freely available online.
For printed copies of the journal contact:
Il Pensiero Scientifico Editore
Tel.: +39 06 86282324 Fax: 06 86282250
E-mail: abbonamenti@pensiero.it

Year 2025
Italy individual print subscription € 57,00 | Italy institutional print subscription € 67,00.
Other countries € 67,00
Each quarterly print issue € 21,00

ISSN 0021-2571 (print), 2384-8553 (online)
Coden: AISSAW 61 (No. 3)

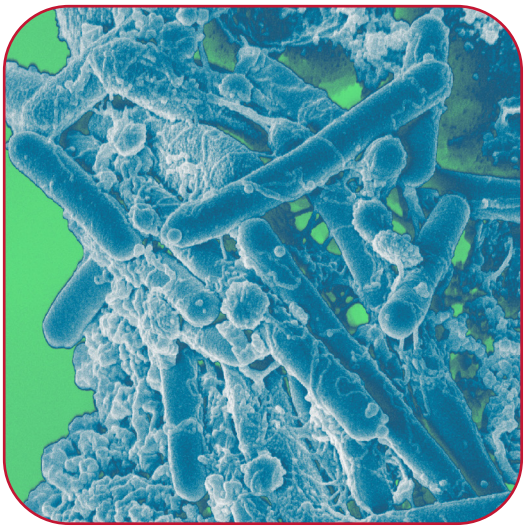
Reg. Stampa - Tribunale di Roma, n. 482 del 29 ottobre 1985 (cartaceo); n. 121 del 16 maggio 2014 (online

Printed in September 2025 by Ti Printing s.r.l.
Via Case Rosse 23, 00131 Rome, Italy

Ann Ist Super Sanità 2025 | Vol. 61, No. 3

Annali
dell'Istituto Superiore di Sanità
A SCIENCE JOURNAL FOR PUBLIC HEALTH

The cover image shows a biofilm detail of Clostridium sporogenes bacterial cells by high resolution scanning electron microscopy. The image is provided by the Microscopy Area, Core Facilities, Istituto Superiore di Sanità, Rome, Italy



ANNALI
dell'Istituto Superiore di Sanità

Vol. 61, No. 3 2025

Contents

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 161-162
DOI: 10.4415/ANN_24_03_01

COMMENTARY
"Undiagnosed" severe disease pseudo-outbreaks in Sub-Saharan Africa: a paradigm of syndemic events

Giovanni Rezza[1] and Marco de Feo[2,3]

[1]*Facoltà di Medicina e Chirurgia, Università Vita-Salute San Raffaele, Milan, Italy*
[2]*Laboratorio di Oncologia Molecolare, Istituto Dermopatico dell'Immacolata, IDI-IRCCS, Rome, Italy*
[3]*Saint Mary's Hospital Lacor, Gulu, Uganda*

Abstract
Several outbreaks of undiagnosed severe disease occurred in the Democratic Republic of Congo over the last year. Although this is not completely unusual, at least one of them raised an international concern until the determinants of the excess death were identified. Far from representing a real threat for people living in wealthy countries, most of these events are context related, and mainly due to a combination of poverty-related conditions, such as malnutrition, historic plagues like malaria, and vulnerability to common respiratory infections. Even though these syndemic events remain usually restricted to well defined geographical areas affected by poor resources, they merit attention since they represent an opportunity to improve health conditions in remote areas and a challenge to strengthen global preparedness against pandemic events.

Key words
- global health
- pandemics
- syndemic events
- tropical diseases
- preparedness

The occurrence of a high number of cases of a severe respiratory disease in the health zone of Panzi, Kwango province of Democratic Republic of Congo (DRC) at the end of last year, raised concern at international level. On December 8, 2024, the World Health Organization released a "Disease Outbreak News" reporting 406 cases with 31 deaths occurred between October 24 and December 5 of an undiagnosed disease characterized by fever, headache, cough, runny nose, and body aches; all severe cases were malnourished, the majority of them children, particularly under 5 years old [1]. The number of cases increased to 891 with 48 deaths (case-fatality rate: 5.4%) by December 16. Difficulty in breathing, anaemia, and severe malnutrition were associated with death. Although an increase in the number of cases is not considered to be unusual at the start of the rainy season, the observed number of deaths was higher than expected. This finding triggered the alert, which was amplified by the possibility that the outbreak might be due to an unknown – newly introduced – pathogen. However, laboratory results showed high levels of positivity to malaria and to common respiratory viruses, in particular influenza A (H1N1, pdm 09) and, to a lesser extent, rhinoviruses and SARS-CoV-2 [2].

The area affected by the "outbreak" was rural and remote, being sited at least 700 km (about 48 hours by road) away from Kinshasa. Although laboratory findings, showing the presence of common pathogens, were reassuring for the rest of the world, this event should not be neglected only because restricted to a context characterized by poor resources, low vaccine coverage, and difficult access to health services.

Actually, the Panzi event fits the classical criteria of a "syndemic", a term firstly used by Singer in the mid-90s and then applied to the COVID-19 synergistic global epidemic [3, 4]. A syndemic occurs when two or more diseases or health conditions cluster and interact within a population because of social and structural factors and inequities, leading to an excess burden of disease and/or mortality, and continuing health disparities [5]. The term "syndemic" perfectly applies to the Panzi "outbreak", where the excess mortality was due to the co-circulation of common respiratory viruses, in presence of severe malaria, and in the context of severe malnutrition.

On February 2025, a similar event occurred in the Equateur Province of DRC, with 53 deaths reported in Basankusu Health Zone, following a small cluster of 8 deaths occurred in the Balomba Health Zone in

Address for correspondence: Giovanni Rezza, Facoltà di Medicina, Università Vita-Salute San Raffaele, Via Olgettina 60, 20132 Milan, Italy. E-mail: rezza.giovanni@hsr.it.

January [6]. However, the excess death number rapidly decreased, and preliminary findings suggested the co-occurrence of several febrile illnesses in a hyperendemic area for malaria. Thus, also this event may be considered a pseudo-outbreak related to a context with underlying predisposing conditions due to the presence of high number of vulnerable individuals affected by common ailments of different nature.

The evidence that underlying conditions and poor-resource context play an important role in determining the occurrence of unusual clinical conditions which may be considered context-specific comes from the observation, once again in central African countries, of a high incidence of fibro-osseous odontogenic tumors, which are found exclusively in rural populations. These communities are characterized by cyclical nutritional deficiencies, environmental climate changes, extreme poverty, and malnutrition. They are often forced to rely on small wild animals, such as rats and bats, for food, and to drink water contaminated with the feces and urine of the same animals. This might increase the risk of infection with Lassa-like arenaviruses, that are commonly detected in odontogenic tumor specimens from children living in some remote areas of central Africa, and might be involved in their pathogenesis [7, 8].

Far for representing real pandemic threats or real menaces for people living in industrialized countries, the pseudo-outbreaks occurred in Panzi and in the Equateur Province of RDC, as well as other geographically restricted clinical entities, should not be downgraded to trivial local events. In fact, high population vulnerability and difficult access to diagnosis and care could affect the response to epidemic events. For this reason, they should be considered paradigmatic global health problems which necessitate adequate response. Although funding restrictions are currently affecting international organizations, financial and human resources to be mobilized in order to fit sustainable development goals in remote areas located in poor resources countries.

Conflict of interest statement

The Authors declare that there are no conflicts of interest.

Received on 7 June 2025.
Accepted on 7 July 2025.

REFERENCES

1. World Health Organization. Undiagnosed disease - Democratic Republic of the Congo. Disease Outbreak News. WHO; 2024. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON546.
2. World Health Organization. Acute respiratory infections complicated by malaria (previously undiagnosed disease) - Democratic Republic of the Congo. Disease Outbreak News. WHO; 2024. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON547.
3. Singer M, Bulled N, Ostrach B, Mendenhall E. Syndemics and the biosocial cnception of health. Lancet. 2017; 389(10072):941-50. doi: 10.1016/S0140-6736(17)30003-X
4. Horton R. Offline: COVID-19 is not a pandemic. Lancet. 2020;396(10255):874. doi: 10.1016/S0140-6736(20)32000-6
5. US Department of Health and Human Services. HIV.gov. Blog. Available from: https://www.hiv.gov.
6. World Health Organization. Cluster of community deaths in Basankusu. Equateur-Democratic Republic of the Congo. Disease Oubreak News. WHO; 2025. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2025-DON557.
7. de Feo M, De Leo C, Romeo U, Muti P, Blandino G, Di Agostino S. Arenavirus as a poten-tial etiological agent of odontogenic tumours in humans. J Exp Clin Cancer Res. 2020;39(1):34. doi: 10.1186/s13046-020-1540-1
8. de Feo M, Dilu Tamba F, Makaka Mutondo A, Kashitu Mujinga G, Odong OS, Castellani C, Pavesi L, Mpingabo PI, Ahuka-Mundeke S, Di Agostino S. Detection of the Lassa virus in a group of odontogenic bone tumor tissues. Anatomia. 2024;3(2):57-67. doi: 10.3390/anatomia3020006

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 163-172
DOI: 10.4415/ANN_25_03_02

Dietary supplements for human health. What do we really know? A systematic review of umbrella reviews

Eugenia Piragine[1,*], Marco Andrea Malanima[2,*], Vincenzo Calderone[1], Salvatore De Masi[3], Carla Ghelardini[4], Alessandro Mugelli[4] and Ersilia Lucenteforte[5]

[1]*Dipartimento di Farmacia, Università di Pisa, Pisa, Italy*
[2]*Dipartimento di Medicina Clinica e Sperimentale, Unità di Statistica Medica, Università di Pisa, Pisa, Italy*
[3]*Clinical Trial Center (CTC), Azienda Ospedaliera Universitaria Careggi, Florence, Italy*
[4]*Dipartimento di Neuroscienze, Psicologia, Area del Farmaco e Salute del Bambino (NEUROFARBA), Sezione di Farmacologia e Tossicologia, Università degli Studi di Firenze, Florence, Italy*
[5]*Dipartimento di Statistica, Informatica, Applicazioni "G. Parenti", Università degli Studi di Firenze, Florence, Italy*
**These Authors contributed equally to this work*

Abstract

Background and objective. The potential benefits of dietary supplements for human health have been known since ancient times, but high-quality evidence on their efficacy is lacking. Furthermore, the overwhelming amount of available studies contributes to the vagueness of this topic. The aim of this systematic review was to summarize the evidence on the health benefits of dietary supplements.

Methods. A Medline search (via PubMed) was performed.

Results. 62 umbrella reviews (also known as reviews of reviews) were retrieved. Most of the results/findings (41.3%) suggested potential beneficial effects of dietary supplements on human health, but with low to very low certainty of evidence. Twenty results/findings (26.7%) supported the efficacy of dietary supplements in improving biochemical parameters and preserving human health, with moderate to high certainty of evidence. All other studies showed uncertain/conflicting results or inefficacy.

Conclusions. The demonstration of the beneficial properties of dietary supplements is far from conclusive and high-quality studies are needed.

Key words

- dietary supplements
- natural products
- efficacy
- review of reviews
- umbrella reviews

INTRODUCTION

Dietary supplements (or food supplements) are defined by the US Food and Drug Administration (FDA) as "vitamins, minerals, herbs or other botanicals, amino acids or other dietary substances to be used to supplement the diet" [1], and by the Directive 2002/46/EC of the European Parliament and the Council as "concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form (such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders) designed to be taken in measured small unit quantities" [2-4]. Although they have only been regulated for a few decades, the potential effects of minerals, vitamins, and botanicals on human health have been known since ancient times [5]. One of the earliest documents on "phytotherapy", known as the Egyptian "Ebers papyrus", dates to 2900 BC and includes more than 700 plant-based health remedies, such as onion, garlic, and pomegranate [6, 7]. In 2600 BC, an additional "list" of natural products with potential benefits for human health was represented in cuneiform on clay tablets by an unknown scholar from Mesopotamia [6]. A few centuries later, the Greeks and Romans used "medicinal herbs" to treat seasonal ailments, respiratory disorders, headaches, heartburn, and a wide plethora of "minor" conditions (e.g., wounds and burns) [6, 7]. The "cult" of natural products in the Middle Ages was preserved in the monasteries of Germany, England, France, and Ireland and was gradually enriched with Chinese, American and Indian herbs by the Arabs, Marco Polo and Vasco Da Gama [6, 7]. Until the isolation of alkaloids from pomegranate, ipecacu-

Address for correspondence: Ersilia Lucenteforte, Dipartimento di Statistica, Informatica, Applicazioni "G. Parenti", Università degli Studi di Firenze, Viale Morgagni 59, 50134 Florence, Italy. E-mail: ersilia.lucenteforte@unifi.it.

anha, and poppy in the early 19th century, which opened the new era of "medicinal chemistry", the use of natural products remained the only remedy for the prevention and treatment of many diseases [5, 8]. However, the advent of pharmaceutical sciences did not spell the demise of phytotherapy. In fact, many drugs currently used in clinical practice are directly isolated from plants (e.g., paclitaxel and morphine) [9], and natural products are widely used as "alternative" medicines, although their efficacy is mainly based on traditional or folk use. In recent decades, the concept of "rational phytotherapy", based on the identification and study of specific active components from plants, has been introduced [7], but this has led to a confusing scenario. Indeed, there is an impressive number of preclinical and clinical studies evaluating the pharmacological value of plant-derived compounds, but they are very heterogeneous in terms of animals/population selected, choice of intervention, dosage, follow-up period and results. The lack of rigorous studies on the ability of vitamins and minerals to maintain, support, or optimize physiological functions also represents a limitation. These supplements can correct deficiencies and contribute to general homeostasis (e.g., vitamin C for scurvy, vitamin D and calcium for bone metabolism, vitamin K for bleeding disorders) [2, 10]. However, over-the-counter products are often used by individuals without signs and symptoms of deficiency, especially in Europe and North America, despite the lack of conclusive evidence regarding their role in supporting physiological balance in such population [10-12]. Thus, there is a kind of "boilerplate" that does not allow us to understand the role of dietary supplements in the "real world" context. The aim of this systematic review of umbrella reviews is to summarize what is known and highlight what is missing regarding the health benefits of dietary supplements, to shed light on this controversial and debated field.

MATERIALS AND METHODS

Study identification and selection

We launched the search string on Medline on June 1st, 2023. Therefore, data on studies published in 2023 are not complete. Our goal was to set up a search strategy to identify reviews of reviews (also known as umbrella reviews) investigating the effects of dietary supplements on human health. We combined search queries containing terms as "food", "dietary", "herbal", "nutritional", "nutraceutical", "natural" as well as "supplements", "remedies", "substances", "ingredients", "dietary supplements" (and related terms), "phytotherapy" using the Boolean operators "AND" and "OR". Filters to identify only studies conducted on humans and written in English were applied (for further detail on search strategy see *Table S1 available online as Supplementary Materials*).

We carried out duplicates detection and the whole screening process of titles and abstracts using the Rayyan tool [13]. The screening was independently carried out by three Authors (EP, MAM and EL).

After duplicates removal, we identified additional studies conducted on animals that had not yet been excluded by applying the previous filters. In particular, records containing terms that referred to studies not conducted on humans in the title such as "animal", "mice", "rat", "murine", "rodents", "rodent", "rabbit", "piglets", "canine", "broiler" were removed.

Then we selected only those records containing keywords such as "meta-analysis", "meta-analyses", "review", "reviews", "systematic review" in the title. Further screening was carried out using other keywords as "umbrella review", "overview of evidence", "overview of reviews", "overview of systematic reviews", "review of reviews", "review of evidence", "review of meta-analyses", "summary of evidence" and "summary of systematic reviews" to obtain the final set of studies assessed for eligibility.

Three Authors (EP, MAM and EL) checked the abstracts of potentially includible umbrella reviews and excluded those that did not fulfill the inclusion criteria.

Inclusion criteria

The inclusion criteria were formulated according to the Population, Intervention, Control, Outcome, and Study design (PICOS) framework.

Population (P): healthy subjects or patients with various types of disease, of any age group, including children, adults, or pregnant women. Umbrella reviews were also included when the population was unspecified, provided it was clear that only human studies were considered. Intervention (I): dietary supplements, regardless of dosage form and route of administration. Control (C): not required. Outcome (O): any effects on human health. Study design (S): umbrella reviews.

Exclusion criteria

We excluded articles that were not umbrella reviews, did not investigate dietary supplements, or did not directly evaluate health outcomes.

Data extraction from the umbrella reviews

For each umbrella review included, we extracted the following information, if reported: number of reviews included classified by type (i.e., systematic review, systematic review with meta-analysis, meta-analysis only); total number of primary studies included or descriptive statistics (mean and standard deviation or median and range) on the number of primary studies in each included review; study design of the primary studies; total number of patients included or descriptive statistics (as above) on the number of patients in each included review; characteristics of the population.

For each umbrella review, a summary of the main results was also provided and, if available, the level of certainty of the conclusions (high/moderate certainty, low certainty, inconclusive) was reported.

Data collection was carried out by two Authors (EP and MAM), using the spreadsheet software Microsoft Excel. Any discrepancies were discussed with a third Reviewer (EL).

RESULTS AND DISCUSSION

Identification and selection of umbrella reviews

Overall, 124,298 records were identified via Medline. After duplicates removal, 121,360 records were selected and screened. Among the 106,313 studies on hu-

mans, 7,105 reviews and meta-analyses were identified. Of them, 122 were finally assessed for eligibility. 62 umbrella reviews were included according to the defined exclusion criteria and 60 were excluded. The complete workflow leading to the inclusion of 62 studies is summarized in the flow chart (*Figure 1*).

The identified records were then plotted by year of publication, considering all the 121,360 non-duplicated records selected in Medline (*Figure 2a*).

Studies directly investigating or summarizing evidence on the effects of the consumption of different dietary supplements on human health have been published since 1945. The number of published papers per year shows little increase for some decades and then around the beginning of the last century an exponential growth starts, with the highest number registered to date during 2021 (9,174 studies).

All the 121,360 identified records were also grouped by the country of publication of the study, which is intended as the authors' affiliation declared country. In case of affiliations belonging to different countries in one paper, each country is counted as 1. The leading publishing country is USA, followed by China and UK (*Figure 2b*).

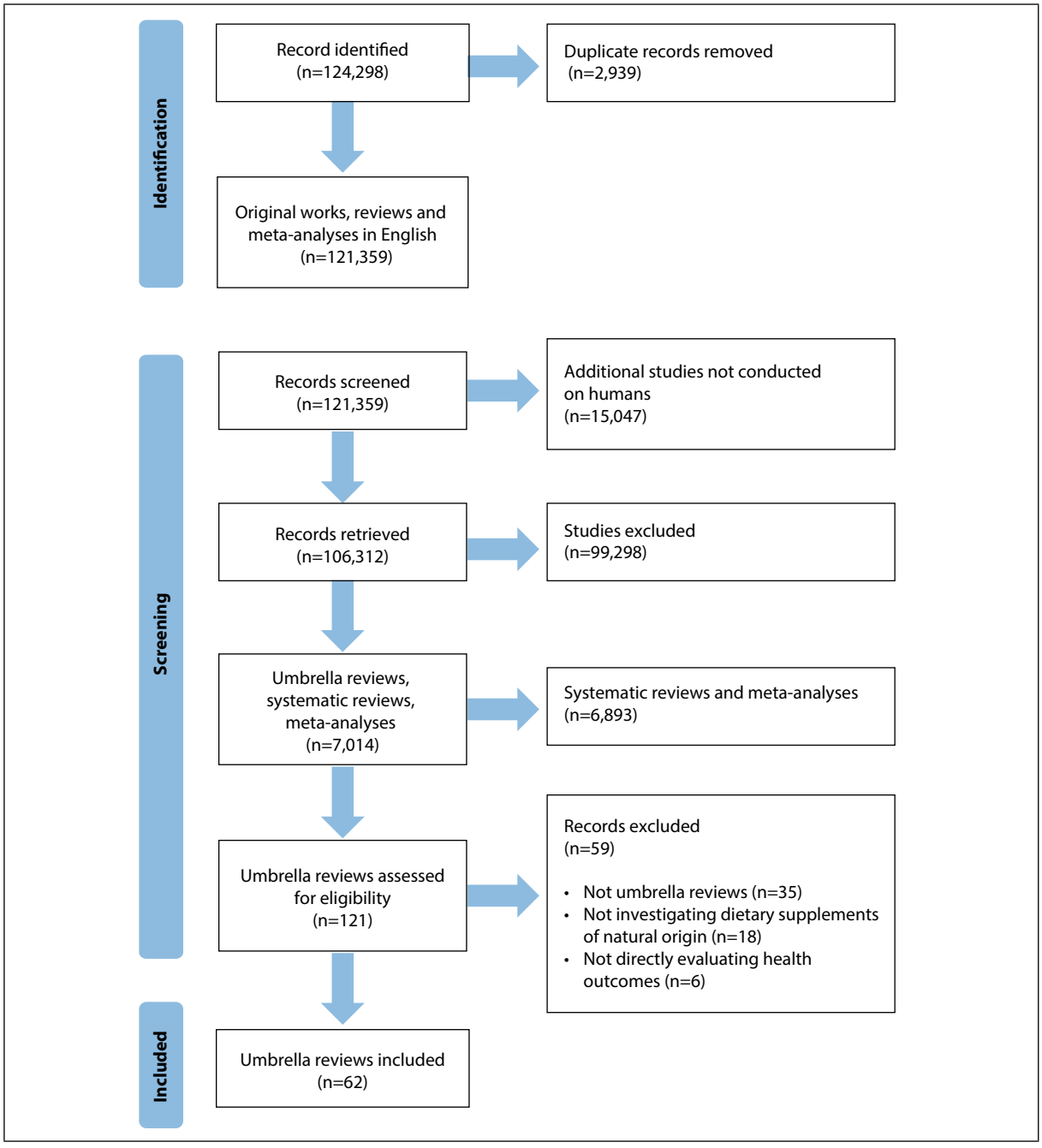


Figure 1
Flow chart of search.

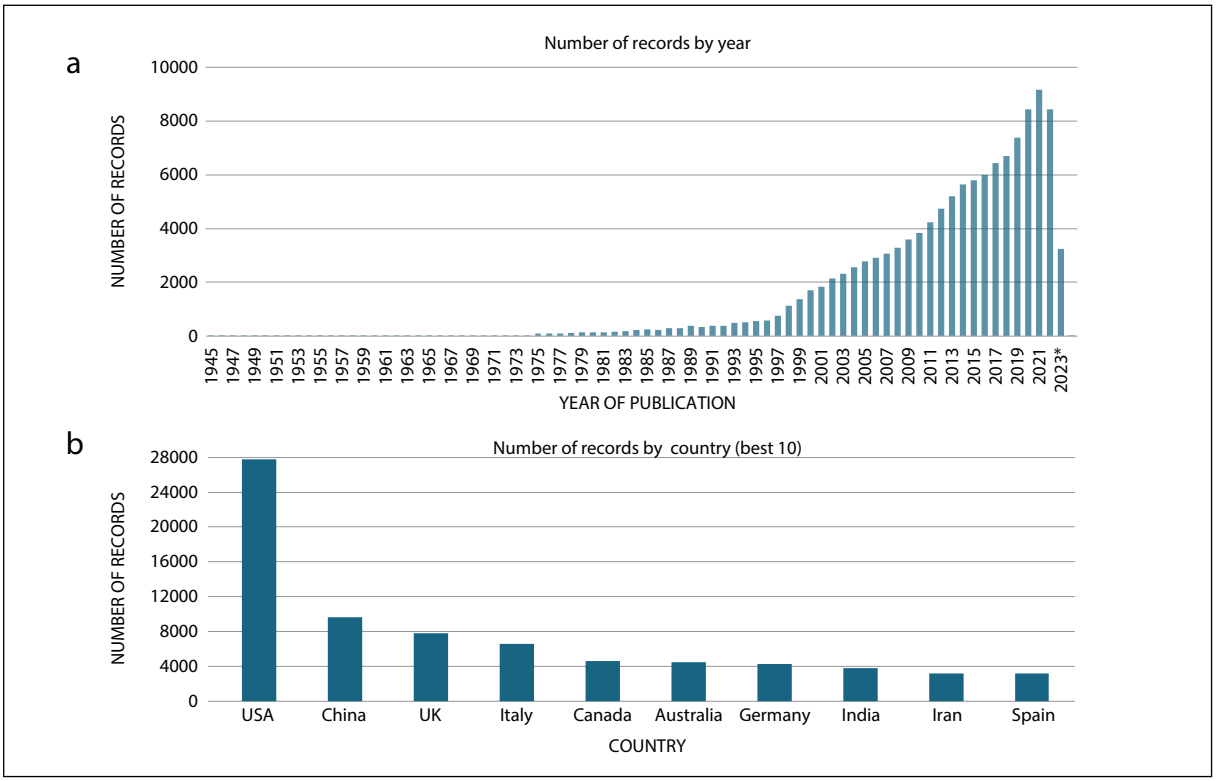


Figure 2
a) Number of non-duplicated records identified on Medline, by year of publication; b) number of non-duplicated records identified on Medline ranked by the best 10 countries of publication.

Figure 3a shows the 7,015 systematic reviews and meta-analyses (including umbrella reviews) obtained during the screening process.

Studies resuming the evidence of the effects of the consumption of different dietary supplements on human health have been published since 1976.

The trend is similar to that illustrated in *Figure 2a*. In fact, the number of published systematic reviews is steady until the beginning of the last century, then an exponential increase is observed with the highest number of published systematic reviews to date in 2021 (1,008).

The same 7,015 records were also plotted by country of publication, which is extracted from authors' affiliation country. As above, in case of authors' affiliations belonging to different countries in one paper, each country is counted as 1 (*Figure 3b*). The leading publishing country is China, followed by USA and Iran.

The number of published umbrella reviews over the years was plotted considering only the 62 records included (*Figure 4*). Umbrella reviews on the effects of the consumption of different dietary supplements have been published since 2011. In particular, an increasing publishing trend seems to be observed since 2018, with the highest number reached in 2022 (21 studies).

Systematic review

Table 1 summarizes the general characteristics of the included reviews. Twenty-four (35.8%) were reviews of systematic reviews (SRs) [14-37], 19 (28.4%) were reviews of meta-analysis (MA) [38-57], 21 (31.3%) were reviews of SRs with MA [14, 15, 19, 58-75], and 3 (4.5%) were i) reviews of Mendelian randomisation studies and SRs [23], ii) reviews of MA and umbrella reviews [39], or iii) reviews of Mendelian randomisation studies and MA [45] (some umbrella reviews included more than one type of review). The number of studies on dietary supplements included in each review ranged from one to 289, and the interventions were very heterogeneous. In fact, forty-six reviews focused on the effects of vitamins [16, 17, 21, 23-25, 28, 29, 32-34, 39, 41, 44-46, 49, 55, 57, 59-61, 65, 68, 71, 73], 21 of minerals [24, 28, 32, 34, 36, 39, 41, 47, 60, 67, 72], 11 of omega-3 fatty acids [17, 21, 24, 39, 42, 44, 46, 47, 52, 56, 62], 10 of prebiotics/postbiotics/synbiotics [17, 18, 26, 27, 38, 39, 46, 48, 53, 74], 10 of proteins and amino acids [15, 17, 19, 29, 35, 69], one of lipid-based nutrients [44], 28 of others interventions/supplements (e.g., curcumin [30, 46, 51, 64], *Camellia sinensis* L. – green tea [31, 64, 66, 67], coenzyme Q10 [20, 24], unspecified antioxidants [21, 63], polyphenols [39, 54], *Allium sativum* L. (garlic) [31, 50]). Some reviews have focused on more than one dietary supplement.

Details on the characteristics of each study are given in *Table S2 available online as Supplementary Materials*. Overall, the population was highly heterogeneous, ranging from healthy to chronically ill people, with a high risk of overlap between patients and/or studies. Twenty results/findings (26.7%) supported the efficacy of dietary supplements in improving biochemical parameters (such as inflammatory biomarkers and fasting

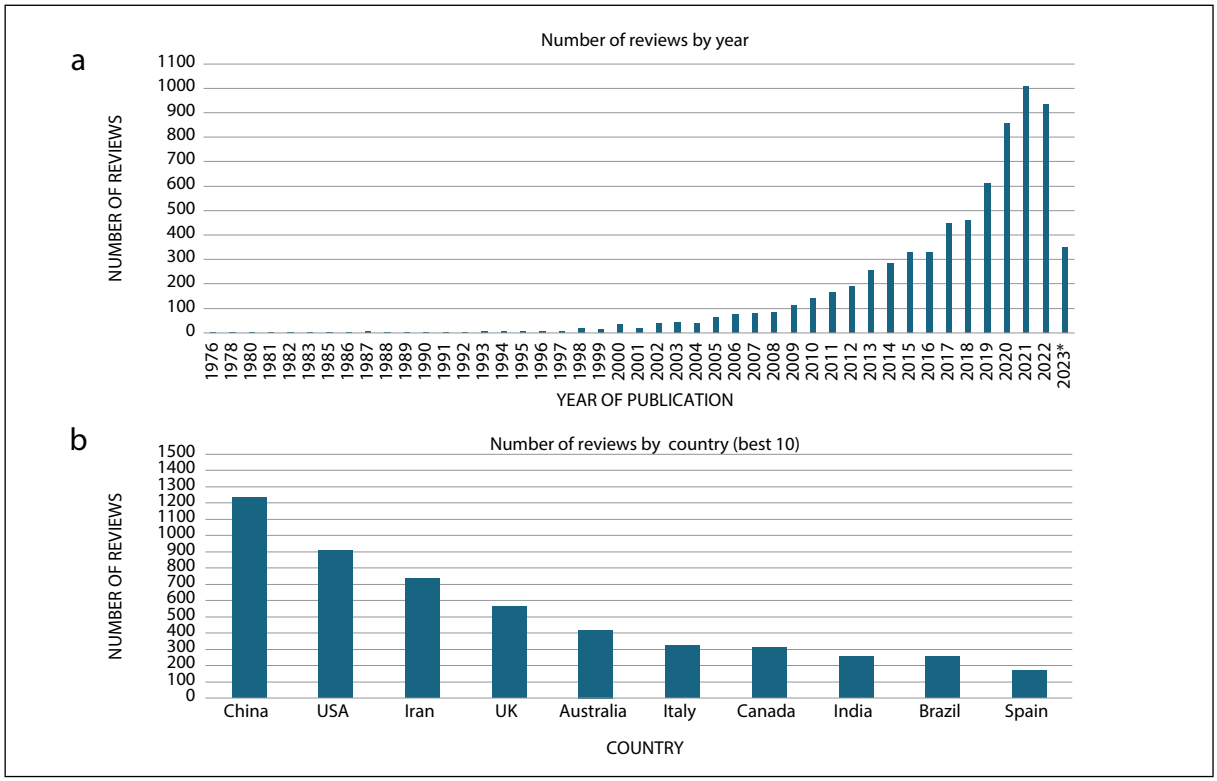


Figure 3
a) Number of non-duplicated systematic reviews and meta-analyses identified on Medline, by year of publication; b) number of non-duplicated systematic reviews and meta-analyses identified on Medline ranked by the best 10 countries of publication.

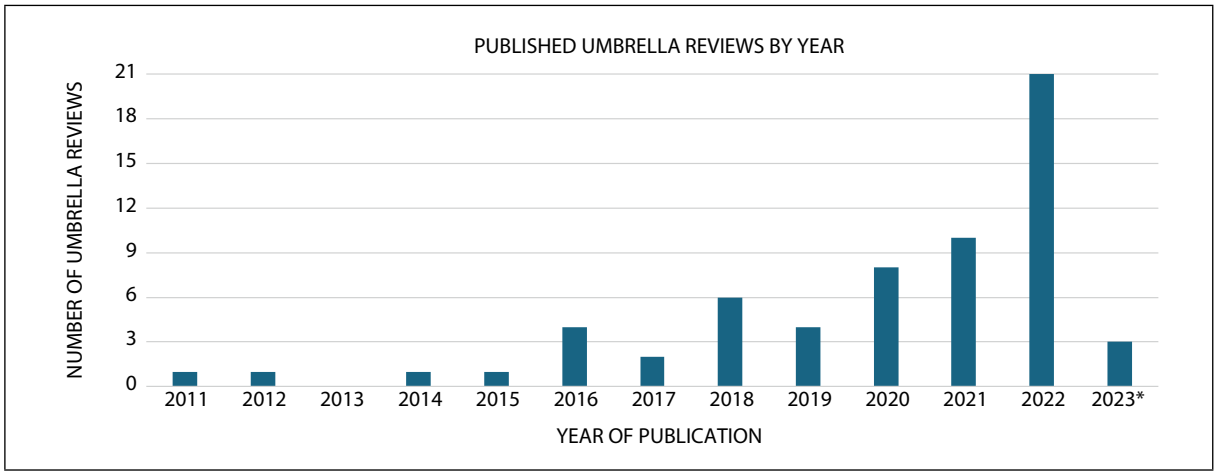


Figure 4
Number of published umbrella reviews investigating the effects of dietary supplements on human health outcomes by year of publication.

glucose) and in preserving human health (e.g., by reducing the risk of anemia, migraine and fractures), with moderate to high certainty of evidence. Most studies focused on vitamin D supplementation and demonstrated its efficacy in reducing the risk of falling in adult patients when administered in the elderly at risk of malnutrition and in the elderly with dementia (risk reduction ranging from 14.0% to 19.0%) [68]. Furthermore, vitamin D supplementation (8-24 weeks) has been associated with a slight, but not significant, reduction in insulin resistance (standardized mean difference, SMD, compared with placebo [95% confidence interval, CI]: -0.25 [-0.53, 0.04] for the homeostatic model assessment index – HOMA index) [46]. In this regard, other dietary supplements could improve glucose, lipid and adipose tissue metabolism. For example, curcumin supplementation (6-12 weeks) reduced fasting glucose levels in women with polycystic ovarian syndrome (SMD

Table 1
Summary of the included studies

Type of the umbrella reviews, n (%)*; median number of the included studies [range]	
Reviews of SRs	24 (35.8%); 15 [5-87]
Reviews of MA	19 (28.4%); 30 [1-195]
Reviews of SRs with MA	21 (31.3%); 12 [4-141]
Others**	3 (4.5%); 74 [13-289]
Main findings, n (%)* **	
Efficacy with low certainty/insufficient evidence or without information on the quality of evidence	31 (41.3%)
Efficacy	20 (26.7%)
Inefficacy with low certainty/insufficient evidence or without information on the quality of evidence	13 (17.3%)
Inconclusive/conflicting results	8 (10.7%)
Inefficacy	3 (4.0%)
Intervention/supplements, n (%)	
Vitamins	46 (74.2%)
Vitamin D	20
Vitamin C	6
Vitamin D + calcium	4
Vitamin B9 (folic acid)	3
Vitamin A	3
β-carotene (precursor of vitamin A)	2
Vitamin E	2
Vitamin B complex	1
Vitamin B3 (niacin)	1
Vitamin B6	1
Vitamin B7 (inositol)	1
Vitamin B12	1
Vitamin K	1
Minerals	21 (33.9%)
Zinc	3
Iron	3
Iron + vitamin B9 (folic acid)	3
Calcium	4
Selenium	3
Chromium	2
Magnesium	1
Iodine	1
Zinc + iron	1
Omega-3 fatty acids	11 (17.7%)
Prebiotics/probiotics/synbiotics	10 (16.1%)
Proteins and amino acids	10 (16.1%)
β-hydroxy-β-methyl butyrate (leucine metabolite)	2
Glutamine	1
Tryptophan	1
Leucine	1
Not specified	5
Lipid-based nutrients	1 (1.6%)
Others	28 (45.2%)
Curcumin	4
Camellia sinensis L. (green tea)	4
Coenzyme Q10	2
Antioxidants (unspecified)	2
Polyphenols	2
Allium sativum L. (garlic)	2
Phytosterols, *Serenoa repens*, β-sitosterol, *Pygeum africannum* Hook f. and Cernilton (rye grass pollen)®	2
Pollen	1
Spicy foods and chili pepper	1
Caffeine	1
Zingiber officinale Roscoe (ginger), *Hibiscus sabdariffa* L., *Aloe vera* spp., *Nigella sativa* L., or *Arthrospira platensis* (spirulina)	1
Cannabis sativa spp. and *Rosa canina* L.	1
Cinnamomum verum Presl (cinnamon)	1
Fish oil	1
Vegetable oil	1
Guar gum, chromium picolinate, *Ephedra* spp. and ephedrine, *Citrus aurantium* L., conjugated linoleic acid, calcium, glucomannan, chitosan, *Camellia sinensis* L. (green tea)	1
Sodium bircarbonate	1

MA: meta-analysis; SRs: systematic reviews; *some umbrella reviews included more than one type of review; **reviews of MA and umbrella reviews (n=1), Mendelian randomisation studies and SRs (n=1), Mendelian randomisation studies and MA (n=1); ***some studies on more than one dietary supplement have reported more than one result.

compared with placebo: -3.31 [-4.89, -1.79]) [46], as well as blood lipid levels in the general population (total cholesterol, TC: -25.13 mg/dl [40.6, -9.28]; low-density lipoprotein cholesterol, LDL-C: -39.83 [75.02, 4.25] after 8-12 weeks, compared with placebo) [64]. Vegetable oils, phytosterols, plant proteins and *Camellia sinensis* L. exhibited lipid-lowering levels (vegetable oils, 2-104 weeks: -6.7 to -19.0 mg/dl for TC and -0.4 to -16.2 mg/dl for LDL-C; phytosterols, 3-85 weeks: -7.7 to -16.4 mg/dl for TC and -10.4 to -23.7 mg/dl for LDL-C; plant proteins, 3-208 weeks: -6.4 to -23.2 mg/dl for TC and -4.76 to -21.7 mg/dl for LDL-C; *Camellia sinensis* L., 2-96 weeks: -0.4 to -27.6 mg/dl for TC and -0.2 to -24.8 mg/dl for LDL-C) [64], while probiotics (8-12 weeks) decreased fasting blood glucose in adult patients (SMD compared with placebo: -4.70 [-8.43, -0.97]) [46]. Also, probiotics reduced body mass index (BMI) and waist circumference in obese people, particularly after 8 weeks of supplementation (SMD for BMI from baseline: -0.11 [-0.40, 0.18] for periods <8 weeks *vs* -0.21 [-0.32, -0.09] for 8-12 weeks; SMD for body weight from baseline: -0.25 [-0.80, 0.30] for periods ≤8 weeks *vs* -0.41 [-0.61, -0.20] for more than 8 weeks) [48].

Many reviews have focused on the effects of dietary supplements in pregnant women showing, for example, a positive association between vitamin D use and reduced risk of preterm delivery (risk ratio, RR: 0.36 [0.14, 0.93]) or low birth weight (RR: 0.40 [0.24, 0.67]) [25]. High magnesium intake [72] and omega-3 supplementation [62] decreased the intensity/frequency of migraine in pregnant women and the risk of pre-eclampsia (RR: 0.75 [0.57, 0.98]) and low-birth weight (RR: 0.72 [0.55, 0.94]), respectively. Finally, vitamin A increased retinol concentrations in maternal serum and breast milk and reduced the risk of anemia and maternal clinical infection in women of reproductive age [32].

Consistent results have been found regarding the anti-inflammatory effects of dietary supplements. For instance, C-reactive protein (CRP) levels were significantly reduced by vitamin C, zinc and melatonin supplementation, while tumor necrosis factor (TNF) and interleukin (IL)-6 levels were significantly lowered by melatonin supplementation. The effects of vitamin D on inflammatory markers, however, were controversial [60, 65]. Omega-3 supplementation has also shown significant effects on CRP, TNF and IL-6 levels [42]. However, beneficial effects on inflammatory biomarkers do not necessarily imply clinical efficacy in the prevention and treatment of inflammatory diseases. For instance, the double-blind, randomized, placebo-controlled ASCEND-Eye trial showed no significant benefit for omega-3 fatty acids on diabetic retinopathy [76]. Furthermore, Cochrane reviews have shown that omega-3 intake has little or no effect in preventing cardiovascular events [77], as well as dry eye symptoms in patients with dry eye disease [78].

Thirty-one results/findings (41.3%) suggested potential beneficial effects of dietary supplements on human health, but with a low to very low certainty of evidence. Although these reviews yielded promising results on the health effects of dietary supplements, some doubts remain on the methodological quality of the included studies. Finally, eight results/findings (10.7%) were uncertain/conflicting, thirteen (17.3%) suggested that dietary supplements are ineffective (certainty of evidence low to very low), and only three (4.0%) concluded that dietary supplements have no beneficial effects on human health (certainty of evidence moderate to high). In this regard, vitamin D supplementation (without calcium) did not prevent preterm birth, stillbirth and cesarean section in pregnant women [16], nor hip fracture or any other fractures in healthy individuals [25]. Furthermore, calcium supplementation had no effect on body weight and BMI in women of reproductive age [32].

CONCLUSIONS

The demonstration of the beneficial properties of dietary supplements is far from conclusive and further high-quality studies are needed to confirm the potential benefits of vitamins, minerals and botanicals in the prevention of diseases or their recurrence, with affordable costs justifying their use. In fact, in most papers the quality of the evidence was low or uncertain or even inconclusive, and the studies showed an effect mainly on biomarkers or soft endpoints. In our opinion, a more regulated process (e.g., through randomized controlled trials), simpler but somehow similar to that of drugs or substance based medical devices, is needed for dietary supplements to clearly demonstrate their benefits and justify the additional costs to patients and the community.

LIMITATIONS

This is a review of umbrella reviews, which increases the risk of missing relevant data not extracted in the original umbrella reviews or in the primary studies they included. Additionally, the selected reviews differ substantially in terms of the type and number of included studies, resulting in the variability of sample size and types of interventions considered. There is also a high risk of overlap between patient populations, potentially leading to an overestimation of the effect. In fact, several umbrella reviews on the same topic may have included the same primary studies and, consequently, the same patient data. This may have artificially increased the statistical power of the result without additional evidence or new data.

Authors' contributions

Conceptualization: AM, EL; methodology: EP, MAM, EL; software: EP, MAM, EL; investigation: EP, MAM, EL; data curation: EP, MAM, EL; writing – original draft preparation: EP, MAM; writing – review and editing: EP, MAM, VC, SDM, CG, AM, EL; supervision: AM, EL.

Conflict of interest statement

The Authors declare no conflict of interest.

Received on 1 December 2024.
Accepted on 26 May 2025.

REFERENCES

1. Young AL, Bass IS. The dietary supplement health and education act. Food Drug Law J. 1995;50(2):285-92.
2. Lentjes MAH. The balance between food and dietary supplements in the general population. Proc Nutr Soc. 2019;78(1):97-109. doi: 10.1017/S0029665118002525
3. Papatesta EM, Kanellou A, Peppa E, Trichopoulou A. Is dietary (food) supplement intake reported in European National Nutrition Surveys? Nutrients. 2023;15(24):5090. doi: 10.3390/nu15245090
4. European Union. Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. Official Journal of the European Union L 183, 12 July 2002. Available from: https://eur-lex.europa.eu/eli/dir/2002/46/oj/eng.
5. Dzobo K. The Role of Natural Products as Sources of Therapeutic Agents for Innovative Drug Discovery. Comprehensive Pharmac. 2022;408-22. doi: 10.1016/B978-0-12-820472-6.00041-4
6. Dias DA, Urban S, Roessner U. A historical overview of natural products in drug discovery. Metabolites. 2012;2(2):303-36. doi: 10.3390/metabo2020303
7. Petrovska BB. Historical review of medicinal plants' usage. Pharmacogn Rev. 2012;6(11):1-5. doi: 10.4103/0973-7847.95849
8. Cragg GM, Newman DJ. Natural products: a continuing source of novel drug leads. Biochim Biophys Acta. 2013;1830(6):3670-95. doi: 10.1016/j.bbagen.2013.02.008
9. Patridge E, Gareiss P, Kinch MS, Hoyer D. An analysis of FDA-approved drugs: natural products and their derivatives. Drug Discov Today. 2016;21(2):204-7. doi: 10.1016/j.drudis.2015.01.009
10. Zhang F, Barr SI, McNulty H, Li D, Blumberg JB. Health effects of vitamin and mineral supplements. BMJ. 2020;369:m2511. doi: 10.1136/bmj.m2511
11. Blumberg JB, Bailey RL, Sesso HD, Ulrich CM. The evolving role of multivitamin/multimineral supplement use among adults in the age of personalized nutrition. Nutrients. 2018;10(2):248. doi: 10.3390/nu10020248
12. Wierzejska RE. Dietary supplements for whom? The current state of knowledge about the health effects of selected supplement use. Int J Environ Res Public Health. 2021;18(17):8897. doi: 10.3390/ijerph18178897
13. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210. doi: 10.1186/s13643-016-0384-4
14. Antonelli M, Donelli D, Firenzuoli F. Therapeutic efficacy of orally administered pollen for nonallergic diseases: An umbrella review. Phytother Res. 2019;33(11):2938-47. doi: 10.1002/ptr.6484
15. Apostolopoulou A, Haidich AB, Kofina K, Manzanares W, Bouras E, Tsaousi G, Stoppe C, Dardavessis TI, Chourdakis M. Effects of glutamine supplementation on critically ill patients: Focus on efficacy and safety. An overview of systematic reviews. Nutrition. 2020;78:110960. doi: 10.1016/j.nut.2020.110960
16. Bialy L, Fenton T, Shulhan-Kilroy J, Johnson DW, McNeil DA, Hartling L. Vitamin D supplementation to improve pregnancy and perinatal outcomes: An overview of 42 systematic reviews. BMJ Open. 2020;10(1):e032626. doi: 10.1136/bmjopen-2019-032626
17. Burrows T, Teasdale S, Rocks T, Whatnall M, Schindlmayr J, Plain J, Latimer G, Roberton M, Harris D, Forsyth A. Effectiveness of dietary interventions in mental health treatment: A rapid review of reviews. Nutr Diet. 2022;79(3):279-90. doi: 10.1111/1747-0080.12754
18. Ellwood J, Draper-Rodi J, Carnes D. Comparison of common interventions for the treatment of infantile colic: A systematic review of reviews and guidelines. BMJ Open. 2020;10(2):e035405. doi: 10.1136/bmjopen-2019-035405
19. Gielen E, Beckwee D, Delaere A, De Breucker S, Vandewoude M, Bautmans I; Sarcopenia Guidelines Development Group of the Belgian Society of Gerontology and Geriatrics. Nutritional interventions to improve muscle mass, muscle strength, and physical performance in older people: An umbrella review of systematic reviews and meta-analyses. Nutr Rev. 2021;79(2):121-47. doi: 10.1093/nutrit/nuaa011
20. Jafari M, Mousavi SM, Asgharzadeh A, Yazdani N. Coenzyme Q10 in the treatment of heart failure: A systematic review of systematic reviews. Indian Heart J. 2018;70(Suppl. 1):S111-7. doi: 10.1016/j.ihj.2018.01.031
21. Khan SU, Khan MU, Riaz H, Valavoor S, Zhao D, Vaughan L, Okunrintemi V, Riaz IB, Khan MS, Kaluski E, Murad MH, Blaha MJ, Guallar E, Michos ED. Effects of nutritional supplements and dietary interventions on cardiovascular outcomes: An umbrella review and evidence map. Ann Intern Med. 2019;171(3):190-8. doi: 10.7326/M19-0341
22. Kim TH, Lim HJ, Kim MS, Lee MS. Dietary supplements for benign prostatic hyperplasia: An overview of systematic reviews. Maturitas. 2012;73(3):180-5. doi: 10.1016/j.maturitas.2012.07.007
23. Maretzke F, Bechthold A, Egert S, Ernst JB, Melo van Lent D, Pilz S, Reichrath J, Stangl GI, Stehle P, Volkert D, Wagner M, Waizenegger J, Zittermann A, Linseisen J. Role of vitamin D in preventing and treating selected extraskeletal diseases: An umbrella review. Nutrients. 2020;12(4):969. doi: 10.3390/nu12040969
24. Martin Ruiz E, Olry de Labry A, Epstein D. Primary prevention of cardiovascular disease: An umbrella review. An Sist Sanit Navar. 2018;41(3):355-69. doi: 10.23938/ASSN.0316
25. Mateussi MV, Latorraca COC, Daou JP, Martimbianco ALC, Riera R, Pacheco RL, Pachito DV. What do Cochrane systematic reviews say about interventions for vitamin D supplementation? Sao Paulo Med J. 2017;135(5):497-507. doi: 10.1590/1516-3180.2017.0230150817
26. McKenzie YA, Thompson J, Gulia P, Lomer MC. British Dietetic Association systematic review of systematic reviews and evidence-based practice guidelines for the use of probiotics in the management of irritable bowel syndrome in adults (2016 update). J Hum Nutr Diet. 2016;29(5):576-92. doi: 10.1111/jhn.12386
27. Michels N, Zouiouich S, Vanderbauwhede B, Vanacker J, Indave Ruiz BI, Huybrechts I. Human microbiome and metabolic health: An overview of systematic reviews. Obes Rev. 2022;23(4):e13409. doi: 10.1111/obr.13409
28. Moorthy D, Merrill R, Namaste S, Iannotti L. The impact of nutrition-specific and nutrition-sensitive interventions on hemoglobin concentrations and anemia: A meta-review of systematic reviews. Adv Nutr. 2020;11(6):1631-45. doi: 10.1093/advances/nmaa070
29. Neil-Sztramko SE, Teggart K, Moore C, Sherifali D, Fitzpatrick-Lewis D, Coletta G, Phillips SM, Newbold KB, Alvarez E, Kuspinar A, Kennedy CC, Santaguida PL, Ganann R. Community-based group physical activity and/or nutrition interventions to promote mobility in older adults: An umbrella review. BMC Geriatr. 2022;22(1):539. doi: 10.1186/s12877-022-03170-9
30. Pagano E, Romano B, Izzo AA, Borrelli F. The clinical

efficacy of curcumin-containing nutraceuticals: An overview of systematic reviews. Pharmacol Res. 2018;134:79-91. doi: 10.1016/j.phrs.2018.06.007
31. Posadzki P, AlBedah AM, Khalil MM, AlQaed MS. Complementary and alternative medicine for lowering blood lipid levels: A systematic review of systematic reviews. Complement Ther Med. 2016;29:141-51. doi: 10.1016/j.ctim.2016.09.019
32. Rajwar E, Parsekar SS, Venkatesh BT, Sharma Z. Effect of vitamin A, calcium and vitamin D fortification and supplementation on nutritional status of women: An overview of systematic reviews. Syst Rev. 2020;9(1):248. doi: 10.1186/s13643-020-01501-8
33. Theodoratou E, Tzoulaki I, Zgaga L, Ioannidis JP. Vitamin D and multiple health outcomes: Umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. BMJ. 2014;348:g2035. doi: 10.1136/bmj.g2035
34. von Salmuth V, Brennan E, Kerac M, McGrath M, Frison S, Lelijveld N. Maternal-focused interventions to improve infant growth and nutritional status in low-middle income countries: A systematic review of reviews. PLoS One. 2021;16(8):e0256188. doi: 10.1371/journal.pone.0256188
35. Phillips SM, Lau KJ, D'Souza AC, Nunes EA. An umbrella review of systematic reviews of beta-hydroxy-beta-methyl butyrate supplementation in ageing and clinical practice. J Cachexia Sarcopenia Muscle. 2022;13(5):2265-75. doi: 10.1002/jcsm.13030
36. Sans S, Bobo G, Zudaire L, Lafarga T, Sabate J, Casals J, Simo J. Nutritional values of raw and cooked "calcots" (Allium cepa L. resprouts), an expanding crop. J Sci Food Agric. 2019;99(11):4985-92. doi: 10.1002/jsfa.9733
37. Grgic J, Grgic I, Pickering C, Schoenfeld BJ, Bishop DJ, Pedisic Z. Wake up and smell the coffee: caffeine supplementation and exercise performance - an umbrella review of 21 published meta-analyses. Br J Sports Med. 2020;54(11):681-8. doi: 10.1136/bjsports-2018-100278
38. Chang C, Yuan X, Zhang X, Chen X, Li K. Gastrointestinal microbiome and multiple health outcomes: Umbrella review. Nutrients. 2022;14(18):3726. doi: 10.3390/nu14183726
39. Fong C, Alesi S, Mousa A, Moran LJ, Deed G, Grant S, Tapia K, Ee C. Efficacy and safety of nutrient supplements for glycaemic control and insulin resistance in type 2 diabetes: An umbrella review and hierarchical evidence synthesis. Nutrients. 2022;14(11):2295. doi: 10.3390/nu14112295
40. Hoang T, Kim J. Phytonutrient supplements and metabolic biomarkers of cardiovascular disease: An umbrella review of meta-analyses of clinical trials. Phytother Res. 2021;35(8):4171-82. doi: 10.1002/ptr.7079
41. Iqbal S, Ekmekcioglu C. Maternal and neonatal outcomes related to iron supplementation or iron status: A summary of meta-analyses. J Matern Fetal Neonatal Med. 2019;32(9):1528-40. doi: 10.1080/14767058.2017.1406915
42. Kavyani Z, Musazadeh V, Fathi S, Hossein Faghfouri A, Dehghan P, Sarmadi B. Efficacy of the omega-3 fatty acids supplementation on inflammatory biomarkers: An umbrella meta-analysis. Int Immunopharmacol. 2022;111:109104. doi: 10.1016/j.intimp.2022.109104
43. Keramati M, Musazadeh V, Malekahmadi M, Jamilian P, Jamilian P, Ghoreishi Z, Zarezadeh M, Ostadrahimi A. Cinnamon, an effective anti-obesity agent: Evidence from an umbrella meta-analysis. J Food Biochem. 2022;46(8):e14166. doi: 10.1111/jfbc.14166
44. Kinshella MW, Omar S, Scherbinsky K, Vidler M, Magee LA, von Dadelszen P, Moore SE, Elango R, The Precise Conceptual Framework Working Group. Effects of maternal nutritional supplements and dietary interventions on placental complications: An umbrella review, meta-analysis and evidence map. Nutrients. 2021;13(2):472. doi: 10.3390/nu13020472
45. Liu D, Meng X, Tian Q, Cao W, Fan X, Wu L, Song M, Meng Q, Wang W, Wang Y. Vitamin D and multiple health outcomes: An umbrella review of observational studies, randomized controlled trials, and mendelian randomization studies. Adv Nutr. 2022;13(4):1044-62. doi: 10.1093/advances/nmab142
46. Moslehi N, Zeraattalab-Motlagh S, Rahimi Sakak F, Shab-Bidar S, Tehrani FR, Mirmiran P. Effects of nutrition on metabolic and endocrine outcomes in women with polycystic ovary syndrome: An umbrella review of meta-analyses of randomized controlled trials. Nutr Rev. 2023;81(5):555-77. doi: 10.1093/nutrit/nuac075
47. Motrico E, Bina R, Kassianos AP, Le HN, Mateus V, Oztekin D, Rodriguez-Munoz MF, Moreno-Peral P, Conejo-Ceron S. Effectiveness of interventions to prevent perinatal depression: An umbrella review of systematic reviews and meta-analysis. Gen Hosp Psychiatry. 2023;82:47-61. doi: 10.1016/j.genhosppsych.2023.03.007
48. Musazadeh V, Zarezadeh M, Ghalichi F, Ahrabi SS, Jamilian P, Jamilian P, Ghoreishi Z. Anti-obesity properties of probiotics; a considerable medical nutrition intervention: Findings from an umbrella meta-analysis. Eur J Pharmacol. 2022;928:175069. doi: 10.1016/j.ejphar.2022.175069
49. Musazadeh V, Keramati M, Ghalichi F, Kavyani Z, Ghoreishi Z, Alras KA, Albadawi N, Salem A, Albadawi MI, Salem R, Abu-Zaid A, Zarezadeh M, Mekary RA. Vitamin D protects against depression: Evidence from an umbrella meta-analysis on interventional and observational meta-analyses. Pharmacol Res. 2023;187:106605. doi: 10.1016/j.phrs.2022.106605
50. Schwingshackl L, Missbach B, Hoffmann G. An umbrella review of garlic intake and risk of cardiovascular disease. Phytomedicine. 2016;23(11):1127-33. doi: 10.1016/j.phymed.2015.10.015
51. Unhapipatpong C, Polruang N, Shantavasinkul PC, Julanon N, Numthavaj P, Thakkinstian A. The effect of curcumin supplementation on weight loss and anthropometric indices: An umbrella review and updated meta-analyses of randomized controlled trials. Am J Clin Nutr. 2023;117(5):1005-16. doi: 10.1016/j.ajcnut.2023.03.006
52. Vesco AT, Lehmann J, Gracious BL, Arnold LE, Young AS, Fristad MA. Omega-3 supplementation for psychotic mania and comorbid anxiety in children. J Child Adolesc Psychopharmacol. 2015;25(7):526-34. doi: 10.1089/cap.2013.0141
53. Zarezadeh M, Musazadeh V, Ghalichi F, Kavyani Z, Nasernia R, Parang M, Jamilian P, Jamilian P, Fakhr L, Ostadrahimi A, Mekary RA. Effects of probiotics supplementation on blood pressure: An umbrella meta-analysis of randomized controlled trials. Nutr Metab Cardiovasc Dis. 2023;33(2):275-86. doi: 10.1016/j.numecd.2022.09.005
54. Zeraattalab-Motlagh S, Jayedi A, Shab-Bidar S. The effects of resveratrol supplementation in patients with type 2 diabetes, metabolic syndrome, and nonalcoholic fatty liver disease: An umbrella review of meta-analyses of randomized controlled trials. Am J Clin Nutr. 2021;114(5):1675-85. doi: 10.1093/ajcn/nqab250
55. Chakhtoura M, Bacha DS, Gharios C, Ajjour S, Assaad M, Jabbour Y, Kahale F, Bassatne A, Antoun S, Akl EA, Bouillon R, Lips P, Ebeling PR, El-Hajj Fuleihan G. Vitamin D supplementation and fractures in adults: A systematic umbrella review of meta-analyses of controlled

trials. J Clin Endocrinol Metab. 2022;107(3):882-98. doi: 10.1210/clinem/dgab742
56. Choi H, Kim JY, Lee KH, Kim JS, Lee JY, Choi EK, Seong HJ, Kim G, Park H, Jung E, Hong SH, Kronbichler A, Eisenhut M, Koyanagi A, Jacob L, Yon DK, Lee SW, Kim MS, Kostev K, Shin JI, Yang JW, Smith L. Omega-3 fatty acids supplementation on major cardiovascular outcomes: An umbrella review of meta-analyses of observational studies and randomized controlled trials. Eur Rev Med Pharmacol Sci. 2021;25(4):2079-92. doi: 10.26355/eurrev_202102_25113
57. Ganmaa D, Enkhmaa D, Nasantogtokh E, Sukhbaatar S, Tumur-Ochir KE, Manson JE. Vitamin D, respiratory infections, and chronic disease: Review of meta-analyses and randomized clinical trials. J Intern Med. 2022;291(2):141-64. doi: 10.1111/joim.13399
58. Ao Z, Huang Z, Liu H. Spicy food and chili peppers and multiple health outcomes: Umbrella review. Mol Nutr Food Res. 2022;66(23):e2200167. doi: 10.1002/mnfr.202200167
59. Ashor AW, Brown R, Keenan PD, Willis ND, Siervo M, Mathers JC. Limited evidence for a beneficial effect of vitamin C supplementation on biomarkers of cardiovascular diseases: An umbrella review of systematic reviews and meta-analyses. Nutr Res. 2019;61:1-12. doi: 10.1016/j.nutres.2018.08.005
60. Corrao S, Mallaci Bocchio R, Lo Monaco M, Natoli G, Cavezzi A, Troiani E, Argano C. Does evidence exist to blunt inflammatory response by nutraceutical supplementation during COVID-19 pandemic? An overview of systematic reviews of vitamin D, vitamin C, melatonin, and zinc. Nutrients. 2021;13(4):1261. doi: 10.3390/nu13041261
61. De Spiegeleer A, Beckwee D, Bautmans I, Petrovic M, Sarcopenia Guidelines Development Group of the Belgian Society of Gerontology and Geriatrics. Pharmacological interventions to improve muscle mass, muscle strength and physical performance in older people: An umbrella review of systematic reviews and meta-analyses. Drugs Aging. 2018;35(8):719-34. doi: 10.1007/s40266-018-0566-y
62. Firouzabadi FD, Shab-Bidar S, Jayedi A. The effects of omega-3 polyunsaturated fatty acids supplementation in pregnancy, lactation, and infancy: An umbrella review of meta-analyses of randomized trials. Pharmacol Res. 2022;177:106100. doi: 10.1016/j.phrs.2022.106100
63. Houze B, El-Khatib H, Arbour C. Efficacy, tolerability, and safety of non-pharmacological therapies for chronic pain: An umbrella review on various CAM approaches. Prog Neuropsychopharmacol Biol Psychiatry. 2017;79(Pt B):192-205. doi: 10.1016/j.pnpbp.2017.06.035
64. Adel Mehraban MS, Tabatabaei-Malazy O, Rahimi R, Daniali M, Khashayar P, Larijani B. Targeting dyslipidemia by herbal medicines: A systematic review of meta-analyses. J Ethnopharmacol. 2021;280:114407. doi: 10.1016/j.jep.2021.114407
65. Moslemi E, Musazadeh V, Kavyani Z, Naghsh N, Shoura SMS, Dehghan P. Efficacy of vitamin D supplementation as an adjunct therapy for improving inflammatory and oxidative stress biomarkers: An umbrella meta-analysis. Pharmacol Res. 2022;186:106484. doi: 10.1016/j.phrs.2022.106484
66. Neyestani TR, Nikooyeh B. A comprehensive overview on the effects of green tea on anthropometric measures, blood pressure, glycemic and lipidemic status: An umbrella review and meta meta-analysis study. Nutr Metab Cardiovasc Dis. 2022;32(9):2026-40. doi: 10.1016/j.numecd.2022.05.021
67. Onakpoya IJ, Wider B, Pittler MH, Ernst E. Food supplements for body weight reduction: A systematic review of systematic reviews. Obesity (Silver Spring). 2011;19(2):239-44. doi: 10.1038/oby.2010.185
68. Poscia A, Milovanovic S, La Milia DI, Duplaga M, Grysztar M, Landi F, Moscato U, Magnavita N, Collamati A, Ricciardi W. Effectiveness of nutritional interventions addressed to elderly persons: Umbrella systematic review with meta-analysis. Eur J Public Health. 2018;28(2):275-83. doi: 10.1093/eurpub/ckx199
69. Rizzoli R, Biver E, Bonjour JP, Coxam V, Goltzman D, Kanis JA, Lappe J, Rejnmark L, Sahni S, Weaver C, Weiler H, Reginster JY. Benefits and safety of dietary protein for bone health-an expert consensus paper endorsed by the European Society for Clinical and Economical Aspects of Osteopororosis, Osteoarthritis, and Musculoskeletal Diseases and by the International Osteoporosis Foundation. Osteoporos Int. 2018;29(9):1933-48. doi: 10.1007/s00198-018-4534-5
70. Schultz TJ, Roupas P, Wiechula R, Krause D, Gravier S, Tuckett A, Hines S, Kitson A. Nutritional interventions for optimizing healthy body composition in older adults in the community: An umbrella review of systematic reviews. JBI Database System Rev Implement Rep. 2016;14(8):257-308. doi: 10.11124/JBISRIR-2016-003063
71. Shah K, Varna VP, Sharma U, Mavalankar D. Does vitamin D supplementation reduce COVID-19 severity? A systematic review. QJM. 2022;115(10):665-72. doi: 10.1093/qjmed/hcac040
72. Veronese N, Demurtas J, Pesolillo G, Celotto S, Barnini T, Calusi G, Caruso MG, Notarnicola M, Reddavide R, Stubbs B, Solmi M, Maggi S, Vaona A, Firth J, Smith L, Koyanagi A, Dominguez L, Barbagallo M. Magnesium and health outcomes: An umbrella review of systematic reviews and meta-analyses of observational and intervention studies. Eur J Nutr. 2020;59(1):263-72. doi: 10.1007/s00394-019-01905-w
73. Xu K, Peng R, Zou Y, Jiang X, Sun Q, Song C. Vitamin C intake and multiple health outcomes: An umbrella review of systematic reviews and meta-analyses. Int J Food Sci Nutr. 2022;73(5):588-99. doi: 10.1080/09637486.2022.2048359
74. Zarezadeh M, Musazadeh V, Faghfouri AH, Sarmadi B, Jamilian P, Jamilian P, Tutunchi H, Dehghan P. Probiotic therapy, a novel and efficient adjuvant approach to improve glycemic status: An umbrella meta-analysis. Pharmacol Res. 2022;183:106397. doi: 10.1016/j.phrs.2022.106397
75. Grgic J, Grgic I, Del Coso J, Schoenfeld BJ, Pedisic Z. Effects of sodium bicarbonate supplementation on exercise performance: An umbrella review. J Int Soc Sports Nutr. 2021;18(1):71. doi: 10.1186/s12970-021-00469-7
76. Sammons EL, Buck G, Bowman LJ, Stevens WM, Hammami I, Parish S, Armitage J; ASCEND Study Collaborative Group. ASCEND-Eye: Effects of omega-3 fatty acids on diabetic retinopathy. Ophthalmology. 2024;131(5):526-33. doi: 10.1016/j.ophtha.2023.11.030
77. Abdelhamid AS, Brown TJ, Brainard JS, Biswas P, Thorpe GC, Moore HJ, Deane KH, Summerbell CD, Worthington HV, Song F, Hooper L. Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2020;3(3):CD003177. doi: 10.1002/14651858.CD003177.pub5
78. Downie LE, Ng SM, Lindsley KB, Akpek EK. Omega-3 and omega-6 polyunsaturated fatty acids for dry eye disease. Cochrane Database Syst Rev. 2019;112(12):CD011016. doi: 10.1002/14651858.CD011016.pub2

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 173-179
DOI: 10.4415/ANN_25_03_03

Needs for a shared operational methodology to draft guidelines and good practices in legal medicine

Patrizio Rossi and Andrea Mele

Sovrintendenza Sanitaria Centrale INAIL, Rome, Italy

Abstract

Introduction. Article 5 of Law n. 24/2017 established the obligation for medico-legal professionals to adhere to guidelines and good clinical-care practices, except in specific cases. However, the methodologies developed for clinical practice are not entirely applicable to the field of legal medicine, which presents unique characteristics in terms of regulatory context, objectives, and evaluative processes. Legal medicine does not primarily focus on diagnosis or treatment but on standardized assessment procedures, legal defensibility, and consistency of judgments.

Objectives. Starting from the experience of the Central Health Department (Sovrintendenza Sanitaria Centrale, SSC) of the Italian National Institute for Insurance against Accidents at Work (Istituto Nazionale per l'Assicurazione contro gli Infortuni sul Lavoro, INAIL), the goal is to develop a dedicated manual outlining the appropriate methods for developing guidelines and best practices in legal medicine, proposing a methodological framework.

Methods. The authors conduct a review of the literature on the topic related to the methodology for developing guidelines and best practices in forensic medicine. They took inspiration from the methodological manual for the production of clinical practice guidelines by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS).

Discussion. The authors highlight the lack of literature specifically addressing the development of guidelines and best practices in forensic medicine. *The methodological manual for the production of clinical practice guidelines* by the Italian National Institute of Health (ISS) requires some adaptations but certainly represents a highly useful tool for creating relevant recommendations for legal medicine. Therefore, the authors propose a specific methodology and a dedicated manual tailored to legal medicine. The manual should be adapted from the ISS methodologies used in clinical settings, revised to reflect the unique needs of medico-legal practice, and developed in close collaboration with the relevant scientific societies and institutions.

Conclusions. The method used for INAIL's SSC recommendations has proven effective in guiding internal medico-legal practices. Building on the ISS methodological manual, the authors propose a tailored approach for developing guidelines (LGML) and best practices (RBPML) in legal medicine. Given the unique challenges of the discipline – often not fully addressed by existing regulations or literature – standardized solutions are necessary to ensure consistent, high-quality medico-legal outcomes. Therefore, the establishment of a dedicated Working Group in collaboration with the ISS is essential to develop a structured methodology. INAIL's prior experience in this field provides a solid foundation for this initiative.

Key words

- medico-legal recommendations
- medico-legal guidelines
- medico-legal good practices
- INAIL recommendations

INTRODUCTION

Article 5 of Law n. 24 of 8 March 2017 "Good clinical care practices and recommendations provided by the guidelines" [1] introduced a legal obligation for healthcare professionals performing services for medico-legal purposes to adhere – except in specific cases – to the recommendations set forth in officially recognized guidelines. These guidelines, pursuant to paragraph 3 of the same article, must be developed by public or private entities, scientific societies, and technical-scientific

Address for correspondence: Patrizio Rossi, Sovrintendenza Sanitaria Centrale, Direzione Generale INAIL, Piazzale Giulio Pastore 6, 00144 Rome, Italy. E-mail: sovrsancentrale@inail.it.

associations of health professionals, provided they are registered in a specific list established and regulated by the Ministerial Decree of 2 August 2017, and published in the Official Gazette n. 186 of 10 August 2017.

This provision significantly departs from earlier legislative drafts, which did not explicitly include healthcare services performed for medico-legal purposes, nor did they recognize technical-scientific associations and public or private institutions, alongside scientific societies, as bodies authorized to produce such guidelines.

In the past, there have been some reservations about the interpretation to be given to the formula used by the legislator [2]. Specifically, there was debate as to whether the law referred solely to clinicians whose work might carry medico-legal implications, or whether, as argued by other authors [3, 4], article 5 should also be understood to encompass the services provided directly by specialists in legal medicine.

The phrasing of the law, explicitly requiring healthcare professionals who perform activities for medico-legal purposes to comply with guidelines, or in their absence, with good clinical-care practices (except when the specific case justifies deviation), appears to support the latter interpretation. Accordingly, even medico-legal experts are now expected to follow recommendations found in validated guidelines and good practices, despite the current lack of such documents within the Italian National Guidelines System (Sistema Nazionale Linee Guida, SNLG).

This makes it evident that specific, tailored guidelines and good practices are necessary for legal medicine, particularly in those contexts where general clinical guidelines may not be applicable [5, 6].

In both legal commentaries and the available literature, the issue has predominantly been addressed with explicit and preferential reference to clinical guidelines. Medico-legal practitioners tend to rely on these clinical guidelines primarily when formulating expert opinions on cases of clinical medical professional negligence. However, they do not typically align their broader professional activities with guidelines specifically tailored to legal medicine.

In this context, the role of guidelines for legal medicine would be, for example, to support medico-legal decision-making processes [7-10]. Unlike clinical settings, where guidelines are mainly intended to assist healthcare professionals in choosing diagnostic or therapeutic interventions, in legal medicine they aim to ensure consistency, transparency, and defensibility in evaluative judgments. A concrete example is their use in expert assessments within judicial proceedings, where medico-legal experts are required to justify both their methods and conclusions. When the expert follows validated and contextually appropriate guidelines, it becomes more challenging for opposing consultants, such as the public prosecutor's expert or the court-appointed assessor, to claim that an alternative procedure should have been employed or that the professional unjustifiably diverged from accepted standards. In this sense, guidelines not only inform the decision-making process but also confer legal protection and methodological credibility in high-stakes or contentious evaluations.

Moreover, medico-legal protocols often derive directly from regulatory frameworks that mandate specific assessment criteria. For instance, permanent disability assessments for occupational injuries at Italian National Institute for Insurance against Accidents at Work (Istituto Nazionale per l'Assicurazione contro gli Infortuni sul Lavoro, INAIL) follow the Legislative Decree of 23 February 2000 and Ministerial Decree of 12 July 2000; civil disability assessments refer to the Ministerial Decree of 5 February 1992; while compensation for civil liability, involving impairments between 1% and 9%, is governed by the Ministerial Decree of 3 July 2003. These documents function more as prescriptive protocols than traditional clinical guidelines. Nevertheless, certain medico-legal assessment criteria are not codified in legislation nor derived from case law. In such instances, practitioners often rely on analogical reasoning, particularly when the specific condition under evaluation does not correspond to a defined percentage in the available assessment tables.

Additionally, various phases of the medico-legal assessment process remain undefined by either statutory law or jurisprudence, thereby necessitating structured guidance to support medico-legal professionals in conducting consistent and defensible evaluations.

Medico-legal practitioners, however, should not engage with the issue merely as users of clinical guidelines, but also because their services must be anchored to the same principles of appropriateness that underlie the guidelines and good clinical-care practices followed by clinical healthcare professionals.

In essence, the quality of medico-legal services must be ensured and assessed according to predefined and discipline-specific standards. This point has already been emphasized by several authors [11, 12], who highlighted the need to complement outcome indicators, typically quantitative, such as service volumes or response times, with process indicators that reflect the quality of the medico-legal assessment across the various steps of the evaluative pathway, from input to output.

To this end, focused attention on guidelines and good practices specific to legal medicine is essential, as they can serve as a foundation for the identification and development of appropriate process indicators or proxies, through a methodology expressly designed for the peculiarities of the field.

OBJECTIVES: FROM THE RECOMMENDATIONS OF THE INAIL CENTRAL HEALTH DEPARTMENT TO GUIDELINES AND BEST PRACTICES IN LEGAL MEDICINE

The idea of providing useful tools to legal medicine operators to standardize practices, establish quality benchmarks for medico-legal services, and define relevant process indicators – prompted the Central Health Department (Sovrintendenza Sanitaria Centrale, SSC) of INAIL to initiate the development of recommendations.

While the grades of recommendation, assessment, development and evaluation Working Group (GRADE) methodology for guideline development and the appraisal of guidelines for research & evaluation (AGREE)

and AGREE II methods [13] for assessing guideline quality have proven robust in the clinical setting – and are appropriately cited in the methodological manual published by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) [14, 15], they present several limitations when applied to the context of legal medicine.

In line with the approach adopted by the Ministry of Health, INAIL recognized the opportunity to utilize the "recommendation" as a more suitable instrument. As a result, the INAIL SSC launched the production of medico-legal recommendations.

These recommendations are defined as "specific documents aimed at offering tools to prevent adverse events, promote accountability, and foster systemic change" (https://www.salute.gov.it/new/it/tema/governo-clinico-e-sicurezza-delle-cure/raccomandazioni-del-ministero/).

They are "leaner" tools, simpler to produce and with a more agile method of revision, compared to the guidelines, which, however, allows to provide appropriate and exhaustive indications aimed at standardizing behaviors and preventing errors in medico-legal activities.

From the "INAIL medico-legal recommendations" checklists and process indicators were extracted and used as reference standards for medico-legal audit [16].

Currently, the production of recommendations involves the development of a draft at the INAIL SSC level by an *ad hoc* multidisciplinary Working Group, which usually studies a critical issue reported or highlighted by the territory, institutional governance or other stakeholders. The draft is then shared with the regional and provincial health departments and/or other central agencies (INAIL Central Directorates and/or Consultancies), depending on the topic addressed and the competencies of the Departments, for the necessary bottom-up and/or top-down feedback. The distribution takes place in such a way that the draft is disseminated by the Departments throughout the territory to collect as many comments as possible. The outcome of the consultation is followed by the possible acceptance of the notes received and the drafting of the final version of the INAIL medical-legal recommendation. The recommendations issued by the SSC must be general and focus on virtuous behaviors based on scientific evidence, regulatory and doctrinal sources, and internal reference on the different issues addressed.

However, the recommendations may impact a local reality which, due to various factors (such as work organization, personnel, equipment, etc.), find it difficult to adhere to them. For this reason, similar to what happens for the diagnostic-therapeutic assistance pathways (percorso diagnostico terapeutico assistenziale, PDTA), the medical-legal assistance pathways (percorso medico-legale assistenziale, PMLA) have been introduced. These pathways consider the organizational aspects and aim to provide optimal assistance to individuals with work-related injuries or illnesses, ensuring the safety of performance and overcoming any difficulties in applying INAIL SSC recommendations [17].

It is easy to highlight how this tool appears unsuitable for guiding the behaviour of doctors who approach INAIL legal medicine from outside the Institute, as the INAIL medico-legal recommendations do not adhere to the methodology proposed for guidelines and good practices in the clinical field as published in the documents edited by the ISS.

It is desirable to generate shared documents published on the ISS website, in the SNLG, with the role of guidelines and best practices for evaluating the conduct and performance quality of medico-legal practitioners, pursuant to article 5 of Law n. 24/2017.

It is necessary to develop a dedicated manual outlining the appropriate methods for developing guidelines and best practices in legal medicine, proposing a methodological framework.

METHODS

A PubMed search for methodologies specifically designed for the development of guidelines and best practices in legal medicine yields no results. Nevertheless, various documents labeled as guidelines are currently in use by medico-legal professionals and widely referenced within the scientific community, although they do not follow standardized or structured development methods. For instance, in the textbook by Ferrara *et al.*, 2013 [18] and in the article by Basso *et al.*, 2017 [19] such documents are referred to as "guidelines" yet they are essentially literature reviews lacking the methodological tools required for formal guideline production. Similarly, most national and international publications in areas such as forensic pathology, toxicology, hematology, and legal genetics serve as reference texts, but they are not based on recognized or systematic method of development and evaluation, as required for creating guidelines.

For clinical matters, the effort of the ISS was to create a manual that drives healthcare professionals in drafting guidelines and good clinical-care practices.

The same operation for legal medicine may appear more complex and, in some cases, presents peculiar differences for several reasons:

- the methodology suggested for the guidelines in the clinical field is not applicable *tout court* to legal medicine;
- the international and national legal medicine guidelines seem do not follow a structured methodology, despite being recognized by the scientific community and used in medico-legal practice;
- the guidelines used in legal medicine are often overcome by the criteria indicated by specific regulations (for example, the application criteria of legal tables that outline specific behaviours to follow) or by jurisprudential conclusions.

DISCUSSION

The discipline has difficulty adhering to the indications provided by the manuals for the production of guidelines and good clinical-care practices edited by the ISS. It is, therefore, necessary to establish specific "rules" for legal medicine.

As the guidelines and good clinical-care practices support healthcare professionals in making the best choices to ensure the health and safety of the patient, in the same way the development of guidelines and

good practices for legal medicine, according to the requirements of article 5 of Law n. 24/2017, can support the activities and decisions of the medico-legal practitioners. Adherence to a shared methodology that guides the investigation and decision-making process, ensuring homogeneity and uniformity of medico-legal judgment, represents, in fact, essential elements for the medico-legal service safety.

The medico-legal discipline, in fact, is characterized by the presence of so-called performance risk, essentially related to benefits (of both economic and non-economic nature, even to the limitation on individual freedom), which arise from the legal context of reference in which the medico-legal activity is performed.

The so-called medico-legal risk is a "spurious" risk since, in the medico-legal activity, two different risk components coexist: a clinical one, when the service may cause damage to the health and safety of the patient, and a medico-legal one, related to the safety of the service [11]. While the diagnostic and/or therapeutic health service aims at the safety and health of the patient, the medico-legal service aims at the safety of the service.

The medico-legal service safety represents a new concept of the healthcare management system, which also concerns individuals who are not direct receivers of the service. The collective interest can be threatened by a medico-legal performance error, for example, in the inappropriate release of a driving licence, inadequate assessment of capacity or social dangerousness, or absolute or temporary disability, or ability for a specific job.

Therefore, the analysis and management of medico-legal health risk must consider this broader connotation compared to the one intended for all healthcare professionals performing diagnostic-therapeutic activities and, consequently, the impacts of medico-legal error on the safety of the service.

To ensure the safety of medico-legal services, it is essential to introduce, also for this discipline, tools for risk prevention: recommendations of the guidelines (linee guida in medicina legale, LGML) and good practices (buone pratiche in medicina legale, BPML) for legal medicine.

As mentioned, guidelines may not be necessary in cases where specific regulations have already been issued for the different areas of evaluation with a precise description of the application criteria; instead, they may find space in regulatory gaps or for debated and not yet regulated topics.

The recommendations contained in the LGML and BPML appear necessary to optimize and personalize medico-legal processes. They should be based on solid evidence, pursuing the same principle of multidisciplinarity and sharing between Institutes and scientific societies involved, as well as the guidelines and good clinical-care practices.

A comparison between professionals interested in researching best practices may also allow the identification of virtuous realities as reference models (benchmark) and induce a positive mechanism of competitiveness, which leads to an effective continuous improvement in the quality and safety of medico-legal services.

As far as INAIL Institutional status is concerned, this comparison has already been defined. Therefore, the Institute, which has exclusive competence in the field of social insurance according to the legislation in force, must always be consulted when guidelines are drawn up by scientific societies.

If the error in clinical practice results in damage to the health and safety of the patient, the error in legal medicine entails no less harmful effects, such as the failure to ensure the necessary protection of subjects in need of assistance, adequate compensation and/or compensation for the damage suffered, the failure to condemn subjects responsible for crimes or the conviction of non-responsible subjects, etc.

As in clinical practice, it is necessary to introduce a system of valid guidelines and good practices, according to art. 5 of Law n. 24/2017, to evaluate the behaviours of healthcare professionals working in legal medicine.

Assuming that the recommendations of the guidelines for legal medicine could be those included in the dedicated regulations, it is quite clear that the slowness of the production process found for clinical practice would be even more amplified. Consequently, even for legal medicine, where the regulatory review process is slow and fraught with obstacles, the recommendations of the BPML could be more easily used. These will provide a rapid systematic literature review and allow relatively short drafting times (around 6 months), providing equally valid support, as it is anchored to some key principles. Similar to the recommendations for good practice in clinical care (raccomandazioni per le buone pratiche clinico assistenziali, RBPCA), the recommendations for good medico-legal practice (raccomandazioni per le buone pratiche medico-legali, RBPML) would guide aspects relating to medico-legal practice and the organization of health services.

To be reliable, the RBPML, with almost identical characteristics – net of the inevitable differences between medico-legal practice and clinical care practice – to the RBPCA [20], must:

be based on a rapid systematic review of existing evidence;

- be developed by a competent, multidisciplinary and multi-professional group of experts representing the competent bodies, institutions and main scientific societies involved;
- take into consideration the problems identified based on the prevalence, the urgency, the rate of medical-legal litigation, and the expression of non-homogeneity of behaviour;
- take into consideration the needs of the protected population for access to particular benefits provided by law;
- be based on an explicit and transparent process that minimizes distortions, prejudices and conflicts of interest;
- provide a clear explanation of any alternative methodological options and their implications on the results;
- take into account the preferences and will of the citizen, inviting the medical examiner to base his assessment on the elements available to him at the time of the assessment, in the event of the subject's refusal to undergo treatment and/or diagnostic tests [21];

- be reconsidered and revised when important new evidence justifies the change.

Referring to the methodological guidelines for drafting recommendations for good clinical care practices published by the ISS, "minimum" methodological requirements can also be referred to for legal medicine.

However, for legal medicine, minimum requirements n. 3 and n. 7 do not appear applicable. As for requirement n. 3, the evaluation of the "certainty of evidence" reported in the methodological indications of the RBPCA in the forensic and medico-legal fields takes on a different meaning and should be reserved for those areas in which the evidence must overcome even reasonable doubt and be endowed with high logical probability [22]. Requirement n. 7 does not concern the strength of the recommendation but the evidence to which the recommendation refers; such evidence is part of the selection process, based on the authoritativeness and concordance of the sources.

The minimum methodological requirements are shown in the following *Table 1*.

As with RBPCA, the production method can be based on the four elements summarized by the acronym PICO:

- P, problem/population: indicates the subject or population of reference for the question (e.g., the problem of "telemedicine applied to legal medicine" [23], or citizens with civilian invalidity or work-related disability, etc.);
- I, interventions: indicates the main intervention taken into consideration;
- C, comparison/control: indicates the main alternative with which the intervention (I) is compared, capable of relating to the outcome (O);
- O, outcome: this is what is hoped to be achieved, the result or purpose of the recommendation.

Regarding topic selection, unlike RBPCA, it is not necessary to identify an additional expert panel, as the group addressing the topic already comprises qualified professionals. Integration of further experts may be considered only if the proposal originates from entities other than the designated Working Group. The Working Group should be structured around a multidisciplinary and inter-institutional core, with the possibility of including field-specific experts as needed.

To gather expert consensus within the Working Group, the RAND/UCLA appropriateness method can be employed. Although traditionally positioned at the final tier of the evidence pyramid as a tool for eliciting expert opinion, this methodology proves particularly valuable in the field of legal medicine, especially in areas where no clear guidance exists through legislation, jurisprudence, or well-established literature [24]. It should be highlighted that medico-legal expertise today is increasingly hyper-specialized in a scientific world in constant evolution.

The Working Group should consist of an odd number of members to ensure that any proposals can be voted on with a clear majority, allowing for the prioritization of actions. From a risk management perspective, if multiple proposals are presented simultaneously, intervention priorities may be established using the priority index (e.g., frequency × severity, or frequency × severity × detectability). These proposals may originate from stakeholders or specific population groups (e.g., individuals with disabilities, injured workers, privately insured parties, victims of duty), who may address the Working Group directly.

The same majority-based decision-making approach may be applied to the formal approval of the recommendation. A methodology that has proven effective within INAIL involves broad consultation with regional branches during the development of centrally drafted recommendations. This collaborative process may also be adopted for RBPML, enabling Working Group members to submit the draft to a selected group of institutional, academic, or scientific society collaborators for feedback and contributions.

The final draft, according to what happens for the RBPCA, can be submitted "to external review by two independent referees, selected by the Working Group,

Table 1
Minimum methodological requirements

1. Identification of regulatory, legal and bibliographic sources related to the topic, describing the process of selecting evidence, also concerning keywords and any filters used. This will also be useful to make the search "repeatable". Evaluation of the authoritativeness and concordance of the available evidence. Certainty (or high logical probability) is necessary if the scope of the recommendations for good medico-legal practice (RBPML) is a criminal process, the greatest probability, instead, if the scope is a civil process, social security, etc. It has to be evaluated the majority of literature, but also only the most authoritative part, the strongest evidence, and the one with the greatest value. Even if the sources are numerically lower than the total evidence available, they are relevant for medico-legal purposes if they are among the most authoritative and concordant. As for clinical scientific evidence, the reference selection must consider the quality of the evidence and the strength and weight of the recommendations [23].
2. The authority and concordance of the references must be evaluated in each phase of the medico-legal process since it is considered important or critical to issue the final judgment.
4. The minimum requirement for the presentation of the summary of evidence is a clear description of the sources and the method used to identify them and assess their degree of authoritativeness and consistency. Synoptic tables can be used to report the domains indicated (e.g., legislation, jurisprudence, scientific literature, and related authoritativeness and concordance).
5. Explicit criteria should provide the basis for making recommendations or decisions. Explicit judgments should be made for each criterion chosen, including those that might be added, and evidence used to support those judgments should be provided. Additional considerations affecting the recommendation or decision should also be documented and accessible.
6. Those who develop RBPML should describe the expected outcomes and, where possible, monitor them through medico-legal audits.

based on requirements of authoritativeness and competence in the area covered. The referees will express observations and comments on the document contents, with particular reference to the consistency between evidence and recommendations and the formulation and applicability of the latter. The report from the external review will be examined by the Working Group, before finalising the document" [20].

Similar to the structure required for RBPCA, the RBPML must include:

1. a detailed description of the Working Group, specifying the roles of involved bodies, institutions, and scientific societies;
2. explicit description of the process and method used to draft the document, reviewing and documenting all stages: topic selection, evidence search strategy, and consensus process for each recommendation;
3. summary of evidence and recommendations;
4. summary of the external audit findings;
5. conflict of interest declaration forms, filled and signed by all RBPML development participants;
6. declaration of commitment not to publish or disclose the RBPML, in whole or in part, before completion of the assessment process.

In March 2025, a document titled "Procedures for the submission and evaluation of recommendations for good clinical care practices" was published. Annex 3 of the document outlines the criteria used to assess the methodological quality of these recommendations. Specifically, recommendations must address the following items:

1. the composition of the development group;
2. the methodology used in the development of the recommendation;
3. the management of conflicts of interest.

However, the development methodology cited refers to the application of the GRADE approach, which was originally designed for clinical care contexts. For the reasons outlined above, this method cannot be applied to medico-legal best practices, which differ in both content and purpose, and are governed by regulatory, contractual, or statutory provisions rather than clinical objectives.

Recently, the SNLG website published a good practice applied to legal medicine [25]. This represents a significant milestone and may serve as a valuable starting point for fostering collaboration among the various institutions involved in the field. It could help identify a shared methodology for the development of good practices, ultimately leading to the much-needed publication of a dedicated manual outlining the appropriate procedures for their formulation.

CONCLUSIONS

The methods tested in the development of recommendations by the Central Health Department of INAIL, responsible for the governance of institutional health activities, have proven effective in guiding medico-legal practices within the institution. However, these documents lack the formal status and recognition afforded to guidelines and good practices validated by the ISS for clinical-care contexts.

Despite the inapplicability of tools designed for clinical medicine, we assert that legal medicine must also be grounded in evidence-based principles. Building upon the methodological framework outlined in the "ISS methodological manual for the production of clinical practice guidelines", we propose a method for the production of recommendations in the form of guidelines (LGML) or best practices (RBPML) dedicated to legal medicine.

The subject's specificities demand resolving problems (P of PICO) that have not been fully or only partially resolved through regulatory intervention, from sources within National institutes focusing on legal medicine, or from relevant literature. Then, there are phases of the medical-legal processes that require a univocal reading and framing to homogenize the behaviours and guarantee quality, uniformity and safety of the medico-legal service outcomes.

Therefore, the establishment of a dedicated Working Group in collaboration with the ISS is essential to develop a structured methodology for producing recommendations in legal medicine. These recommendations should serve as a reference standard for practitioners, with exceptions allowed only in well-justified cases. In this evolving landscape, the experience gained through the drafting and dissemination of recommendations by INAIL's Central Health Department can serve as a valuable foundation.

Conflict of interest statement

The Authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Received on 14 March 2025.
Accepted on 26 May 2025.

REFERENCES

1. Italia. Legge 8 Marzo 2017 n. 24. Disposizioni in materia di sicurezza delle cure e della persona assistita, nonché in materia di responsabilità professionale degli esercenti le professioni sanitarie. Gazzetta Ufficiale – Serie Generale n. 64, 17 marzo 2017. Available from: https://www.gazzettaufficiale.it/eli/id/2017/03/17/17G00041/s.
2. Mele A, Gallo M. L'art. 5 della Legge 8 Marzo 2017, n. 24: le linee guida in medicina legale. Riv Infort Mal Prof. 2016;3:491.
3. Del Sordo S, Genovese U. Articolo 5. Buone pratiche clinico-assistenziali e raccomandazioni previste dalle Linee Guida. In: Genovese U, Martini F (Eds). La nuova

responsabilità professionale in Sanità. Santarcangelo di Romagna (RN): Maggioli; 2017. p. 41.
4. Frati P, La Russa R, Campolongo AA, Viola RV, Romano S, Volonnino G, Fineschi V. Le innovazioni procedurali della novella Gelli e le reali prospettive di arginare il fenomeno del contenzioso sanitario. Responsabilità Civile e Previdenza. 2019;3:1056-72.
5. Mele A, Rossi P. L'audit, la root cause analysis e il safety walk round in medicina legale. In: Atti del Convegno nazionale di medicina e sanità INAIL salute, benessere e sicurezza del lavoratore al centro della sanità. Roma: 26-29 giugno 2023. p. 975.
6. Rossi P, Mele A. Il ruolo medico-legale e l'approccio evidence based in ambito assicurativo sociale. Riv Infort Mal Prof. 2023;1:2.
7. Caputo M, Centonze F. La risposta penale alla malpractice: il dedalo di interpretazioni disegnato dalla riforma Gelli-Bianco. Riv Ital Med Leg Dirit Campo Sanit. 2017;4:1361.
8. Buccelli C, Abignente, I, Niola M, Paternoster M, Graziano V, Di Lorenzo P. La rilevanza delle linee guida nella determinazione della responsabilità medica. Le novità introdotte dalla cd. Legge Balduzzi, le problematiche connesse, i tentativi di risoluzione. Riv Ital Med Leg. 2016;2:663.
9. Conti A. Il significato delle linee guida prima delle recenti norme. Riv Ital Med Leg Dirit Campo Sanit. 2019;2:635.
10. Ricciardi GW, Iannone P, Trojano V, Cirese V, Mariotti, P, Caminiti R. Linee guida e buone pratiche clinico-assistenziali. In: Gelli F, Hazan M, Zorzit D (Eds). La nuova responsabilità sanitaria e la sua assicurazione. Milano: Giuffrè; 2017. p. 151.
11. Rossi P, Comacchio A, Mele A. La gestione del rischio sanitario medico-legale. Dalla clinical governance ai processi medico legali. Milano: Giuffrè; 2014.
12. Comacchio A, Goggiamani A, Mele A, Rossi P. Dagli esiti alla prevenzione: indicatori di processo versus indicatori di esito in medicina legale. Riv Ital Med Leg. 2015;4:1675.
13. Agree Next Step Consortium. AGREE II. Checklist per valutare la qualità delle linee guida. Bologna: Fondazione Gimbe; 2019. Available from: https://www.gimbe.org/pubblicazioni/traduzioni/AGREE_IT.pdf.
14. Centro Nazionale per l'Eccellenza Clinica, la Qualità e la Sicurezza delle Cure. Manuale metodologico per la produzione di Linee Guida di Pratica Clinica. Versione 1.3.1. Roma: Istituto Superiore di Sanità; 2019.
15. Centro Nazionale per l'Eccellenza Clinica, la Qualità e la Sicurezza delle Cure. Manuale metodologico per la produzione di Linee Guida di Pratica Clinica. Versione 1.3.3. Roma: Istituto Superiore di Sanità; 2023.
16. Mele A, Rossi, P, Gallo M. La legge n. 24/2017: linee guida, buone prassi e audit come strumenti di miglioramento della qualità in medicina legale assicurativa previdenziale. In: XII Convegno nazionale di medicina legale previdenziale "Nuove frontiere della medicina legale previdenziale". Bologna, 28-30 novembre 2018.
17. Rossi P, Mele A. Dalle raccomandazioni medico-legali ai percorsi medico-legali assistenziali (PMLA) in ambito INAIL. Riv Infort Mal Prof. 2023;3:227.
18. Ferrara SD, Baccino E, Bajanowski T, Boscolo-berto R. Malpractice and medical liability. European guidelines on methods of ascertainment and criteria of evaluation. Int J Legal Med. 2013;545-57.
19. Basso C, Aguilera B, Banner J, Cohle S, Amati G. Guidelines for autopsy investigation of sudden cardiac death: 2017 update from the association for European cardiovascular pathology. Virchows Arch. 2017;691-705.
20. Istituto Superiore di Sanità. Indicazioni metodologiche per la stesura di raccomandazioni per le buone pratiche clinico assistenziali. Versione 1.0. Roma: ISS; 2024.
21. Mele A, Lauro A. L'importanza della cartella clinica nell'accertamento medico legale. La cartella clinica elettronica nel contesto della sanità italiana: potenzialità, prospettive e sinergie. Napoli: Direzione Regionale Campania-INAIL; 2019.
22. Istituto Nazionale Assicurazione contro gli Infortuni sul Lavoro – Sovrintendenza Sanitaria Centrale. Raccomandazione SSC n. 4/2023. Approccio evidence based per la tutela delle patologie da lavoro; Roma: INAIL; 2023.
23. Rossi P, Bramante L, Broccoli L, Mele A, Vantaggiato DR, Iera S. La telemedicina nella medicina legale in ambito assicurativo sociale. Riv Infort Mal Prof. 2022;3:311.
24. Fitch K, Bernstein SJ, Aguilar MD, Burnand B, LaCalle JR, Lazaro P, van het Loo M, McDonnell J, Vader J, Kahan JP. Rand/Ucla appropriateness method user's manual. Santa Monica (CA): RAND Corporation; 2000.
25. Centro Nazionale per l'Eccellenza Clinica, la Qualità e la Sicurezza delle Cure. Buone pratiche cliniche di valutazione medico legale delle menomazioni alla integrità psicofisica comprese tra 10 e 100 punti di invalidità permanente. Roma: Istituto Superiore di Sanità; 2025.

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 180-190
DOI: 10.4415/ANN_25_03_04

Uncovering accessibility gaps. Geospatial and diagnostic practices analysis of the Centres for Cognitive Disorders and Dementias (CCDD) in Apulia and Basilicata, Italy

Ezia Rizzi[1], Francesco Giaquinto[2], Marika Iaia[2], Michele Dell'Abate[3], Luigi Macchitella[4], Giorgia Tosi[1], Daniele Luigi Romano[1], Nicola Vanacore[5] and Paola Angelelli[2]

[1]Dipartimento di Psicologia e Milano Centro per le Neuroscienze (NeuroMi), Università di Milano-Bicocca, Milan, Italy
[2]Dipartimento di Medicina Sperimentale, Laboratorio di Psicologia Applicata e Intervento, Università del Salento, Lecce, Italy
[3]Dipartimento di Scienze Umane e Sociali, Università del Salento, Lecce, Italy
[4]Associazione "La Nostra Famiglia" – IRCCS "E. Medea", Ospedale Scientifico per la Neuroriabilitazione, Unità per le Disabilità Severe dell'Età Evolutiva e Giovane Adulta (Neurologia dello Sviluppo e Neuroriabilitazione), Brindisi, Italy
[5]Centro Nazionale per la Prevenzione e il Controllo delle Malattie, Istituto Superiore di Sanità, Rome, Italy

Abstract

Background. This study analysed accessibility, patient and healthcare professionals' characteristics, neuropsychological practices, and patient care gaps at Centres for Cognitive Disorders and Dementias (CCDD) in Apulia and Basilicata, Italy.

Methods. Geographic information systems (GIS) analysis and online survey were employed. CCDDs clinicians completed a self-report questionnaire covering "Characteristics of the CCDD" and "Neuropsychological assessment", from July 2021 to January 2023. Geographical coordinates were used to identify peripheral areas, based on the Italian strategy for Inner Areas.

Results. Thirty-three CCDDs were identified. Geospatial analysis revealed ultra-peripheral municipalities and inadequate public transport to CCDDs in several areas. Most patients were women aged 70-89. Neurologists played a key role in diagnosis and test administration. Diagnostic criteria and neuropsychological tools varied: international criteria were rarely applied, recommended tests were underutilised, and some cognitive domains undervalued.

Conclusion. These findings highlight the need for effective healthcare interventions for cognitive disorders and the potential for teleneuropsychology to bridge care gaps.

Key words

- inequalities in healthcare
- geographical accessibility
- Centres for Cognitive Disorders and Dementia
- neuropsychological assessment
- accessibility

INTRODUCTION

Exploring differences in access to healthcare services is one of the priorities in public health [1], particularly about dementia, a prevalent condition affecting millions of people worldwide. Dementia is a degenerative condition related to ageing and is the most common cause of cognitive and behavioural decline, affecting 55 million people globally, with around 10 million new cases annually (https://www.who.int/publications/i/item/9789241513487). The proportion of older adults is increasing in Italy and many other countries [2], leading to a greater impact of cognitive decline on the population. In Southern Italy, severe difficulties in essential functions (i.e., perceptual, motor and memory skills) are higher compared to the Central and Northern regions (32.1% *vs* 25.5% and 22.9%, respectively). There is also a lower proportion of older adults in the South visiting specialist doctors or undergoing specialist ex-

Address for correspondence: Paola Angelelli, Dipartimento di Medicina Sperimentale, Università del Salento, Via di Valesio Edificio 5, 73100 Lecce, Italy. E-mail: paola.angelelli@unisalento.it.

ams compared to the national average (63.2% *vs* 66.1%, and 43.2% *vs* 49.3%, respectively) (https://www.istat.it/it/files/2021/07/Report-anziani-2019.pdf). Women tend to use outpatient health services more frequently, especially between the ages of 65 and 74 (https://www.istat.it/it/files/2021/07/Report-anziani-2019.pdf). The regions of Basilicata (562,869 inhabitants; mean age is 45.7) and Apulia (4,029,000; mean age 44.6 years), in Southern Italy, have unevenly distributed populations, with a higher prevalence of chronic diseases in Basilicata compared to national averages (https://www.istat.it/it/files/2021/07/Report-anziani-2019.pdf). Both regions have a significant number of patients suffering from dementia (10,000 *vs* 55,000 patients in Basilicata and Apulia, respectively), with dementia and neurologic diseases being the leading cause of death in Basilicata (https://regione.basilicata.it/giunta/site/Giunta/detail.jsp?otype=1012&id=3077556 and https://www.sanita.puglia.it/documents/36031/53941903/PDTA+Alzheimer.pdf/930c654f-b1e2-4949-b00c-0273bb2ea0ed). The analysis of the essential levels of assistance/care reveals critical performance in prevention, community health services, and hospital assistance within the two regions [3].

In response to healthcare needs, the Italian Government approved the National Dementia Plan in 2015 [4] The Plan aimed to establish Centres for Cognitive Disorders and Dementias (CCDD) dedicated to evaluating, diagnosing, and treating cognitive disorders and dementias. These centres, which can be public, territorial, outpatient, hospital, university, or research institutes, have the authority to formulate official diagnoses and define legally recognized Therapeutic Pharmacological Plans. The CCDDs' essential characteristics include multidisciplinary and multi-professionalism to cater to each patient's care needs effectively [4]. In Italy, the 2023 census by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) [5] reports a total of 587 CCDDs, with 268, 105, and 214 located in Northern Italy, Central Italy, and Southern Italy and the Islands, respectively. The regions of Apulia and Basilicata had 31 and 3 CCDDs, respectively [5]. It is common to encounter disparities in healthcare access, especially in rural or remote areas and among vulnerable populations. Nevertheless, the accessibility of CCDDs has not been taken into consideration in previous research.

Accessibility to healthcare services represents a crucial concern that impacts the well-being of communities and individuals [6] and supports policy decisions regarding the allocation of resources for care provision [7], that better meet the needs of the community [8]. A valuable tool in addressing accessibility challenges in the healthcare sector is the geospatial analysis [9]. It involves the use of geographic information systems (GIS) and spatial data to understand the distribution of healthcare facilities, their proximity to populations, and the barriers that might hinder people from accessing services. Several studies [8] have investigated the spatial characteristics of healthcare facilities, including their location, distribution, and proximity to various modes of transportation, particularly for facilities catering to older adults. According to a recent study by Kim *et al*. [6], the combination of qualitative and geospatial methods is a new and promising way to gain a comprehensive understanding of health issues. However, as reported above, to our knowledge, no Italian study has yet explored the accessibility of essential healthcare services such as CCDDs.

A second point relates to the internal organisation of CCDDs in terms of their location in hospitals or universities, waiting times, patient flow, healthcare professionals involved, and the diagnostic protocols used (including factors such as reference diagnostic criteria and types of neuropsychological tests). In the first survey by the Italian National Institute of Health [5], the CCDDs' location, staff composition, and services varied significantly across the three macro-geographical areas of Italy. Notably, CCDDs located in the Southern part of the country were less commonly found in hospitals or universities, had fewer patients and monthly referrals, shorter wait times for initial visits, and a lower proportion of psychologists administering psychodiagnostics tests compared to CCDDs in the other two areas. They also tended to be less integrated into coordinated care pathways (Therapeutic, Diagnostic and Care Pathways, DTCP) [5]. Despite being critical to the team, psychologists and neuropsychologists have the lowest percentage of permanent employment in CCDDs [10]. A recent survey [11] examining the current work situation of self-identified neuropsychologists in Italy reports that the majority of participants (71.7%) worked in the field of the diagnosis of dementia. However, the survey does not offer data on the distribution of respondents on a regional basis, nor on how many of them work in the CCDDs.

As far as the diagnostic protocols are concerned, the study by Di Pucchio *et al*. [12] specifically addressed the neuropsychological tests used in Italian CCDDs. The results showed that more than half of the included CCDDs based their screening procedures mainly on the administration of rough cognitive (e.g., Mini-Mental State Examination) and functional (e.g., Activities of Daily Living and Instrumental Activities of Daily Living) scales or a small set of tests. However, the study does not investigate adherence to known diagnostic criteria or protocols, while much has been done internationally to standardise the protocols. The international criteria for diagnosing dementia and neurocognitive disorders are well-established, serving as an important reference for standardising clinical practice [13, 14]. European Consensus efforts have also aimed to harmonise diagnostic protocols. Festari *et al*. [15] provided data on neuroimaging and biomarker usage in diagnosing Mild Cognitive Impairment (MCI) and mild dementia, revealing varying usage levels among European clinicians. According to that study, 93% of European clinicians use Magnetic Resonance Imaging (MRIs), while 92% and 68% use Cerebrospinal Fluid (CSF) biomarkers and Fluorodeoxyglucose-Positron Emission Tomography (FDG-PETs), respectively. It is less common to use cardiovascular MIBG-scintigraphy (38%), polysomnography (60%), amyloid-PET (54%), and electroencephalography (EEG) (33%). Most clinicians (77%) did not use the new tau-PET tracers' methodology. A consensus

framework developed by the Joint Program for Neurodegenerative Diseases (JPND) and the Italian Ministry of Health [16] addressed harmonising neuropsychological assessments for neurodegenerative dementias in Europe. The study emphasised the need for standardised testing methodologies and the limited availability of psychometric information on these tests. In fact, it was found the use of heterogeneous and non-standardized neuropsychological tests in European countries, along with variations in administration and scoring methods, which leads to incomparable results. After a thorough analysis, the authors reached a consensus on general recommendations for neuropsychological assessment procedures and tools. In this line, a methodology for producing normative data and cut-off values, facilitating early detection and cross-country comparisons in test validation, was also proposed [17].

Overall, in light of the data reported so far and the issues that have emerged, the main objective of our study is threefold. Firstly, it aims to investigate the accessibility of CCDDs (Centres for Cognitive Disorders and Dementias) in the regions of Apulia and Basilicata. Secondly, it seeks to update information regarding the organisation and activities of these centres (e.g., by characterising their staff, equipment, patients, and types of diagnoses). Lastly, the study aims to survey the neuropsychological procedures employed in clinical practice to diagnose dementia.

METHODS

CCDD involvement

As a starting point, we used the CCDDs list provided by the ISS survey conducted in 2014-2015 [5]. To our knowledge, this was the most updated publicly available list of CCDDs. Following further research on the territory and comparing the official website list of each Italian Regions, the chief medical officer and Directors of Medical Services of these CCDDs were contacted by phone. We ended up with the identification of a total of thirty-three CCDDs (30 in Apulia and 3 in Basilicata; see *Figure S1 available online as Supplementary Materials*) and contacted them with a letter of intent explaining the project in detail. The Ethical Committee of Salento University and the Local Health Authority of Lecce (Italy) approved the study (Protocol n. 174371/2020). Participants were volunteers and did not receive any compensation. They provided Informed Consent to complete the questionnaire. All data were collected between July 2021 and January 2023. No personal information about the age or gender of the clinicians was required.

Procedure

GIS analysis

The addresses and geographical coordinates of all CCDDs present in Puglia and Basilicata were used for the geospatial analysis of the location and spatial distribution of CCDDs. The Basilicata region comprises 131 municipalities, divided into two provinces, Matera (n=31) and Potenza (n=100), and the health regional system is organised into six health districts (i.e., Potenza, Val d'Agri, Senise, Lauria, Melfi, and Venosa). The Apulia region comprises 257 municipalities divided into six provinces and as many health districts (i.e., the Metropolitan City of Bari: 41; Barletta-Andria-Trani, BAT: 10; Brindisi: 20; Foggia: 61; Lecce: 96; Taranto: 29). First, each municipality was assigned to a single CCDD according to the following criteria: whether a CCDD is present in a health district, then it is the reference for all municipalities in that district; whether more than one CCDD is present in a health district, then the municipalities in the same district are assigned to the geographically closest CCDD (km). In the absence of CCDDs in a health district, each municipality in that district is assigned to the geographically closest CCDD (km) of another district in the same province. In our sample, there was at least one CCDD per province. Using the Google Maps application, it was possible to derive three variables for each municipality: distance in kilometres from the reference CCDD (Distance), time travel in minutes to the reference CCDD by own car (TimeCar), and by public transport (TimePublic). Information about public transport availability was derived from Google Maps, which used online sources such as the Italian railway public service (e.g., Trenitalia) and regional public bus service (e.g., Sita Sud srl). Referring to the strategy for Inner Areas in Italy developed by the Italian Agency for Territorial Cohesion [18], municipalities were classified in terms of distance from the "service delivery centres".

Online CCDD survey

Clinicians were required to complete a self-report survey employed by the Qualtrics platform (https://www.qualtrics.com) using a link shared via mail. The survey was divided into two consecutive sections. The first section, "Characteristics of the CCDD", required information that defines the characteristics of the CCDD: name, location of the service (e.g., hospital, university, territorial), years of operation, number and indicative socio-demographic information about the patients, composition of the medical staff, type of diagnoses, diagnostic procedures (e.g., use of biomarkers, neuroimaging, etc.). The second part, "Neuropsychological assessment", asked whether a standardised or tailored neuropsychological protocol is used, what specific measures are included in the protocol (selected from a list of 9 composite batteries, 29 neuropsychological tests, and 14 clinical scales), scoring procedures (e.g., raw scores, normative correction, etc.), normative data used, diagnostic criteria used, and knowledge about the national guidelines on the Diagnostic, Therapeutic and Care Pathways (DTCP) for dementia. The questionnaire consisted of closed-ended matrices answered on a 5-point scale Likert scale, ranging from 0 (very rarely) to 5 (very often) and checkbox questions (i.e., multiple-choice-type questions), allowing participants to choose multiple options (e.g., tests used in neuropsychological assessment). Open-ended questions were added to the checkbox options in case the participant did not find their answer in the checkbox list.

Mobile phones, computers, and tablets could all be used to complete the survey. Compiling took up to a total of about 15/20 minutes. Clinicians could decide

whether to complete both sections consecutively or save the first part and complete the second later. Participants had ten days to complete the second part of the survey.

Data analysis

We used t-tests and analyses of variance to explore the differences between areas in terms of Distance, time travel by own car (TimeCar), and by public transport (TimePublic). Geographical maps were then produced to visually represent the distribution of population, the allocation of municipalities to CCDDs, and the accessibility of CCDDs according to travel time by private car and by public transport. Jamovi version 2.3 (https://www.jamovi.org) and Quantum GIS version 3.22.13 LTR (http://www.qgis.org) were used for statistical analyses and geographical maps creation, respectively.

To analyse the survey data, we first performed descriptive statistics on the data collected from the online survey. For multiple-choice questions, we calculated the frequencies of responses in each category – sometimes, respondents were allowed to choose more than one answer. These cases were clearly marked in the results section. Plots were generated using the ggplot2 package in R Studio (http://www.rstudio.com/.25). In all the analyses, statistical significance was set at $p<0.05$.

RESULTS

CCDDs accessibility

Geospatial analysis revealed notable differences between the two regions. The distribution of the population is represented in *Figure S2 available online as Supplementary Materials*, classifying municipalities into seven categories based on number of inhabitants: under 1,000; between 1,000 and 5,000; between 5,000 and 15,000; between 15,000 and 60,000; between 60,000 and 100,000; between 100,000 and 250,000; and over 250,000.

The average distance (km) of the municipalities from the reference CCDDs is significantly higher in Basilicata than in Apulia ($Distance_{Apulia}$=21.3±17.9; $Distance_{Basilicata}$=63.6±41.1; t_{386}=-14.07, $p<0.001$), as it is the travel time (min) by car ($TimeCar_{Apulia}$=23.8±16.6; $TimeCar_{Basilicata}$=59.7±32.4; t_{386}=-14.44, $p<0.001$). Public transport is present in all municipalities of the Apulia Region ($TimePublic_{Apulia}$=60.6±42.0). Conversely, public connections to the CCDDs of reference are available in only 26 out of 131 municipalities in Basilicata, with an average travel time of 251.2±234.8 ($TimePublic_{Basilicata}$=251.2±234.8). The discrepancy in journey times between public transportation and private cars/vehicles (TimePublic=78.1±97.6; TimeCar=25.8±19.7; t_{282}=-10.1, $p<0.001$) is significant.

Municipalities were classified into "service delivery centres" if a CCDD was located in the municipality, "enclosure area", with time travel less than 20 minutes; "intermediate area", between 20 and 40 minutes; "peripheral area", between 40 and 75 minutes; and "ultra-peripheral area", if the time travel exceeds 75 minutes. The analysis of the accessibility of CCDDs according to travel time by private car revealed ultra-peripheral areas in Basilicata and the province of Foggia (Apulia) (see *Figure 1*). In fact, the provinces where the municipalities are furthest away from the CCDDs considering the distance in km and the travel time (min) by own means are Potenza ($Distance_{Potenza}$=65.1±45.1; $TimeCar_{Potenza}$=61.7±34.2), Matera ($Distance_{Matera}$=58.5±24.4; $TimeCar_{Matera}$=53.2±21.4) and Foggia ($Distance_{Foggia}$=39.6±20.7; $TimeCar_{Foggia}$=40.0±20.5).

When considering travel time by public transport (if available), the spread of peripheral and ultra-peripheral areas extends across all provinces, sparing only the "service delivery centres" and a few neighbouring municipalities (see *Figure 1*). Excluding from the comparisons Potenza and Matera, in which public transport service is practically absent, the provinces of Apulia Region with the longest travel times are Foggia ($TimePublic_{Foggia}$=95.9±45.2) and Taranto ($TimePublic_{Taranto}$=73.3±44.1).

In terms of individual CCDDs, Potenza (n=81), Maglie (n=37) in the Province of Lecce, and Foggia (n=33) are the CCDDs that more municipalities refer to, in decreasing order of frequency. Those that are the farthest away in terms of kilometres and most difficult to reach by private means are Potenza ($Distance_{Potenza\_CCDD}$=74.7±44.4; $TimeCar_{Potenza\_CCDD}$=69.0±34.1), Matera ($Distance_{Matera\_CCDD}$=58.5±24.4; $TimeCar_{Matera\_CCDD}$=53.2±21.4) and San Giovanni Rotondo in the Province of Foggia ($Distance_{SanGiovanniRotondo\_CCDD}$=42.8±29.8; $TimeCar_{SanGiovanniRotondo\_CCDD}$=49.6±29.3). In terms of population coverage, the CCDDs that serve the most inhabitants are Taranto (n=432,829), Foggia (n=299,240), and Potenza (n=260,977). Meanwhile, those that cover a smaller portion of the population are Triggiano (n=81,197) and Mola di Bari (n=68,903), both in the Province of Bari, and Copertino (n=36,922) in the Province of Lecce.

Survey section one: CCDD characteristics

Twenty CCDDs (60.6%) participated in the research, three from Basilicata (100.0%) and 17 from Apulia (56.7%). Twelve neurologists, three geriatricians, one psychiatrist, and four psychologists or neuropsychologists (i.e., psychologists with expertise in neuropsychology) compiled the first section of the survey. The second section of the survey was compiled by seventeen (51.5%) CCDDs (i.e., two from Basilicata and 15 from Apulia) and involved neurologists, geriatricians, psychologists or neuropsychologists, and psychiatrists. Non-responding CCDDs included nine hospitals, three territorial facilities, and one university/research service. We define CCDD services as non-responders if they meet any of the following criteria: (i) being contacted by phone but unable to participate; (ii) having inactive phone numbers or numbers attributed to other hospital wards; (iii) accepting to receive the survey link but not completing it. Regarding the geographical distribution of respondents, all CCDDs in Basilicata and the province of Taranto completed the survey, while non-respondents were unevenly distributed among the other provinces (non-respondents: Bari 62.5%, Foggia 50.0%, Lecce 44.0%, Brindisi, and BAT 33.0%).

Regarding the responding CCDDs, they have been active for an average of 14.79 years (SD=9, range=2-32),

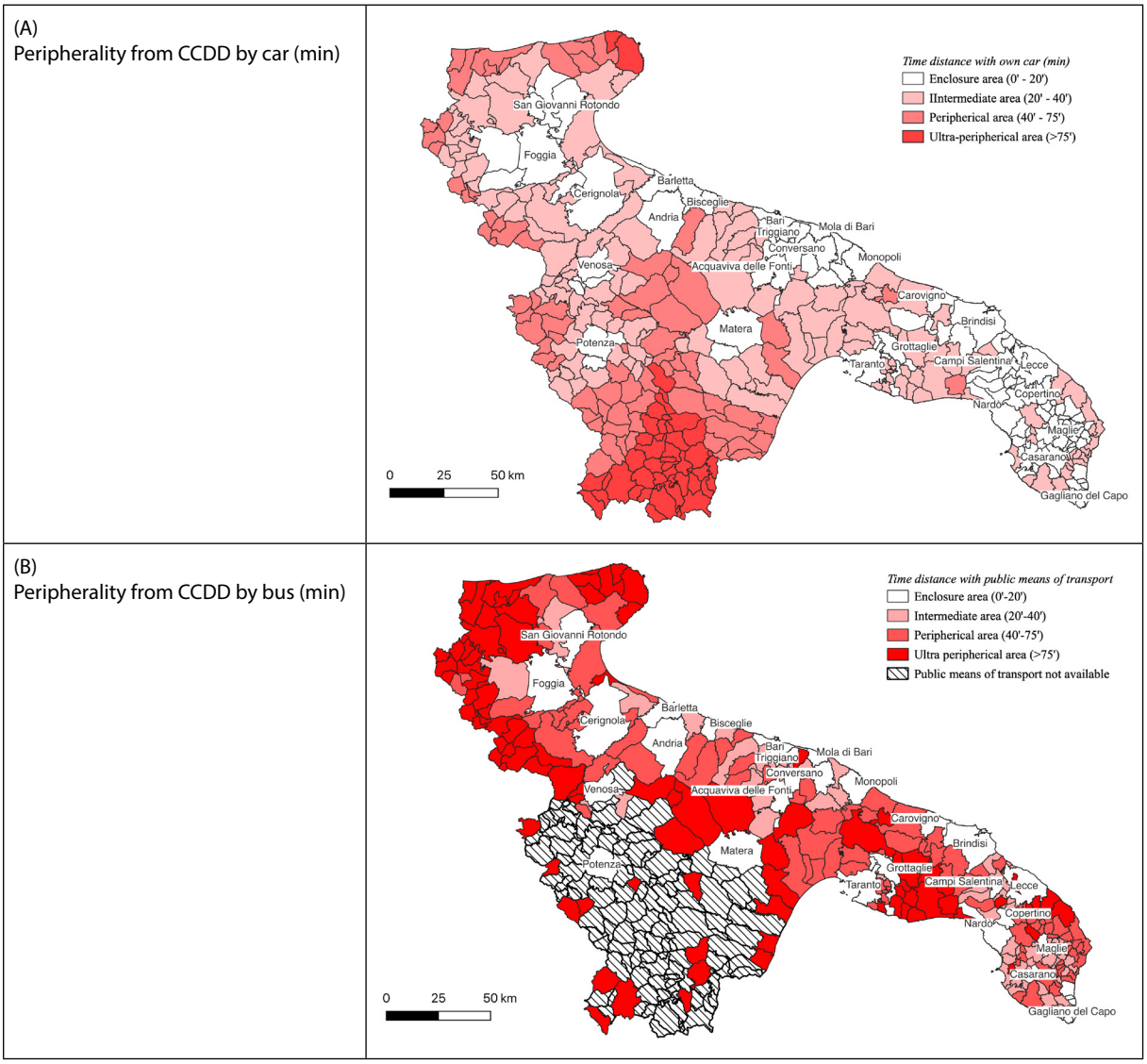


Figure 1
Peripherality. The map (A) depicts the peripherality of each municipality relative to its assigned CCDD, measured in terms of travel time by car. The map (B) depicts the peripherality of each municipality relative to its assigned CCDD, measured in terms of travel time by public means of transport. Referring to the strategy for Inner Areas in Italy developed by the Italian Agency for Territorial Cohesion (Barca *et al.*, 2014 [18]), municipalities were classified into "service delivery centres" if a CCDD is located in the municipality (labels), "enclosure area", with time travel less than 20 minutes (white); "intermediate area", between 20 and 40 minutes (pink); "peripheral area", between 40 and 75 minutes (dark pink); and "ultra-peripheral area", if the time travel exceeds 75 minutes (red). The analysis (A) shows the presence of two ultra-peripheral areas in Basilicata and the province of Foggia. The analysis (B) shows the presence of many ultra-peripheral areas and the absence of Public Transport services that connect municipalities to CCDDs in Basilicata.

and the service is usually provided in hospitals (14 hospital services, one university, and five territorial services). Clinicians have worked in the Centres for an average of 15.21 years (SD=11.94, range=2-40). Additionally, in addition to their medical specialty, most clinicians who completed the survey were Medical Executives (7 out of 20). Concerning referral, neurologists (8/20) often refer patients to the service. People were most likely to find general information about CCDDs on the online reservation platform of the public health service – CUP (14/20), the CCDD website (6/20) and the website of Apulia and Basilicata Region (3/20). According to respondents' estimates, an average of 605 citizens per year require access to the service (SD=373.50, range 50-1,500), most of which are women (58.14%) compared to 42.72% males. Respondents also rated the frequency of access requests by patients' age range (i.e., 40-49, 50-59, 60-69, 70-79, 80-89, >90) and years of education (i.e., 0-5, 6-8, 9-13, >13). Ten out of 20 centres are often contacted by people aged 70 to 89, and 12/20 are very often contacted by people older than 90. Sixteen out of 20 centres indicated patients' education range between 6 and 8 years of school (which correspond to partially or fully attending middle school). High-educated citizens consult the services less frequently. Non-Italian citizens rarely require access to the

service. Regarding the diagnoses issued by the CCDDs (see *Figure 2*), patients are very often diagnosed with Alzheimer's dementia (12/20) and often with Vascular dementia (12/20). Parkinson's disease and mild cognitive impairment are diagnosed sometimes (10/20 and 8/20, respectively). Lewy Body dementia has the lowest frequency of diagnosis (7/20). Concerning instrumental exams to support the diagnosis, structural and functional neuroimaging are employed, respectively very often (12/20) and often (9/20) (see *Figure S3 available online as Supplementary Materials*).

Survey section two: neuropsychological assessment characteristics

Clinicians use standard protocols (5/17), which can be modified, if necessary (9/17), or *ad-hoc* protocols (4/17), in neuropsychological evaluation. Regarding the composite neuropsychological battery, Mini-Mental State Examination (MMSE) is the most widely used tool (see *Table 1*), while the most used cognitive tests are Clock Drawing Tests, Verbal Fluency Tests, Frontal Assessment Battery (FAB), Babcock short-story, and Rey Auditory Verbal Learning Tests (RAVLTs) (see *Table 2*). The Geriatric Depression Scale (GDS) (16/17), Neuropsychiatric Inventory (NPI) (9/17) and Hamilton Depression Rating Scale (HDRS) (7/17) are the most used scales to assess emotional and behavioural diseases. Clinicians usually choose the Instrumental Activities of Daily Living Scale (IADL) (15/17) and the Index of Independence in Activities of Daily Living (ADL) (15/17). To correct patients' scores obtained in neuropsychological testing, clinicians employ normative data from the Italian population. Corrected scores are based on Italian Normative Data published in the literature (10/17), in the test manual (10/17), and International Normative Data (2/17). The score is reported as Corrected Scores (16/17), Equivalent Scores (5/17), and also Raw Scores (5/17). The standardised diagnostic criteria most used is the DSM-5 (9/17), only five CCDDs consult consensus conferences. Three CCDDs declare to use the DSM-IV-TR. Sixteen out of 17 clinicians (i.e., psychology, geriatrician and neurologist) know the existence of the national guidelines on Diagnostic, Therapeutic and Care Pathways (DTCP) for dementia.

DISCUSSION

This study aimed to map the CCDDs in two Italian regions: Apulia and Basilicata. The study focused on the accessibility of CCDDs, clinical practices adopted by the services, patients' characteristics, the type of diagnoses, and professional figures working in the services. Moreover, the study analysed the neuropsychological assessment used by the CCDD services. The survey involved universities, hospitals and territorial healthcare services (ASL) indicated as CCDD. It is important to highlight that this is the first study to use a mixed methods approach, consisting of geospatial analysis and surveys to provide an updated map of available CCDDs, their accessibility and clinical practices.

Firstly, we examine the accessibility of CCDDs in these two regions and provide visual maps of geospatial access indicators. These indicators consider the distance from each municipality to the reference CCDD based on the type of transport (i.e., private *vs* public). The GIS approach enabled the study of the distribution of CCDDs in the territory and the analysis of their accessibility profile. The differences between Apulia and Basilicata are emblematic of Italy's diverse territorial fabric. In Basilicata, the first data that emerges is the lack of public transport service in many municipalities due to the predominantly mountainous terrain and poor road network. This fact highlights that many citizens are forced to use their own means of transport to reach a CCDD, which takes more than an hour. Given

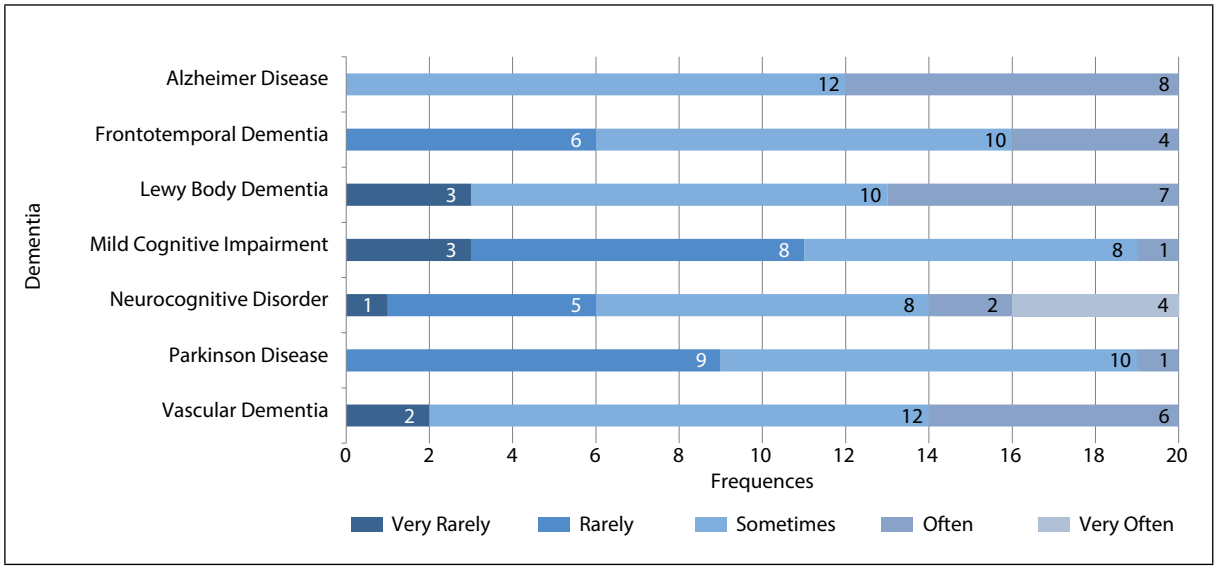


Figure 2
Type of diagnosis. The graph reports the distribution of responses (on a closed-ended matrix question answered on a 5-point scale Likert scale), regarding types of diagnoses issued.

Table 1
Global functioning battery. The Table shows the frequency of responses and the number of CCDD that completed the survey. Participants selected more than one answer

Neuropsychological Battery	Frequency	Number of CCDDs
Mini Mental State Examination (MMSE)	17	17
Clinical Dementia Rating (CDR)	10	17
Montreal Cognitive Assessment (MoCA)	5	17
Addenbrooke's Cognitive Examination Revised (ACE-R)	5	17
Alzheimer's Disease Assessment Scale (ADAS)	3	17
Severe Impairment Battery (SIB)	3	17
Milan Overall Dementia Assessment (MODA)	3	17
Wechsler Adult Intelligence Scale (WAIS)	3	17
Brief Neuropsychological Exam (ENB)	1	17
Frontal Assessment Battery (FAB)	13	17

CCDDs: Centres for Cognitive Disorders and Dementias.

Table 2
Neuropsychological tests. The Table reports the frequency of use of individual neuropsychological tests used to evaluate cognitive abilities, as well as the number of CCDDs that completed the survey. Participants selected more than one answer

Neuropsychological test	Frequency	Number of CCDDs
Clock Drowing Test	16	17
Short Stories	13	17
Verbal Fluency	12	17
Rey Auditory Verbal Learning Test (RAVLT)	12	17
Visual Search-Attentional Matrix	11	17
Rey-Osterrieth Complex Figure (ROCF)	11	17
Digit Span	9	17
Raven's Progressive Matrices	9	17

CCDDs: Centres for Cognitive Disorders and Dementias.

the characteristics of patients attending a CCDD, who are older adults and often unable to drive, this increases the dependency on caregivers and significantly adds to the burden of care [19].

The presence of only three CCDDs in Basilicata, primarily concentrated near the border with Apulia, indicates an uneven distribution of services across the region. Although the service better covers the most populated areas, policymakers should consider opening new CCDDs or branches of existing ones in the southern part of the province of Potenza. In Apulia, however, the distribution and number of CCDDs are adequate. However, the main problem with access to services in this region is communication. The absence of an official list has made it extremely difficult to identify CCDDs in the region, with a high probability that some CCDDs have been omitted. Concerning public accessibility, this highlights a significant challenge in easily sending and receiving information about the location of an essential service for people with dementia and their families. The geospatial analysis highlighted ultra-peripheral areas in the provinces of Potenza and Foggia. Excessive distance from a CCDD could jeopardise easy access to diagnostic assessment and the possibility of participating in psychosocial interventions, which require a certain consistency over time to be effective. As suggested in American studies for rural areas, remote services (telemedicine) could be a reasonable solution to reduce the gap in the distribution of services [20].

A recent study conducted by Tarlow *et al*. [21] proposes an effective approach to bolstering the accessibility of local health services in rural regions. The study explored the implementation of a "hub and spoke" telehealth model, which considered various factors such as geography, socioeconomic conditions, transportation, and healthcare-related challenges faced by clients. The authors also examined policies aimed at reducing disparities and bridging the digital divide. Additionally, local community leaders were involved in identifying access points based on available resources, with an administrative hub located in the city or town with the largest population. Considering the southern Italian towns' geographical characteristics, a central hub could be established to facilitate telemedicine services with a nurse who can provide in-person assistance to patients and caregivers, particularly those who may not be sig-

nificantly aided by technology due to advanced age. This service could also enable early access to treatment in the early stages of the disease, when patients may delay seeking medical attention due to the distance from healthcare facilities or a lack of accompanying support.

Some important evidence emerges about the characteristics of the population. Our results show that 58.14% of females require access to the service compared to 42.72% of males. Among the 20 centres, ten are often contacted by people aged 70 to 89, and 12 are often contacted by people older than 90. Sixteen out of 20 facilities indicated that patients' education ranged from 6 to 8 years (corresponding to partially or fully attending middle school). The frequency scores indicate that patients are very often diagnosed with Alzheimer's dementia (12/20) and often with Vascular dementia (12/20). Mild Cognitive Impairment and Parkinson's disease are sometimes diagnosed (10/20 and 8/20, respectively); Lewy Body dementia is the least common (7/20). Our results are consistent with prevalence reported in previous studies [22]. A comparison of our results with the Italian study confirms the high prevalence of Alzheimer's disease in Basilicata and Apulia.

As concerns the instrumental exams to support the diagnosis, structural and functional neuroimaging are employed, respectively, very often (12/20) and often (9/10) in Basilicata and Apulia, despite the suggested methods. In fact, as indicated by the European consensus to diagnose MCI and mild dementia [15], 93% of European clinicians use MRIs, while 92% and 68% use CSF biomarkers and FDG-PETs, respectively. Seventy-seven per cent of clinicians have not used tau-PET tracers [23, 24]. Moreover, Gustavsson *et al*. [25] proposed that estimating the prevalence of amyloid-positive populations could provide relevant Alzheimer's disease (AD) prevalence estimates. Based on this, it is evident that instrumental exams in Basilicata and Apulia are rarely used to support diagnostic diagnoses, as suggested in Consensus Conferences and academic memory clinics across Europe. It is essential to underline that using the appropriate and suggested tools may prevent misdiagnoses, improve patient outcomes, guide caregivers to provide better care, and could be fundamental for the effective prescription of the upcoming disease-modifying therapies for Alzheimer's disease.

The majority of CCDDs in the target regions participated in and completed the survey. Only in the province of Bari was the proportion of respondents lower than that of non-respondents. In these two regions, CCDDs are mainly located in hospitals and, to a lesser extent, in territorial services. Only one CCDD is located in a university. No significant differences were found between respondents and non-respondents in terms of setting location. Another important finding of our study is the diversity of diagnostic criteria and tools used in clinical practice, despite the well-established international criteria [14]. The diagnostic criteria most used is the DSM-5 (9/17), and only five CCDD consult consensus conferences. Three CCDDs declare to use DSM-IV-TR, which could be considered unusual criteria to diagnose dementia.

According to an analysis of the neuropsychological tests conducted in 501 Italian CCDDs [12], the most commonly used tests for cognitive disorders and dementia are MMSE (i.e., used in all CCDDs involved), Clock Drawing Test, Semantic and phonemic Fluency, Rey Auditory Verbal Learning Tests (RAVLTs), Babcock Short-Story, and Trail Making Test. Our research confirms these results, identifying MMSE as the test used in all the 17 CCDDs as first-level screening. Also, we identified other neuropsychological tests used in the CCDDs, such as the Frontal Assessment Battery (FAB), Rey-Osterrieth Complex Figure (ROCF) and Spinnler and Tognoni's Figure Copying Tasks for visuospatial and constructional ability, as well as Raven's Progressive Matrices considered as second level assessment in clinical practice. The survey demonstrates an important aspect: four out of 17 CCDDs perform only a first-level neuropsychological evaluation, administering only MMSE, CDR, Clock Drawing Test and some behavioural batteries as GDS, and three of them are hospital services. The importance of adequate neuropsychological assessment cannot be overstated, as it is crucial for accurately identifying the type of dementia even at an early stage, avoiding misdiagnosis, and providing the opportunity for early intervention. However, considering the recommendations of some international consensus conferences [16, 17], it is worth noting that some recommended tests (e.g., Free and Cue Selective Reminding Test (FCSRT) and Set Test; for the FCSRT, see also recent meta-analysis by Macchitella *et al*. [26]), and cognitive domains and skills (e.g., social cognition) were underused or undervalued. Research has consistently demonstrated that timely and precise diagnosis and care, including pharmacological, behavioural, and psychological interventions, can significantly slow the progression of dementia and enhance the quality of life of patients and caregivers [27]. Additionally, the adoption of uniform diagnostic criteria and instruments would facilitate patient assessment across CCDDs and ensure consistent care for patients, even when attending different healthcare services [15, 16]. Neuropsychological assessments in CCDDs are typically performed by neurologists, neuropsychologists, or psychologists with expertise in neuropsychology. It is essential to have a diverse range of competencies to correctly identify and care for patients affected by cognitive disorders or dementia. All of the CCDDs that participated in our survey employ multidisciplinary teams; it is crucial to involve experts in neuropsychology who are specifically trained to conduct comprehensive assessments of individuals' cognitive functioning. Some guidelines for the diagnosis of dementia recommend that a thorough neuropsychological evaluation should be conducted by neuropsychologists or by "*someone trained in neuropsychology*" [28]. Notably, in Italy as well as at the international level, specific and advanced training in neuropsychology is only provided in psychology degree programs and postgraduate courses in neuropsychology, and psychologists with this specific and advanced training are considered neuropsychologists. Despite this, to date, Italian law does not set any limits on practising neuropsychology; therefore, any psychologist, physician, pedagogist, or rehabilitation therapist may use some

diagnostic tools (such as tests) that are not classified as for psychologists' use only or offer neuropsychological rehabilitation, even if they have never attended education or training in clinical neuropsychology [10].

We found no obvious differences in the organisation and procedures used by territorial, hospital and university CCDDs. All CCDDs perform a first-level neuropsychological assessment; however, the second-level neuropsychological assessment in the Basilicata and Puglia CCDDs lacks common criteria and procedures. As a result, evaluations obtained in different CCDDs, or the same CCDD at different time points cannot be directly compared, making it difficult to track patients' health over time. Instead, consistent evaluation criteria are essential to collaboration among medical practitioners. From a different point of view, neuropsychological evaluations are often referenced by other healthcare professionals such as neurologists and geriatricians and clear, consistent criteria would facilitate their understanding and efficient use of information. Improving the coordination of medical interventions is an important goal set by the Ministerial Decree n. 70 of 04/02/2015 [29], which presents qualitative, structural, technological, and quantitative standards relating to hospital assistance. In order to achieve such standards, each region needs to develop a DTCP setting common guidelines for hospital services as well as a system to monitor the effectiveness and efficiency of the chosen treatments. Almost all the clinicians who completed the survey affirmed to be acknowledged with the existence of national guidelines about DTCP for dementia, although there are no DTCPs in Apulia and Basilicata. The detailed geographical data collected during this study will be a precious instrument to tailor Apulia and Basilicata's DTCP to the specific distribution of population and services on the territory, for instance, considering tele-neuropsychology and telemedicine to reach the most isolated communities.

CONCLUSION

In conclusion, using a mixed-method approach, the present study provides a comprehensive map of the services addressing cognitive disorders and dementia in these two southern Italian regions, highlighting strengths and criticalities, given the recent effort to provide a unitary theoretical, legislative and operational framework. These findings underscore the necessity to harmonise access to CCDDs in the two regions studied and the procedures for assessing cognitive, behavioural and functional symptoms. Due to the geographical challenges of the territory and the difficulties in travel and public transportation, offering telemedicine and teleneuropsychology services would be ideal. The administration of online neuropsychological tests has been investigated in several studies over the last few years, with promising results and applications [30, 31].

Our survey suggests a fundamental issue for future research, and our results also emphasise the importance of adhering to the National Dementia Plan to gain a better understanding of the epidemiology of dementia and to establish an integrated care pathway from diagnosis to treatment of these disabling pathologies by developing DTCP in the two regions. Additionally, incorporating cognitive stimulation into CCDD is advisable to prevent cognitive decline and improve disease outcomes. Clinical trials have demonstrated the effectiveness of Cognitive Training and Cognitive Rehabilitation programs for patients with MCI and dementia. Combining cognitive interventions with psychosocial support might yield more comprehensive benefits for the population [32]. Cognitive Reserve studies underscore the promotion of wellness by emphasising the advantages of maintaining physical, cognitive, and socially active lifestyles for public health [33]. To proactively address dementia risk factors and assist affected patients, the Health Care System must consider and incorporate all these aspects into the prevention, support, and treatment perspective.

Ethics approval and consent to participate

The Ethical Committee of Salento University and the Local Health Authority of Lecce (Italy) approved the study (Protocol n. 174371/2020). Participants were volunteers and did not receive any compensation.

Availability of data and materials

The data that support the findings of this study are available from the corresponding Author, ER, upon reasonable request.

Funding

This research benefited from a grant from Fondazione Con il Sud for the project "Demenza Network" (Ref N 2018-PDR-01233).

Acknowledgements

The Authors express their gratitude to the general managers of the ASLs of Apulia and Basilicata, as well as to all the healthcare professionals who participated in the survey.

Conflict of interest statement

Authors have no competing interest to declare.

Received on 1 December 2024.
Accepted on 26 May 2025.

REFERENCES

1. Graves BA. Integrative literature review: a review of literature related to geographical information systems, healthcare access, and health outcomes. Perspect Health Inf Manag. 2008;5:11.
2. Rousson V, Paccaud F. A set of indicators for decomposing the secular increase of life expectancy. Population Health Metrics. 2010;8(1):1-9. doi: 10.1186/1478-7954-8-18
3. Betti M, De Tommaso CV, Maino F. Health inequalities in Italy. Comparing regions among prevention, commu-

nity health services and hospital assistance. Soc Dev Issues. 2023;45(1):61-76.
4. Presidenza del Consiglio dei Ministri Conferenza Unificata. Provvedimento 30 ottobre 2014. Accordo, ai sensi dell'articolo 9, comma 2, lett. c) del decreto legislativo 28 agosto 1997, n. 281, tra il Governo, le regioni e le province autonome di Trento e di Bolzano, le province, i comuni e le comunità montane sul documento recante: "Piano nazionale demenze - Strategie per la promozione ed il miglioramento della qualità e dell'appropriatezza degli interventi assistenziali nel settore delle demenze". Gazzetta Ufficiale - Serie Generale n. 9, 13 gennaio 2015.
5. Bacigalupo I, Giaquinto F, Salvi E, Carnevale G, Vaccaro R, Matascioli F, Remoli G, Vanacore N, Lorenzini P. Permanent Table of the National Dementia Plan Study Group and the CCDDs Study Group. Neurol Sci. 2024;45(2):525-38. doi: 10.1007/s10072-023-06958-8
6. Kim J, Kim DH, Lee J, Cheon Y, Yoo S. A scoping review of qualitative geographic information systems in studies addressing health issues. Soc Sci Med. 2022;314:115472. doi: 10.1016/j.socscimed.2022.115472
7. Pierse T, Keogh F, O'Shea E, Cullinan J. Geographic availability and accessibility of day care services for people with dementia in Ireland. BMC Health Serv Res. 2020;20(1):476. doi: 10.1186/s12913-020-05341-z
8. Nykiforuk CI, Flaman LM. Geographic information systems (GIS) for health promotion and public health: a review. Health Promot Pract. 2011;12(1):63-73. doi: 10.1177/1524839909334624
9. Cromley EK. GIS and disease. Annu Rev Public Health. 2003;24:7-24. doi: 10.1146/annurev.publhealth.24.012902.141019
10. Salvadori E, Pantoni L. Società Italiana di NeuroGeriatria (SINEG). The role of the neuropsychologist in memory clinics. Neurol Sci. 2020;41(6):1483-8. doi: 10.1007/s10072-020-04253-4
11. Onida A, Di Vita A, Bianchini F, Rivera D, Morlett-Paredes A, Guariglia C, Arango-Lasprilla JC. Neuropsychology as a profession in Italy. Appl Neuropsychol Adult. 2019;26(6):543-557. doi: 10.1080/23279095.2018.1466782
12. Di Pucchio A, Vanacore N, Marzolini F, Lacorte E, Di Fiandra T; I-DemObs Group; Gasparini M. Use of neuropsychological tests for the diagnosis of dementia: a survey of Italian memory clinics. BMJ Open. 2018;8:e017847. doi:10.1136/bmjopen-2017-017847
13. American Psychiatric Association, American Psychiatric Association DSM-5 Task Force. Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.
14. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack Jr CR, Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011;7(3):263-9. doi: 10.1016/j.jalz.2011.03.005
15. Festari C, Massa F, Cotta Ramusino M, Gandolfo F, Nicolosi V, Orini S, et al. European consensus for the diagnosis of MCI and mild dementia: preparatory phase. Alzheimers Dement. 2023;19(5):1729-41. doi: 10.1002/alz.12798
16. Costa A, Bak T, Caffarra P, Caltagirone C, Ceccaldi M, Collette F, et al. The need for harmonization and innovation of neuropsychological assessment in neurodegenerative dementias in Europe: consensus document of the Joint Program for Neurodegenerative Diseases Working Group. Alzheimers Res Ther. 2017;9(1):27. doi: 10.1186/s13195-017-0254-x
17. Boccardi M, Monsch AU, Ferrari C, Altomare D, Berres M, Bos I, et al. Harmonizing neuropsychological assessment for mild neurocognitive disorders in Europe. Alzheimers Dement. 2022;18(1):29-42. doi: 10.1002/alz.12365
18. Barca F, Casavola P, Lucatelli S. Strategia nazionale per le aree interne: definizione, obiettivi, strumenti e governance. Roma: Ministero dello Sviluppo Economico, Dipartimento per lo Sviluppo e la Coesione Economica, Unità di Valutazione degli Investimenti Pubblici; 2014.
19. Merriman N, Mackey L, Fernandez EG, Curran F, Caulfield B, Power D, et al. 190 connected health sustaining home stay in dementia (chess): factors associated with the burden experienced by caregivers of people with dementia. Age Ageing. 2022;51(3):afac218.163. doi: 10.1093/ageing/afac218.163
20. Sekhon H, Sekhon K, Launay C, Afililo M, Innocente N, Vahia I, et al. Telemedicine and the rural dementia population: a systematic review. Maturitas. 2021;143:105-14. doi: 10.1016/j.maturitas.2020.09.001
21. Tarlow KR, McCord CE, Du Y, Hammett J, Wills, T. Rural mental health service utilization in a Texas telepsychology clinic. J Clin Psychol. 2020;76(6):1004-14. doi: 10.1002/jclp.22903
22. Filippi M, Cecchetti G, Cagnin A. et al. Redefinition of dementia care in Italy in the era of amyloid-lowering agents for the treatment of Alzheimer's disease: an expert opinion and practical guideline. J Neurol. 2023;270:3159-70. doi: 10.1007/s00415-023-11642-0
23. Sancesario GM, Toniolo S, Chiasserini D, Di Santo SG, Zegeer J, Bernardi G, et al. The clinical use of cerebrospinal fluid biomarkers for Alzheimer's disease diagnosis: the Italian selfie. J Alzheimers Dis. 2017;55(4):1659-66. doi: 10.3233/JAD-160975
24. Nobili F, Arbizu J, Bouwman F, Drzezga A, Agosta F, Nestor P, et al. EANM-EAN recommendations for the use of brain 18 F-Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) in neurodegenerative cognitive impairment and dementia: Delphi consensus. Eur J Neurol. 2018;25(10):1201-17. doi: 10.1111/ene.13728
25. Gustavsson A, Norton N, Fast T, Frölich L, Georges J, Holzapfel D, et al. Global estimates on the number of persons across the Alzheimer's disease continuum. Alzheimers Dement. 2023;19(2):658-70. doi: 10.1002/alz.12694
26. Macchitella L, Tosi G, Giaquinto F, Iaia M, Rizzi E, Chiarello Y, et al. Genuine memory deficits as assessed by the Free and Cued Selective Reminding Test (FCSRT) in the behavioural variant of frontotemporal dementia. A systematic review and meta-analysis study. Neuropsychol Rev. 2024;34(3):823-37. doi: 10.1007/s11065-023-09613-3
27. Porsteinsson AP, Isaacson RS, Knox S, Sabbagh MN, Rubino I. Diagnosis of early Alzheimer's disease: clinical practice in 2021. J Prev Alzheimers Dis. 2021;8(3):371-86. doi: 10.14283/jpad.2021.23
28. Waldemar G, Dubois B, Emre M, Georges J, McKeith IG, Rossor M, et al. Recommendations for the diagnosis and management of Alzheimer's disease and other disorders associated with dementia: EFNS guideline. Eur J Neurol. 2007;14(1):e1-26. doi: 10.1111/j.1468-1331.2006.01605.x
29. Ministero della Salute. Decreto ministeriale 2 aprile 2015, n. 70. Regolamento recante definizione degli standard qualitativi, strutturali, tecnologici e quantitativi relativi all'assistenza ospedaliera. Gazzetta Ufficiale – Serie Generale n. 127, 4 giugno 2015.
30. Rizzi E, Vezzoli M, Pegoraro S, Facchin A, Strina V, Daini R. Teleneuropsychology: normative data for the

assessment of memory in online settings. Neurol Sci. 2023;44(2):529-38. doi: 10.1007/s10072-022-06426-9

31. Sperling SA, Acheson SK, Fox-Fuller J, Colvin MK, Harder L, Cullum CM, et al. Tele-neuropsychology: from science to policy to practice. Arch Clin Neuropsychol. 2024;39(2):227-48. doi: 10.1093/arclin/acad066
32. Giaquinto F, Iaia M, Rizzi E, Macchitella L, Romano DL, Tosi G, Angelelli P. Cognitive training for Alzheimer's disease and other forms of dementia: insights from a systematic review and Bayesian meta-analysis. J Alzheimers Dis. 2025;105(4):1252-74. doi: 10.1177/13872877251334795
33. Giaquinto F, Tosi G, Abbatantuono C, Pepe I, Iaia M, Macchitella L, et al. The indirect effect of cognitive reserve on the relationship between age and cognition in pathological ageing: a cross-sectional retrospective study in an unselected and consecutively enrolled sample. J Neuropsychol. 2023;17(3):477-90. doi: 10.1111/jnp.12323

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 191-198
DOI: 10.4415/ANN_25_03_05

Can we trust administrative data in joint arthroplasty? A validation study against the Italian Arthroplasty Registry data as a gold standard

Enrico Ciminello[1], Riccardo Valentini[2], Paola Laricchiuta[1], Saif Aldeen Madi[3], Eugenio Carrani[1], Tiziana Falcone[1], Stefania Ceccarelli[1], Paola Ciccarelli[1] and Marina Torre[1]

[1]*Segreteria Scientifica del Presidente, Istituto Superiore di Sanità, Rome, Italy*
[2]*Dipartimento di Ingegneria Informatica, Automatica e Gestionale, Sapienza Università di Roma, Rome, Italy*
[3]*Dipartimento di Informatica, Sapienza Università di Roma, Rome, Italy*

Abstract

Introduction. Hospital Discharge Data (HDD) can be a valuable source of information for epidemiological research, but in Italy its accuracy in arthroplasty has not yet been determined on a large scale. The aim is to assess Italian HDD accuracy in reporting clinical information on hip/knee arthroplasties, using RIAP data collected by the Italian Arthroplasty Registry (RIAP) as a reference.

Methods. Coding systems for procedures and diagnoses in RIAP data and HDD for years 2007-2021 are mapped to a common list of items describing surgical procedures and related diagnoses. The ability of HDD in predicting procedures and diagnoses is evaluated by sensitivity, specificity and accuracy, while using RIAP data as a reference.

Results. Surgical procedures and causes for elective and urgent arthroplasties are predicted by HDD with at least 96% sensitivity. Performances drop when evaluating procedures and diagnoses at fine-grain level and for rare events.

Discussion. HDD reports reliable clinical information in arthroplasty and is an effective tool for epidemiological purposes. Nonetheless, a cautious approach must be considered when dealing with high-detail and rare events.

Key words

- registries
- administrative data
- discharge records
- validation study
- arthroplasty
- public health

INTRODUCTION

Hip and knee arthroplasties have experienced a significant increase over the last fifteen years. In OECD countries, the rates of total hip (THA) and total knee (TKA) arthroplasties increased by 22% and 35% between 2009 and 2020 and reached an average of 172 and 119 per 100,000 population, respectively [1, 2]. Moreover, future projections indicate that these numbers are expected to grow in the future [3-5]. In Italy, from 2001 to 2021 the average annual increase rate of THA and TKA was 2.3% and 5.4%, respectively [6].

Hospital Discharge Data (HDD) includes administrative, demographic, and clinical information on all the hospital admissions performed at the national level, enabling large-scale epidemiological studies at the population level. Conceived as a tool to define hospital reimbursement for the admission, HDD does not consider specific device and surgery details, which would allow for an effective surveillance of implants. To fill this gap, in 2006 the Italian Ministry of Health and the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) set up, as a joint effort, the Italian Arthroplasty Registry (Registro Italiano ArtroProtesi, RIAP) with the aim of establishing a national data collection system for monitoring outcomes of procedures and safety of the implanted devices [7]. Waiting for the Regulation that will make data collection mandatory [8], the RIAP data collection is currently on a voluntary basis and covers only about 35% of the national volume [9]. Therefore, HDD might represent a useful tool for carrying out epidemiological studies, due to its national coverage of hospital stay records, which equals 98.9% [10].

In Italy, for arthroplasties, HDD have been used in studies measuring risk adjusted mortality after surgery [11]. However, several authors emphasized the need to assess the reliability of HDD in providing clinical knowledge before using these data for secondary research to perform unbiased statistical and epidemio-

Address for correspondence: Enrico Ciminello, Segreteria Scientifica del Presidente, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: enrico.ciminello@iss.it.

logical population-based analyses [12-17]. Currently available Italian validation studies have targeted other sub-populations of HDD [18-20], or are related to arthroplasty but including data on a smaller scale [21] or addressed the type of surgical procedures only [22, 23].

The present paper aims to evaluate the accuracy of clinical information on the type of arthroplasty procedures and diagnoses reported in the HDD when compared with the data collected by RIAP.

MATERIALS AND METHODS

Data source

RIAP collects information from regions and health structures participating on a voluntary basis. The list of regions and structures with details of the period of their participation available in the Italian Arthroplasty Registry Report [9]. The information collected in registry records includes an HDD part, containing patient demographics and data on hospitalization, clinical procedures and diagnoses, and an additional part, referred to as Minimum Dataset (MDS), containing registry-specific variables that cover knowledge specific to arthroplasties and associated devices. Surgical procedures and diagnoses are filled in both parts, but with different levels of detail depending on the different purposes of the variable collections. Procedure and diagnosis variables in HDD are coded using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) standard, while the MDS has its own coding system [24, 25]. RIAP participating institutions link the HDD and the MDS parts in each record and upload them on dedicated platforms [26]. Subsequently, data is prepared, integrated and cleansed, to flow into the RIAP Ontology-based data layer (composed by an ontology and a relational database) [27].

Study population

The study population consisted of all records stored in the RIAP database, related to hip and knee arthroplasties performed in years 2007-2021 that successfully passed a syntactic and semantic quality check [28] and that report the codes for type of intervention and cause of intervention listed in *Table A1* and *Table A2 available online as Supplementary Materials*. The syntactic check admitted only those records whose values have been entered correctly (i.e., falling within the correct domain as described by RIAP record sets [24, 25]), while the semantic check ensured the compatibility of diagnoses with procedures and of each procedure type with previous procedures *(Figure 1)* [27].

Statistical analysis

Analysis on procedures

The ICD-9-CM and the MDS codes for procedures were mapped to two categories and five sub-categories related to hip, and two categories and four sub-categories related to knee. The mapping is shown in *Supplementary Table A1 available online*. If an ICD-9-CM code of interest appeared in any of the 11 available fields of the HDD part of a record, then the procedure was labelled with the category and sub-category associated with that code. For instance, if the code 81.51 was recorded in any of the fields, then it was associated with the intervention category "Primary" and the sub-category "Total primary". In the same way, the MDS part was labelled according to the code reported for the type of intervention. For example, if the code recorded in the type of intervention field was equal to "A1" in a record of hip arthroplasty, then the MDS part was associated to the category "Primary" and sub-category "Total primary". The reporting of procedure types by the HDD was checked against the MDS part, which was assumed to be the gold standard as it is specifically designed for the monitoring and the clinical exploration of the arthroplasty domain in Italy. In other words, the MDS labelling was considered as the true value of the variable, while the HDD labelling was considered its prediction. Hence, the correctness of the HDD in reporting clinical information was checked by looking at sensitivity, specificity, accuracy and kappa statistics derived by comparing true and such deterministically predicted values.

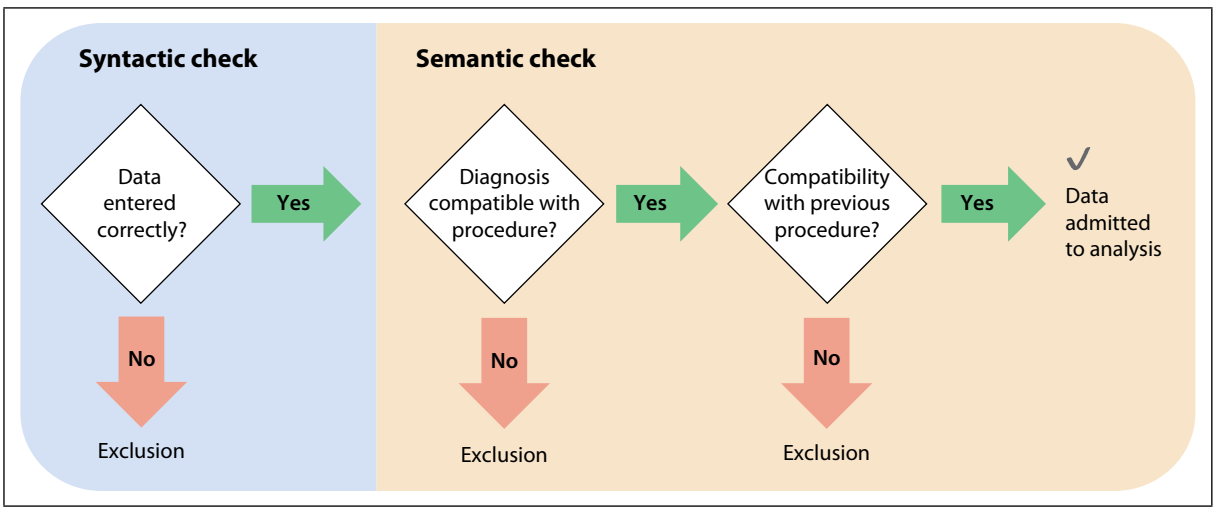


Figure 1
An illustration of RIAP's quality check process.

Analysis on diagnoses

The analysis of the diagnoses followed an approach similar to the one used for the procedures. The ICD-9-CM and MDS codes were mapped to the list of categories shown in *Supplementary Table A2 available online*. If a given ICD-9-CM code appeared in any of the six fields available for diagnoses in a record, then the HDD part of such intervention was labelled with the diagnosis. The same occurs with codes used for the cause of intervention (CAU1 or CAUR, depending on the record being considered as primary or revision in the registry database). Also in this case, the correctness of HDD was evaluated using sensitivity, specificity, accuracy and kappa statistics.

Possible geographical differences in the quality of the reported information were explored by a leave-one-out analysis, where the process was iteratively repeated and the evaluation measures were computed while leaving one geographical area (Italian region) out of the analysis at a time. The consistency of the results was assessed by reporting the resulting range of variation for the considered metrics.

The analysis was performed by using the software R version 4.2.3 (2023-03-15 ucrt) - Shortstop Beagle.

RESULTS

Between 2007 and 2021, a total of 578,419 records passed the RIAP quality checks and were related to hip and knee arthroplasties. From those, 46,433 records were excluded as they were related to spacer substitutions or they did not present the codes of interest in the field "cause of intervention". The final cohort consisted of 531,986 records (345,671 hip and 186,315 knee).

Table 1 shows the distribution of procedures and diagnoses among the analyzed records. Primary arthroplasties accounted for 94.3% of the analyzed procedures for hip (71.7% were total primary arthroplasties and 22.6% were partial primary arthroplasties) and 95.4% for knee. Revisions accounted for 5.7% of hip records (composed by 1.5% total revisions, 3.4% partial revision, 0.7% removal) and 4.6% of knee records (3.4% total revision, 1.1% partial revision, 0.1% removal).

Table 1
Distribution of procedures and diagnoses in the study population (N=531,986)

Hip		
Procedures	**N**	**%**
Primary	326,022	94.3
Total primary	*247,717*	*71.7*
Partial primary	*78,305*	*22.6*
Revision	19,649	5.7
Total revision	*5,343*	*1.5*
Partial revision	*11,906*	*3.4*
Removal	*2,400*	*0.7*
Overall	345,671	100
Diagnoses	**N**	**%**
Osteoarthritis	203,125	58.8
Reumatoid arthritis	970	0.3
Neoplasy	806	0.2
Necrosis	10,163	2.9
Malformation	7,894	2.3
Fracture	102,699	29.7
Sepsis	56	0.0
Pseudoarthrosis	309	0.1
Aseptic loosening	8,842	2.6
Periprosthetic fracture	2,373	0.7
Dislocation	2,910	0.8
Infection	1,610	0.5
Metallosis	4	0.0
Wear	1,719	0.5
Pain	1,250	0.4
Prosthesis fracture	313	0.1
Ostheolysis	628	0.2
Instability	453	0.09
Rigidity	187	0.04
Overall	345,671	100
Knee		
Procedures	**N**	**%**
Primary	177,701	95.4
Revision	8,614	4.6
Total revision	*6,427*	*3.4*
Partial revision	*1,960*	*1.1*
Removal	*227*	*0.1*
Overall	186,315	100
Diagnoses	**N**	**%**
Osteoarthritis	174,820	93.8
Reumatoid arthritis	1,194	0.6
Neoplasy	97	0.1
Necrosis	1,590	0.9
Aseptic loosening	3,716	2.0
Periprosthetic fracture	151	0.1
Dislocation	182	0.1
Infection	1,766	0.9
Wear	258	0.1
Pain	1,783	1.0
Prosthesis fracture	118	0.1
Instability	453	0.2
Rigidity	187	0.1
Overall	186,315	100

Continues

Table 1
Continued

The most frequent diagnoses for primary hip arthroplasties were osteoarthritis (58.8%) and fracture (29.7%), while aseptic loosening was the most common revision cause (2.6%). In knee, fracture cannot occur as a cause of joint replacement and osteoarthritis occurs in 93.8% of cases. Aseptic loosening was the most frequent diagnosis in knee revisions, associated to 2% of knee arthroplasties.

Table 2 and *Table 3* report the validity and accuracy data obtained from the analysis of the HDD codes (ICD9-CM) when compared to the MDS codes related to the procedures and diagnoses of interest, respectively.

All the metrics showed a high value for both main procedure categories (primary and revision) with sensitivity and specificity above 95% and accuracy above 99% (kappa 0.93 and 0.95) for both hip and knee. When considering also sub-categories, sensitivity, specificity and accuracy reached values above 90% for all kinds of procedures, except for the lower sensitivity values in partial revisions (69.9% hip; 65.5% knee) and removals (21.9% hip; 33.5% knee).

The large majority of diagnoses had a level of specificity above 98% and accuracy higher than 97% with the only exception of osteoarthritis, which showed lower values: 89.3% specificity and 93.3% accuracy were observed for hip, while 77.1% specificity and 95.8% accuracy were observed for knee arthroplasties. The sensitivity outcomes for diagnoses varied widely, resulting over 96% for osteoarthritis and fracture (in case of hip), equal to 72.9% and 64.4% for infection for hip and knee, respectively, and lower than 60% for the other revision associated diagnoses for both knee and hip.

The leave-on-out analysis confirmed that the geographical area of transmission does not affect the results, in particular when looking at procedure categories and diagnoses with high prevalence. Sensitivity of primary categories reaches 99.04% - 99.68% for hip and 99.15% - 99.64% for knee, while the values for the categories of revision are in the range 93.24% - 97.72% for hip and 92.58% - 96.51% for knee. On the other hand, the values for revision subcategories had wider range of variation by geographical area, but still low levels for the considered metrics, as observed in the overall analysis. The results for procedures from the leave-one-out analysis are reported in *Table B1 available online as Supplementary Material*. The sensitivity in reporting osteoarthritis is in the range 96.01% - 96.46% for hip and in the range 93.62%-98.59% for knee. The highest sensitivity in detecting causes of revision is infection for both hip and knee, with ranges of variation equal to 71.75% - 77.08% and 62.4% - 69.63%, respectively. The results for diagnoses from the leave-one-out analysis are reported in *Table B2 available online as Supplementary Material*.

DISCUSSION

This study, performed on large scale and involving more than five-hundred thousand administrative records, shows that the Italian HDD collects accurate information on arthroplasty procedures and the most frequent related diagnoses. The HDD can discriminate between macro-categories of operated joints and type of intervention, either primary or revision. Moreover, it can distinguish between elective and urgent interventions, as clinical information reported on fractures and osteoarthritis is reliable in over than 95% of records. The small portion of misclassified procedures might be explained by the surgeons' tendency to use the most frequent ICD9-CM codes to indicate the area of intervention (arthroplasty) instead of providing detailed codes that can discriminate procedures at a deeper level. An example of this can be observed when taking into account the relatively low values of sensitivity in partial revision classification (67.99%) and in total revision classification (92.93%) for hip. This could mean that surgeons correctly report a revision procedure, but

Table 2
Prediction metrics of investigated procedures

Hip	**Sensitivity (%)**	**Specificity (%)**	**Accuracy (%)**	**Kappa**
Primary	99.58	96.39	99.4	0.94
Total primary	98.43	97.02	98.03	0.95
Partial primary	96.56	98.85	98.33	0.95
Revision	97.22	99.56	99.43	0.95
Total revision	92.93	98.07	97.99	0.58
Partial revision	67.99	99.56	98.48	0.75
Removal	21.92	99.89	99.35	0.32
Knee	**Sensitivity (%)**	**Specificity (%)**	**Accuracy (%)**	**Kappa**
Primary	99.58	95.89	99.41	0.93
Revision	96.08	99.73	99.57	0.95
Total revision	93.43	99.35	99.14	0.88
Partial revision	65.51	99.86	99.5	0.73
Removal	33.48	99.63	99.55	0.15

Table 3
Prediction metrics of investigated diagnoses

Hip	Sensitivity (%)	Specificity (%)	Accuracy (%)	Kappa
Osteoarthritis	96.12	89.3	93.31	0.86
Reumatoid arthritis	30.21	99.78	99.59	0.29
Neoplasy	41.56	99.91	99.77	0.46
Necrosis	51.57	99.22	97.82	0.57
Malformation	16.52	99.74	97.84	0.25
Fracture	97.64	97.43	97.49	0.94
Sepsis	7.14	99.99	99.97	0.08
Pseudoarthrosis	62.14	99.37	99.34	0.14
Aseptic loosening	61.26	98.64	97.68	0.56
Periprosthetic fracture	54.4	99.84	99.53	0.61
Dislocation	45.57	99.57	99.11	0.46
Infection	72.86	99.53	99.41	0.53
Metallosis	0	100	100	0
Wear	27.52	99.92	99.56	0.38
Pain	1.68	99.83	99.48	0.02
Prosthesis fracture	20.45	99.79	99.72	0.11
Ostheolysis	21.97	99.9	99.75	0.24
Knee	**Sensitivity (%)**	**Specificity (%)**	**Accuracy (%)**	**Kappa**
Osteoarthritis	96.99	77.15	95.76	0.67
Reumatoid arthritis	29.4	99.78	99.33	0.36
Neoplasy	58.76	99.98	99.96	0.58
Necrosis	27.92	99.87	99.26	0.39
Aseptic loosening	27.91	99.12	97.7	0.31
Periprosthetic fracture	46.36	99.98	99.94	0.54
Dislocation	6.59	98.94	98.85	0.01
Infection	64.38	99.74	99.41	0.67
Wear	14.73	99.98	99.87	0.23
Pain	20.13	99.43	98.67	0.22
Prosthesis fracture	21.19	99.72	99.67	0.07
Instability	10.82	99.93	99.86	0.11
Rigidity	14.97	99.99	99.96	0.19

choose the code for "Total revision" to identify a "Partial revision". Similarly, the same can be observed for knee revisions, among which "Partial revision" and "Removal" cases have low sensitivity, as the codes of "Total revision" are mostly used to identify "Revision" in general.

This kind of situation is much more common when it comes to the diagnoses. The HDD does not predict the causes of intervention as it does with the procedures, and sensitivity hardly shows values higher than 50% for the rarest diagnoses, which are not always captured. This result might be partly due to the role of "Osteoarthritis", for which sensitivity and specificity are respectively over 95% and lower than 90%, as it includes the large majority of cases of elective intervention causes. These elective causes are then often misclassified resulting in a very low sensitivity. The opposite happens for the causes of urgent interventions (i.e., "fractures"), which are correctly classified in almost all records of interest.

These findings partially confirm, on a larger and national scale, the evidence found by Baglio *et al*. [21] on total hip replacements, who found 96.2% sensitivity of the Lazio Region Hospital Information System in reporting primary hip replacements and 89.3% sensitivity in reporting diagnoses with the main focus on osteoarthritis/arthritis and fractures. Also, Roof *et al*. [29] evaluated how accurate administrative data is in reporting knee revision, in this case by using ICD-10 coding. They found similar results to this study, as they detected a sensitivity of 98% in identifying that a revision procedure has occurred, but the percentage decreases to 76%

when predicting the correct type of revision in terms of the replaced component. However, other studies worldwide have shown different results. For example, Bozic *et al*. [30] assessed quality in reporting hip and knee revision procedures and related diagnosis by ICD-9-CM in four high-volume total joint arthroplasty centers in the USA. They found that sensitivity in predicting clinical information on procedures by administrative data was over 80% only for patellar component revisions in knee and for femoral and acetabular component revision in hip. Looking at the ability of administrative data to correctly predict diagnoses, Rennert-May *et al*. [31] found a sensitivity of 85% in their study based on ICD-10 coding and focusing on post-operative surgical site infection. Also, Wilson *et al*. [32], in their paper about accuracy in reporting diagnoses related to knee arthroplasty by ICD-10 coding, found levels of sensitivity comparable to those found in this work.

Other authors investigated the validity of Italian HDD in detecting diagnoses of interest in different health domains and evaluated its reliability for epidemiological purposes. They found good levels of sensitivity in identifying target diagnoses by testing ICD9-CM codes against external source of information, used as gold standard [33-35]. Moreover, from an international perspective, it is worth mentioning the study by Yamana *et al*. on validity of administrative data in Japan [36]. Indeed, they found a pattern similar to that described in this study, reporting a good performance in correctly detecting procedures and quite low levels of sensitivity in identifying diagnoses.

This study has several potential limitations. First, the RIAP data is assumed to be the gold standard and to correctly report both procedures and causes of intervention. However, no audit was performed to validate the accuracy of the reported clinical information, even though the dataset concerned has successfully undergone the RIAP quality check process. Second, the RIAP data covers just over 30% of arthroplasty procedures performed in Italy, with a non-homogeneous spatial distribution. This is because participation in the registry is on a voluntary basis and some regions were never covered, while others did not ensure a constant participation over time. As a consequence, this could introduce an information bias because of geographic and time specific coding practices with unpredictable impact on results in terms of magnitude and direction. Also, it could limit the generalizability of the findings of the present study, although it is worth noting that, in the study period, 13 regions, two autonomous provinces and seven single hospitals located in three different regions participated in the registry, and half of them provided information for nine or more years [9]. Nonetheless, the present study did not highlight any systematic patterns in the quality of the reported information by geographical area within the regions in RIAP. Indeed, the good reliability of HDD when used at the macro category level for procedures (primaries and revisions) and for identifying elective and urgent hospitalization was confirmed, because of the high levels of sensitivity for "Osteoarthritis" and "Fracture", which are consistent by region. On the other hand, detailed sub-categories for procedure and rare diagnoses show wider ranges of variation, but always on a low level of performance. Third, the quality in filling HDD may depend on reimbursement patterns and on Diagnosis Related Group (DRG) codes, which are computed as function of procedures and diagnoses reported in the HDD. A thorough analysis of DRG patterns and changes depending on reported ICD9-CM codes lies in the health economics field and is beyond the aim of this study but might be developed as a further work in collaboration with other bodies of the public National Healthcare System. Fourth, despite the number of codes considered covers all cases of clinical interest with over 200 ICD9-CM codes taken into account, relevant codes of interest may have been excluded unintentionally. Last, the approach to mapping between ICD9-CM and MDS codes is arbitrary and different choices of mapping between codes may lead to different conclusions.

In order to overcome coding and mapping issues, a data driven approach is recommended in the future to select ICD9-CM codes of interest in a sound manner and to build a more reliable mapping. In particular, supervised machine learning approaches may be able to detect associations that escape deterministic observation and arbitrary assumptions. The other mentioned issues could be addressed when the RIAP registry will be further developed at the national level.

In conclusion, the Italian HDD related to arthroplasties and their causes performs well in reporting clinical information when used at the level of macro categories, but caution is required when investigating sub categories of procedures and rare causes of intervention. These findings provide evidence for a careful use of HDD for epidemiological studies on arthroplasties and highlight the need to promote a more accurate coding for HDD. Further, developing a mandatory countrywide arthroplasty registry is crucial to obtain a more accurate picture of arthroplasty, not only to ensure an efficient implant surveillance, but also to allow comparisons and fill research gaps, pursuing the ultimate goal of a better clinical practice to enhance patient safety.

Acknowledgements

This study was carried on within the following projects:

"Italian implantable prostheses registry (RIPI): realisation of a platform integrating data flows for orthopaedic prostheses, spinal devices, pacemakers and defibrillators, heart valves", coordinated by the Italian National Institute of Health and supported by the General Directorate of Medical Devices and the Pharmaceutical Service of the Italian Ministry of Health.

"Italian implantable prostheses registry (RIPI): realization of a platform integrating data flows for orthopedic prostheses, spinal devices, pacemakers and defibrillators, heart valves," coordinated by the Italian National Institute of Health and supported by the General Directorate of Medical Devices and Pharmaceutical Service of the Italian Ministry of Health and within the "Project ECS 0000024 Rome Technopole – CUP B83C22002820006, NRP Mission 4 Component 2 Investment 1.5, Funded by the European Union – NextGenerationEU", Partner

Italian National Institute of Health, Spoke 2 (Technology transfer, new entrepreneurship, business incubation and acceleration) and Flagship project FP4 (Development, innovation and certification of medical and non-medical devices for health).

The Authors acknowledge Mascia Masciocchi, Attanasio Cornacchia and Alessia Biondi for their management support of the RIPI project.

Authors' contributions

ECi and MT: concept of the study; ECi: design of the study, data analysis and statistics; SAM, RV and ECa: data management, extraction and processing; ECi, PL, TF, PC, SC and MT: drafting of the manuscript; MT: coordination of the project. All Authors contributed to the interpretation and discussion of the results and content of the manuscript and approved the final version to be published.

Conflict of interest statement

The Authors declare no conflict of interest.

Received on 16 April 2025.
Accepted on 25 June 2025

REFERENCES

1. Organisation for Economic Co-operation and Development. Hip and knee replacement. In: Organisation for Economic Co-operation and Development. Health at a glance 2021: OECD Indicators. Paris: OECD Publishing; 2021.
2. Organisation for Economic Co-operation and Development. Hip and knee replacement. In: Organisation for Economic Co-operation and Development. Health at a glance 2023: OECD Indicators. Paris: OECD Publishing; 2023.
3. Romanini E, Decarolis F, Luzi I, Zanoli G, Venosa M, Laricchiuta P, Carrani E, Torre M. Total knee arthroplasty in Italy: reflections from the last fifteen years and projections for the next thirty. Int Orthop. 2019;43(1):133-8.
4. Nemes S, Rolfson O, W-Dahl A, Garellick G, Sundberg M, Kaerrholm J, Robertsson O. Historical view and future demand for knee arthroplasty in Sweden. Acta Orthop. 2015;86(4):426-31.
5. Inacio MCS, Paxton EW, Graves SE, Namba RS, Nemes S. Projected increase in total knee arthroplasty in the United States: an alternative projection model. Osteoarthr Cartilage. 2017;25(11):1797-803.
6. Ciminello E, Madi SA, Laricchiuta P, Torre M. Appendice A. Interventi di artroprotesi: analisi dei dati SDO nazionali 2020 e 2021. In: Registro Italiano Artroprotesi. RIAP: Report Annuale 2022. Roma: Il Pensiero Scientifico Editore; 2023.
7. Torre M, Romanini E, Zanoli G, Carrani E, Luzi I, Leone L, Bellino S. Monitoring outcome of joint arthroplasty in Italy: Implementation of the National Registry. Joints. 2017;5(2):70-8. doi: 10.1055/s-0037-1603899
8. Toccaceli V, Torre M. A far-reaching Regulation for the Italian National Registry of Implantable Prostheses: a possible model for other health registries. Ann Ist Super Sanità. 2021;57(2):132-7. doi: 10.4415/ANN_21_02_04
9. Ciccarelli P, Ceccarelli S, Biondi A, Urakcheeva I, Torre M. Italian Arthroplasty Registry. Annual Report 2022 – Addendum. Rome: Il Pensiero Scientifico Editore; 2023.
10. Ministero della Salute. Rapporto annuale sull'attività di ricovero ospedaliero: Dati SDO 2020. Roma: Direzione Generale della Programmazione Sanitaria Ufficio 6 Roma; 2020.
11. Messina G, Forni S, Rosadini D, Falcone M, Collini F, Nante N. Risk adjusted mortality after hip replacement surgery. A retrospective study. Ann Ist Super Sanità. 2017;53(1):40-5.
12. Langan S, Benchimol E, Guttmann A, Moher D, Petersen I, Smeeth L, Sørensen H, Stanley F, Von Elm E. Setting the RECORD straight: developing a guideline for the REporting of studies Conducted using Observational Routinely collected Data. Clin Epidemiol. 2013;5(1):29-31. doi: 10.2147/CLEP.S36885
13. Ehrenstein V, Petersen I, Smeeth L, Jick SS, Benchimol EI, Ludvigsson JF, Soerensen HT. Helping everyone do better: a call for validation studies of routinely recorded health data. Clin Epidemiol. 2016;49-51.
14. De Coster, Quan H, Finlayson A, Gao M, Halfon P, Humphries KH, Johansen H, Lix LM, Luthi JC, Ma J, Romano PS, Roos L, Sundararajan V, Tu JV, Webster G, Ghali WA. Identifying priorities in methodological research using ICD-9-CM and ICD-10 administrative data: report from an international consortium. Bmc Health Serv Res. 2006;6(1):1-6.
15. Benchimol EI, Manuel DG, To T, Griffiths AM, Rabeneck L, Guttmann A. Development and use of reporting guidelines for assessing the quality of validation studies of health administrative data. J Clin Epidemiol. 2011;64(8):821-9.
16. Terris DD, Litaker DG, Koroukian SM. Health state information derived from secondary databases is affected by multiple sources of bias. J Clin Epidemiol. 2007;60(7):734-41.
17. Widdifield J, Bombardier C, Bernatsky S, Paterson JM, Green D, Young J, Ivers N, Butt DA, Jaakkimainen RL, Thorne JC. An administrative data validation study of the accuracy of algorithms for identifying rheumatoid arthritis: the influence of the reference standard on algorithm performance. Bmc Musculoskel Dis. 2014;15(1):1-9.
18. Ferrante P. Asbestosis and silicosis hospitalizations in Italy (2001-2015): results from the National Hospital Discharge Registry. Eur J Public Health. 2019;29(5):876-82.
19. Rinaldi R, Vignatelli L, Galeotti M, Azzimondi G, De Carolis P. Accuracy of ICD-9 codes in identifying ischemic stroke in the General Hospital of Lugo di Romagna (Italy). Neurol Sci. 2003;24(1):65-9.
20. Spolaore P, Brocco S, Fedeli U, Visentin C, Schievano E, Avossa F, Milan G, Toso V, Vanuzzo D, Pilotto L, et al. Measuring accuracy of discharge diagnoses for a region-wide surveillance of hospitalized strokes. Stroke. 2005;36(5):1031-4.
21. Baglio G, Sera F, Cardo S, Romanini E, Guasticchi G, Labek G, Torre M. The validity of hospital administrative data for outcome measurement after hip replacement. Ital J Public Health. 2009;6(2):14-27.
22. Madi SA, Ciminello E, Valentini R, Bacocco DL, Laricchiuta P, Carrani E, Torre M. Registry data as a useful tool to measure the validity of hospital discharge data. A study of the Italian Arthroplasty Registry on hip arthroplasty. In: ISAR 2021. 10th International Congress of Arthroplasty Registries. Abstract Book. Copenhagen,

Denmark: November 11-13, 2021.
23. Madi SA, Ciminello E, Bacocco DL, Laricchiuta P, Mari V, Cornacchia A, Carrani E, Torre M. Accuracy of hospital discharge data in reporting knee arthroplasty procedures: a study of the Italian Arthroplasty Registry. In: ISAR 2022. 11th International Congress of Arthroplasty Registries. Abstract Book. Dublin, Ireland: September 3-5, 2022.
24. Carrani E, Pascucci S, Mari V, Cornacchia A, Torre M. Minimum Data Set aggiuntivo alla SDO (Anca). Rev. 13th. Roma: Segreteria Scientifica della Presidenza, Istituto Superiore di Sanità; 2022.
25. Carrani E, Pascucci S, Mari V, Cornacchia A, Torre M. Minimum Data Set aggiuntivo alla SDO (Ginocchio). Rev. 10th. Roma: Segreteria Scientifica della Presidenza, Istituto Superiore di Sanità; 2022.
26. Bacocco DL, Carrani E, Ciciani B, Di Sanzo P, Leotta F, Torre M. Design and implementation of the new Italian healthcare digital interoperable registry for implantable medical devices. Software Pract Exper. 2022;52(11):2368-92.
27. Valentini R, Carrani E, Torre M, Lenzerini M. Ontology-based data management in healthcare: The case of the Italian Arthroplasty Registry. In: Basili R, Lembo D, Limongelli C, Orlandini A (Eds). International Conference of the Italian Association for Artificial Intelligence. AIxIA 2023 – Advances in Artificial Intelligence. Roma: November 6-9, 2023. Cham: Springer; 2023. doi: https://doi.org/10.1007/978-3-031-47546-7_7
28. Carrani E, Cornacchia A, Torre M. Procedura controllo di qualità dei dati. Roma: Segreteria Scientifica della Presidenza, Istituto Superiore di Sanità; 2020.
29. Roof MA, Lygrisse K, Keitel L, Siddiqi A, Emara A, Piuzzi NS, Chen AF, Callaghan J, Schwarzkopf R, Bedard NA. How accurate is ICD-10 coding for revision total knee arthroplasty? J Arthroplasty. 2021;36(12):3950-8.
30. Bozic KJ, Chiu VW, Takemoto SK, Greenbaum JN, Smith TM, Jerabek SA, Berry DJ. The validity of using administrative claims data in total joint arthroplasty outcomes research. J Arthroplasty. 2010;25(6):58-61.
31. Rennert-May E, Manns B, Smith S, Puloski S, Henderson E, Au F, Bush K, Conly J. Validity of administrative data in identifying complex surgical site infections from a population-based cohort after primary hip and knee arthroplasty in Alberta, Canada. Am J Infect Control. 2018;46(10):1123-6.
32. Wilson JM, Broida SE, Maradit-Kremers H, Browne JB, Springer BD, Berry DJ, Lewallen DG, Bedard NA. Is the American joint replacement registry able to correctly classify revision total knee arthroplasty procedural diagnoses? J Arthroplasty. 2023;38(6):S32-5.
33. Borsari L, Malagoli C, Ballotari P, De Girolamo G, Bonora K, Violi F, Capelli O, Rodolfi R, Nicolini F, Vinceti M. Validity of hospital discharge records to identify pregestational diabetes in an Italian population. Diabetes Res Clin Pr. 2017;123(1):106-11.
34. Cozzolino F, Montedori A, o, Abraha I, Eusebi P, Grisci C, Heymann AJ, Lombardo G, Mengoni A, Orso M, Ambrosio G. A diagnostic accuracy study validating cardiovascular ICD-9-CM codes in healthcare administrative databases. The Umbria Data-Value Project. PLoS One. 2019;14(7):e0218919.
35. Bogliun G, Beghi E, Italian GBS Registry Study Group. Validity of hospital discharge diagnoses for public health surveillance of the Guillain-Barré syndrome. Neurol Sci. 2002;23(1):113-7.
36. Yamana H, Moriwaki M, Horiguchi H, Kodan M, Fushimi K, Yasunaga H. Validity of diagnoses, procedures, and laboratory data in Japanese administrative data. J Epidemiol. 2017;27(10):476-82.

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 199-208
DOI: 10.4415/ANN_25_03_06

Paternity and parental leave in Italy: the parents' perspective

Francesca Zambri[1], Vincenza Di Stefano[1, 2], Annachiara Di Nolfi[1, 2], Barbara Vatta[3], Annina Lubbock[3], Giorgio Tamburlini[3], Maddalena Cannito[4], Mara Marzella[5], Elise M. Chapin[6], Flavia Splendore[1,2], Gabriella Tambascia[1, 2], Alessandro Volta[7], Mara Piasentin[3], Paola Scardetta[1], Angela Giusti[1] and the 4E-PARENT Working Group*

[1]*Centro Nazionale per la Prevenzione delle Malattie e la Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy*
[2]*Dipartimento di Biomedicina e Prevenzione, Università degli Studi di Roma "Tor Vergata", Rome, Italy*
[3]*Centro per la Salute delle Bambine e dei Bambini Onlus, Trieste, Italy*
[4]*Dipartimento di Culture, Politica e Società, Università di Torino, Turin, Italy*
[5]*Deep Blue, Rome, Italy*
[6]*Comitato Italiano per l'UNICEF Fondazione ETS, Rome, Italy*
[7]*Dipartimento Salute Infanzia, Cure Primarie - AUSL, Reggio-Emilia, Italy*
**The members of the 4E-PARENT Working Group are reported before the References*

Abstract

Background. Growing recognition of fathers' role in childcare highlights paternity and parental leave policies. The aim of this study is to investigate the perspectives of parents in Italy on the paternity and parental leave utilisation by fathers.

Materials and methods. A cross-sectional study was carried out, using web-based questionnaires targeting parents of children born between 2018 and 2023. Descriptive statistics and multivariate logistic regression models were used to analyse quantitative data, while qualitative content analysis was applied to open-ended responses.

Results. A total of 3,811 mothers and 720 fathers responded. Paternity leave was used by 72.6% of fathers. Non-use was primarily attributed to ineligibility (58.4%). Fathers' parental leave utilisation was low (20.4%). Most parents agreed that mothers need longer leave for the dyad's needs, like breastfeeding. Living in southern Italy and having lower educational levels reduce the likelihood to take leave.

Conclusions. Paternity and parental leave are underutilised by fathers in Italy. There is a need for better-paid and more accessible leave policies to promote active fatherhood and gender equality.

Key words

- paternity leave
- parental leave
- active fatherhood

INTRODUCTION

In recent years, the role of fathers in childcare has gained increasing relevance in public debates. In this context, parenting-related leave policies, including maternity, paternity, and parental leave, are essential tools for encouraging active paternal involvement in family life. Maternity leave was initially conceived primarily to protect and safeguard the health of female workers during pregnancy and postpartum. Only later, particularly in the 20th century, as women's participation in the labor market became economically strategic, did maternity leave policies evolve to also facilitate their reintegration into the workforce. Over time, these policies have gained additional significance due to their positive impact on the well-being of children and families and have legislated to provide women with the opportunity for quick reintegration into the workforce [1, 2]. When used by both parents and when time-appropriate for both mother and father, they promote responsive parenthood, co-parenting and active parental involvement in family life, facilitating a more equal distribution of household responsibilities [3-5]. Moreover, parenting-related leaves increase the time spent with children [6], promoting children's well-being with a positive influence on their physical, psycho-social, emotional, behavioural, and cognitive development, especially during the first years of life, a crucial period for early child development [7]. Specifically, they encourage the active involvement of fathers in the care of children [8-10].

While several studies emphasize the benefits of paternity leave for fostering fathers' involvement in parenting and promoting gender equity [11, 12], other research

Address for correspondence: Vincenza Di Stefano, Centro Nazionale per la Prevenzione delle Malattie e la Promozione della Salute, Istituto Superiore di Sanità, Via Giano della Bella 34, 00161 Rome, Italy. E-mail: vincenza.distefano@guest.iss.it.

suggests that these effects are not uniform. Some studies argue that the positive outcomes often attributed to paternity leave may be confounded by socio-economic characteristics, as fathers who are already more engaged or have greater resources are more likely to take advantage of leave policies [9, 13]. This highlights the need for a nuanced understanding of how leave policies interact with individual and contextual factors.

A father's active involvement from birth has several benefits for both the father and the children. It transforms the father's neurobiological set-up, reorienting it to nurturing, increasing oxytocin levels, salience and parent-infant synchrony and ensuring appropriate and timely parental response [14, 15]. Moreover, fathers' involvement fosters the development of a comprehensive "parental caregiving" neural network, which remains largely consistent across parents [15]. Children exposed to highly nurturing fathers exhibit enhanced cognitive competence at 6 months and demonstrate superior levels of development and problem-solving skills in later stages [16]. Later in life, children experience enhanced language development and improved school performance [17]. They also exhibit improved stress management and frustration coping skills, resulting in fewer behavioural issues during adolescence, including reduced tendencies towards violence and antisocial behaviour [18]. It also has an impact on reducing violence against women and children [19]. Furthermore, while evidence has long shown that breastfeeding rates are influenced by various factors, including sociodemographic aspects [20, 21], and inappropriate postnatal hospital practices – such as the use of breast milk substitutes without clinical indication [22] – there has been a growing focus in recent years on the role of social and family support. Notably, it has emerged that fathers/partners involvement improves breastfeeding initiation, duration, and exclusivity rates [23, 24].

Although parental leave policies allow both parents to take time off, they are not granted to all categories of workers. In addition, in several EU countries substantial differences remain in leave available for both parents, and adequately-paid leave for fathers is too short to support them in bonding with their newborns or to promote gender equality [25].

The context of family policies in Italy has been widely studied in the literature. Naldini and Saraceno [26] and Saraceno and Keck [27] analyzed how policies supporting paid work and caregiving responsibilities have evolved in their role in promoting gender equity. More recently, Cannito [28] explored the factors influencing the uptake of parental leave by parents, while Dottori *et al*. [29] investigated the social and cultural determinants that limit fathers' access to leave. However, the literature still highlights a significant gap between existing policies and their tangible impact on the sharing of parenting responsibilities. Paternity leave in Italy is among the shortest in Europe. It includes 10 mandatory days, which can be taken from 2 months before the expected date of delivery to 5 months after delivery [30].

Table 1 summarizes the main leave categories in Italy [30-32].

In this framework, the European project 4E (Early, Equal, Engaged, Empathetic) PARENT (CERV-2022-DAPHNE n. 101095956) (https://4e-parentproject.eu/), the follow-up of the PARENT project [33],

Table 1
Main leave categories in Italy

Type of leave	Duration	Compensation	Conditions	Covered employee categories
Maternity leave	5 months (2 before +3 after; 1+4; 0+5) (7 if the workplace presents risks for breastfeeding)	Generally paid from 80% to 100% of salary	Mandatory. Extension in case of premature birth, multiples or complications	All categories of female workers
Mandatory paternity leave	10 working days, from 2 months before the expected date of delivery to 5 months after birth	100% of salary	Mandatory. Can be split into non-consecutive days. Minimum notice of 5 days	Private and public sector employees. Not available to self-employed fathers and fathers who work freelance
Optional paternity leave	1 working day, from 2 months before the expected date of delivery to 5 months after birth	100% of salary	As an alternative to the mother, who must give up her mandatory maternity leave day.	Private and public sector employees. Not available to self-employed fathers and fathers who work freelance
Parental leave	6 months per parent. Can be extended to 7 months for the father, with a maximum of 11 months in total if the father uses at least 3 months. Up to child's 12 years of age	80% of salary for the first month according to the 2023 budget law 30% of salary for the following 9 months (up to child's 6 years of age)	Can be taken in days or hours. 5 days' notice (2 days' notice if parental leave is taken on an hourly basis)	Public and private sector employees. Self-employed and freelancers are only entitled to a maximum of 3 months. Not available to: a) parents whose employment has ceased or been suspended; b) domestic workers; c) parents working from home
Daily rest periods (formerly "breastfeeding breaks")	2 hours per day if the working day is at least 6 hours, 1 hour per day if the working day is less than 6 hours	100% of salary	Can be taken individually or cumulatively	Employees and remote workers

aims to promote engaged fatherhood and caring masculinity from the beginning of pregnancy, in order to achieve gender equity and to prevent gender-based violence (https://4e-parentproject.eu/). The project's specific objectives are to develop a proposal for policy change, to strengthen advocacy and communication, to respond to parents' need to be listened to and to facilitate communication on gender stereotypes in order to contribute to cultural change and knowledge sharing. Within this framework, this pilot study aims to describe the perspectives of fathers and mothers regarding the utilisation of both paternity and parental leaves by fathers, identifying factors that influence fathers' involvement in childcare and the barriers to greater leave uptake.

MATERIALS AND METHODS

As part of the project 4E-PARENT, a cross-sectional study was carried out using web-based questionnaires addressed to mothers and fathers of children born between 2018 and 2023. Participation in the questionnaires was voluntary. The data were analysed through descriptive statistics and multivariate logistic regression models to investigate determinants of paternity and parental leave utilisation. In addition, qualitative content analysis was performed on responses to open-ended questions.

Questionnaire description

The web-based questionnaires were developed by the research team based on current paternity and paternal leave policies in Italy and evidence-based factors that promote or hinder fathers' involvement through the lens of paternity/parental leave. The development process was participatory: an interdisciplinary working group including researchers, professionals from public health institutions and NGOs, and representatives from parent associations (including fathers' groups) contributed to the design and review of the items. The questionnaire was also discussed within the 4E-PARENT project stakeholder network. A pre-testing phase was conducted with a small sample of parents (n=10) to assess clarity, comprehension, and interpretability of the questions. Feedback from this step was used to refine the wording and structure of the items. The final version includes 17 semi-structured questions organized in 5 sections (*the Questionnaire is available online as Supplementary Material*):

- Section 1: demographic characteristics and personal details (3 questions);
- Section 2: utilisation of both paternity and parental leave by fathers (4 questions);
- Section 3: reasons for non-utilisation (2 questions);
- Section 4: agreement/disagreement with current leave policies, using a 5-point Likert scale, ranging from "1-Completely agree" to "5-Completely disagree" (4 questions);
- Section 5: agreement/disagreement with several gender stereotypes using a 5-point Likert scale, ranging from "1-Completely agree" to "5-Completely disagree" (1 question).

There was also a section for comments (3 open-ended questions).

Data collection and analysis

The study used a convenience sample, with voluntary participation. Participants were eligible if they were mothers or fathers of at least one child born between 2018 and 2023. The web-based questionnaires were disseminated between August and December 2023 through the 4E-PARENT official website (https://4e-parentproject.eu/), social media channels (such as Facebook and Instagram), and through newsletter, managed by project partners. While it is not possible to determine the exact number of individuals reached, the overall pool was estimated to include several hundred potential participants. The data collection was designed to ensure anonymity. The questionnaire was hosted by the Centro per la Salute delle Bambine e dei Bambini's (CSB) own web platform that did not collect any personally identifying information such as Internet Protocols (IPs), names or email addresses. Therefore, anonymity was respected in compliance with the GDPR. Survey responses were recorded in an electronic data sheet.

Descriptive analyses were performed using frequencies and percentages for categorical data.

An analysis of determinants of paternity and parental leaves utilisation was conducted through the development of multivariate logistic regression models, for both mothers' and fathers' responses. The 5-point Likert scale variables of agreement/disagreement (1=Completely disagree to 5=Completely agree) were collapsed into three levels as follows: Agree: responses 5 (Completely agree) and 4 (Agree); Neutral: response 3 (Neither agree nor disagree); Disagree: responses 2 (Disagree) and 1 (Completely disagree). Multivariate logistic regression models were built using the strategy suggested by Hosmer and Lemeshow. Each variable was examined by univariable analysis and included in the multivariate logistic model when the p-value was <0.15. Prior to model estimation, we assessed multicollinearity among the independent variables using the Variance Inflation Factor (VIF). The influence of the independent variables on each binary outcome investigated (paternity leave utilization and parental leave utilization) was expressed as adjusted odds ratios (ORadj) and 95% confidence interval (CI). Statistical significance was set at a p-value<0.05. Model fit was assessed using the Hosmer-Lemeshow goodness-of-fit test. A p-value>0.05 was considered to indicate a good fit between the model and the data. The statistical analysis was performed using STATA 17.0 software (Stata Corporation, College Station, TX, USA).

The dependent variables in the regression models were: the use of paternity leave (yes/no) and the use of parental leave (yes/no). The independent variables included: educational level, categorized as high (Bachelor's degree or higher), medium (high school diploma), low (less than high school); geographic area of residence (North, Centre, South); child's year of birth, categorized as "2021 or later" *vs* "before 2021"; all variables derived from items using 5-point Likert scales (ranging from 1=Completely disagree to 5=Completely agree), recoded into three categories for the analysis (Disagree 1-2, Neutral 3, Agree 4-5).

The open-ended questions were coded inductively

and deductively, according to a categorical analysis [34]. The NVivo software was used to conduct coding, categorical analysis and mapping. Two expert researchers in qualitative methods and experience in public health and gender studies independently analysed the responses. Initial coding was done separately, followed by consensus meetings to compare and reconcile differences, ensuring consistency and reliability in the identification of themes and categories. In cases of disagreement, a third researcher was consulted to mediate and reach shared decisions.

Ethical considerations

Participants provided informed consent electronically before completing the questionnaire. The survey platform did not collect personal identifiers (e.g., IP addresses, names or emails). Given the nature of dissemination the data were collected without direct identifiers. Participants were assured of the anonymity. This approach ensured compliance with data protection regulations while maintaining participant confidentiality.

RESULTS

Main characteristics of the respondents

The responders completing all sections of the questionnaire were 3,811 mothers and 720 fathers. The socio-demographic characteristics of these respondents are reported in *Table 2*.

We collected responses from all Italian regions and the majority of respondents were from Northern Italy (60.3% mothers; 56.7% fathers). The educational level was high (bachelor's degree or higher) in most cases for both mothers (73.7%) and fathers (57.8%). Most of the children the questionnaire referred to were born in 2023 (27.9% mothers; 30.8% fathers).

Paternity leave utilisation

Most fathers (72.6%) and mothers (61.5%) reported that fathers used paternity leave, with the majority of this leave being publicly funded (58.7% fathers; 61.7% mothers), followed by company-paid leave (23.1% according to fathers; 23.9% according to mothers) (*Table 3*).

Among fathers who did not use paternity leave, most reported that they were not eligible. Other reasons included being unemployed, having unused vacation or leave time, or having paternity leave yet to be used. As for mothers, most of them declared that the fathers were not eligible. Other reasons included personal choice not to use the leave or the company not supporting use of leave, difficulties in utilisation or lack of information on how the fathers could use the paternity leave.

Figure 1 shows the opinions on the utilisation of longer paternity leave among fathers who used it (n=523) and mothers who reported that fathers took paternity leave (n=2,343) for their most recent child. Most fathers (91.6%) and mothers (90.6%) agreed that fathers would have used a longer paternity leave if it had been fully paid (at 100% of salary). Only a small proportion of fathers (4.1%) and mothers (4.1%) believed that a longer paternity leave was unnecessary because the mother was at home; most disagreed (fathers 88.8%; mothers 92.7%). Additionally, 47.1% of fathers and 56.5% of mothers stated that fathers would use a longer paternity leave, but they would face challenges at work.

Parental leave utilisation

As for the utilisation of parental leave at the time of the last childbirth, the majority of both mothers (84.9%) and fathers (79.6%) reported that fathers did not use parental

Table 2
Socio-demographic characteristics of respondents

	Mothers N=3,811	Fathers N=720
Geographic area of residence		
Northern	2,296 (60.3%)	408 (56.7%)
Centre	820 (21.5%)	198 (27.5%)
Southern	695 (18.2%)	114 (15.8%)
Missing	-	-
Educational level*		
High	2,809 (73.7%)	416 (57.8%)
Middle	908 (23.8%)	258 (35.8%)
Low	94 (2.5%)	46 (6.4%)
Year of birth of last child		
2023	1,063 (27.9%)	222 (30.8%)
2022	891 (23.4%)	179 (24.9%)
2021	742 (19.5%)	137 (19.0%)
2020	481 (12.6%)	95 (13.2%)
2019	362 (9.5%)	57 (7.9%)
2018	272 (7.1%)	30 (4.2%)

*High: II level University Master Course, I level University Master Course, PhD, Master's Degree, bachelor's Degree. Middle: High school leaving qualification. Low: Lower secondary school qualification, Elementary school qualification.

Table 3
Paternity and parental leave utilisation

	Mothers N=3,811	Fathers N=720
Paternity leave for most recent child		
Yes	2,343 (61.5%)	523 (72.6%)
No	1,468 (38.5%)	197 (27.4%)
Type of paternity leave	**(n=2,343)**	**(n=523)**
Publicly-funded leave	1,446 (61.7%)	307 (58.7%)
Company-paid leave	561 (23.9%)	121 (23.1%)
Both	250 (10.7%)	84 (16.1%)
Missing	*86 (3.7%)*	*11 (2.1%)*
Parental leave for most recent child		
Yes	577 (15.1%)	147 (20.4%)
No	3,234 (84.9%)	573 (79.6%)
Days of parental leave utilization	Median 10 (IQR 5-20)	Median 10 (IQR 5-20)

leave (*Table 3*). The median duration of parental leave was 10 days (IQR 5-20) for both mothers and fathers.

Figure S1 (*available online as Supplementary Material*) shows opinions on the utilisation of a longer and better-paid parental leave among fathers who used it (n=147) and mothers who reported that fathers took parental leave (n=577) for their most recent child. Most fathers (76.9%) and mothers (81.6%) agreed the fathers would have used a longer paternal leave if they were better paid. However, some fathers (35.4%) and mothers (46.1%) indicated, although fathers might have used a longer and better-paid parental leave, they would have faced challenges at work.

Current and future leave policies and gender stereotypes

Figure S2 (*available online as Supplementary Material*) presents opinions on a proposal to extend work leave: increasing paternity leave days, extending leave to categories not currently covered (e.g., freelancers), and raising parental leave pay from 30% to no less than 80%. Most fathers (80.0%) and mothers (80.6%) disagreed with the statement that "the current leave policies are more or less adequate, because in the early years (especially the first year) it is the mother's presence that is crucial". Additionally, a small proportion of mothers (6.0%) and fathers (6.9%) endorsed the stereotype that the mothers should stay home for child-rearing and housekeeping while fathers provide the main income. Furthermore, for most mothers (59.5%) and fathers (57.4%), while the proposal to extend work leave is deemed necessary, the actual utilisation could be a challenge (*Figure S2 available online as Supplementary Material*).

As for the importance of leave for fathers, both mothers (98.1%) and fathers (98.1%) agreed that fatherhood is an enriching experience and therefore it is a father's right to be present from the beginning. In addition, mothers (98.5%) and fathers (97.4%) agreed that work leave is important because it enables the father to share the burden of care with the mother, especially after birth, a particularly stressful period. They also believed that father-child bonding is established after birth through shared time together (mother 92.6%; fathers 90.6%) (*Figure S3 available online as Supplementary Material*).

As for equal leave (in duration and pay), 28.3% of mothers and 32.2% of fathers agreed that the equal leave should be used at different times (mothers in the first few months, fathers later). Some mothers (33.0%) and fathers (32.9%) believed that equal leave is a fair goal but expressed concerns about fathers and employer's readiness for such change. Furthermore, most fathers (72.4%) and mothers (69.0%) agreed that the father should have more leave, but, in general, that the mothers require longer leave than fathers due to the dyad specific needs, including breastfeeding (*Figure 2*).

Logistic regression model

The logistic model shows that, for fathers, a low educational level (ORadj 0.34; 95% CI 0.13-0.86; p<0.05), living in Central (ORadj 0.49, 95% CI 0.28-0.87; p<0.05) and Southern Italy (ORadj 0.32, 95% CI 0.15-0.64; p<0.05), and accepting traditional family role divisions (ORadj 0.30, 95% CI 0.14-0.65; p<0.05) are

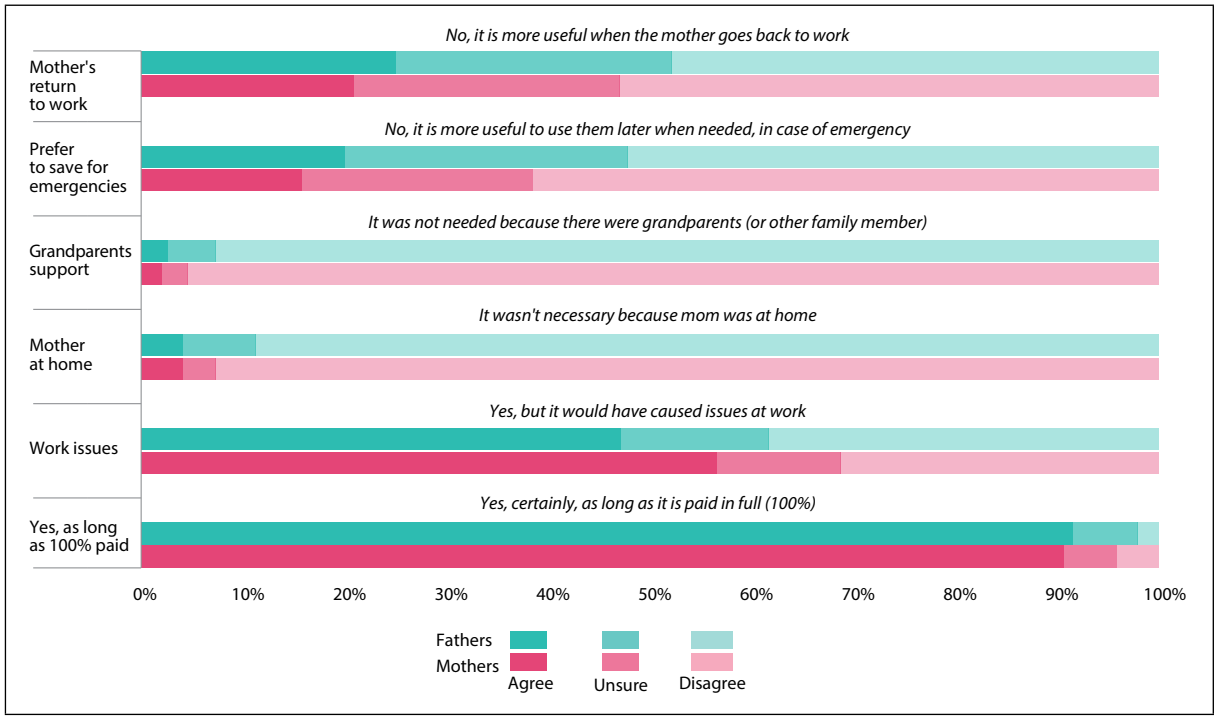


Figure 1
Fathers' and mothers' opinions on a longer paternity leave utilization (n mothers=2,343; n fathers=523).
Question: *"Would you/the father have/has taken longer paternity leave in the first month of baby's life?".*

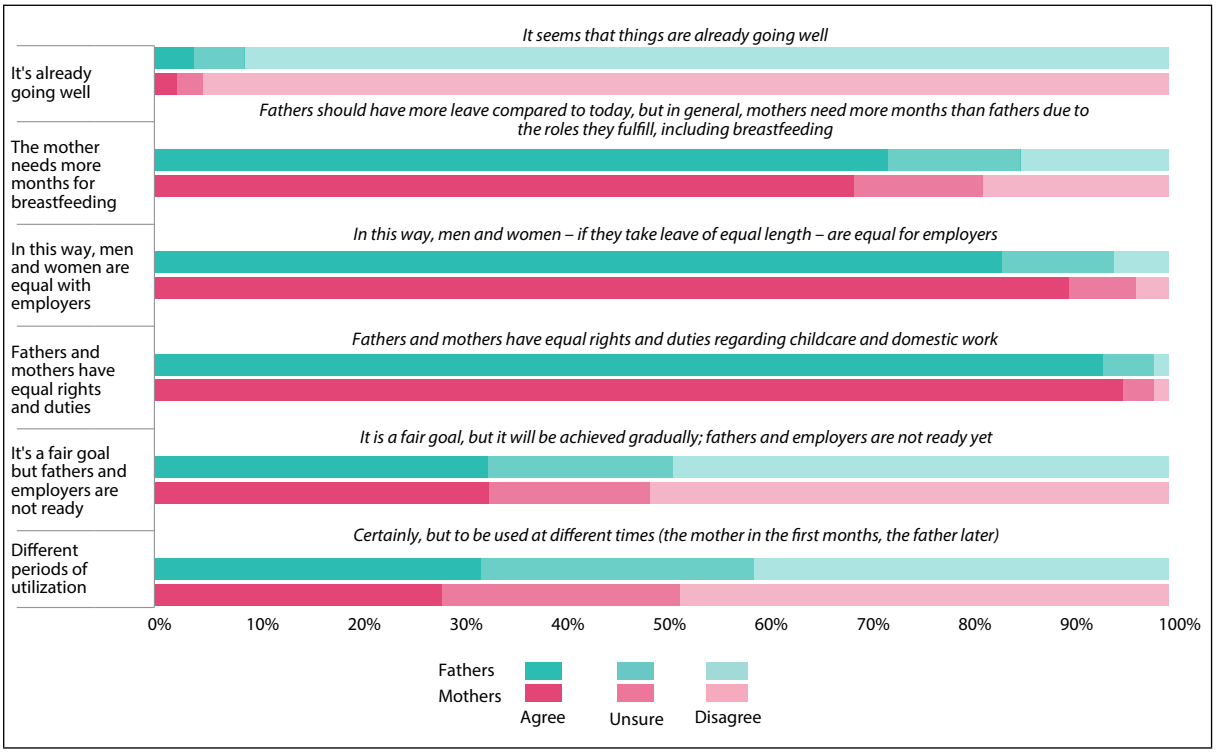


Figure 2
Fathers' and mothers' opinions on equal leave (equal in duration and pay) (n mothers=3,811; n fathers=720).
Question: *"Leave available for mothers (maternity leave and parental leave not reserved for fathers) and leave available for fathers (paternity leave and parental leave reserved for fathers) should be equal in duration and pay over the first 2-3 years of the child's life".*

associated with a reduced likelihood of using paternity leave. Conversely, having a child born in 2021 or later increases the likelihood of using paternity leave (OR-adj 1.82, 95% CI 1.21-2.73; p<0.05). The same results are observed for mothers, except for the low education level, which was not statistically significant.

Moreover, for fathers, living in Southern Italy was statistically significant (ORadj 0.24, 95% CI 0.09-0.69; p<0.05) in reducing the likelihood of using paternal leave. For mothers, both a middle educational level (ORadj 0.72, 95% CI 0.54-0.97; p<0.05) and living in Southern Italy (ORadj 0.67, 95% CI 0.49-0.92; p<0.05) were significant factors (*Table S1 available online as Supplementary Material*).

All VIF values were below 2.5, indicating no significant multicollinearity. Therefore, all selected variables were retained in the final models. Moreover, the Hosmer-Lemeshow goodness-of-fit test indicated an adequate fit for all logistic regression models, with p-values >0.05.

Insights from open-ended responses on leave uptake and cultural barriers

Among open-ended answers, what emerged was the need for a cultural change to promote equal opportunities for mothers through the support of fathers, recognizing parenting as a shared responsibility. Moreover, some fathers reported that *"many fathers do not feel fully responsible for the care of their children in the early years and therefore do not use paternity/parental leave"*. Another theme was about the remuneration and economic impact of taking leave because *"without adequate pay, it becomes a privilege for a very few"* considering that the *"30% of salary is not even enough to buy diapers"*. As for paternity leave, the mothers reported that having equal leave would lead to a reduction in the gender gap at the job-interview stage because women would no longer suffer discrimination. As for parental leave, both mothers and fathers expressed a preference for greater flexibility in how it can be used, including the option to share it between them and to take it by the hour based on their family's needs (*Figure S4 available online as Supplementary Material*).

DISCUSSION

Our study involved 3,811 mothers and 720 fathers, showing significant differences in the utilisation of paternity and parental leave between different Italian regions and between different educational levels. The majority of participants were from Northern Italy, and the majority of fathers used paternity leave, with a prevalence of public leave.

A systematic review of European countries suggested that men's use of paternity leave is determined by both political/regulatory and organisational forces, affecting various organisational, psychological, and family-related areas including career development, health, and relationships with children [35]. Another study found that the introduction and expansion of paid parental leave policies are associated with improved well-being

during adolescence and young adulthood [18]. Although extending the duration of leave may not produce significant long-term results, the introduction of paid leave policies, shows evidence of statistically significant benefits [18]. The main channel of impact is the increased investment of parental time during the early years. Among several actions, institutional factors such as the availability and quality of early (0-2 years) education services can be crucial [18], in addition to better-paid leave, tailored services and cultural change. This confirms the importance of sensitive and caregiving parenting for the child's maturity and cognitive development [36].

In our study, most fathers and mothers reported that fathers used paternity leave, primarily public leave, followed by company-paid leave. The reported take-up rates in our study are notably higher than those reported in official data; for example, the OECD family database indicates that only 32% of fathers took paternity leave following births in 2019 [37]. This discrepancy suggests that our findings may overestimate the extent of leave-taking, and it is crucial to interpret them with caution in light of these limitations.

Among fathers who did not use paternity leave, most stated they were not eligible, with other reasons including unemployment, companies not being supportive of fathers taking leave or being self-employed. In Italy, many categories of workers are not covered by paternity and parental leave. While legislation allows self-employed workers to take parental leave, the benefits and duration are less favourable compared to those for employees [38]. Taking parental leave can lead to a total loss of income for some, which may be financially unsustainable, particularly if their business is the family's primary source of income. Furthermore, many self-employed individuals work independently or without any collaborators. As a result, they may have no one to delegate their responsibilities to during their leave, making it challenging for them to take time off from work.

Most fathers and mothers agreed that fathers would have taken longer paternity leave if it had been always paid at 100%, though many felt that work-place related pressures would make it difficult to use more leave. According to the National Social Security Institute (Istituto Nazionale Previdenza Sociale, INPS) paternity leave uptake shows an increasing trend, with fathers residing in Central and Northern Italy, those with full-time employment, and those in large companies (with more than 100 employees) being more likely to take paternity leave [39]. These data confirm our findings that being from the North or the Centre increases the likelihood of using paternity and parental leave for both mothers and fathers.

As for parental leave, our findings show that the majority of both mothers and fathers reported that fathers did not use parental leave. However, most fathers and mothers agreed that fathers would have used longer parental leave if it had been possible and better-paid, although many believe they would have faced work-related challenges in doing so. The INPS reported an increase in the number of parents benefiting from parental leave, along with a significantly unequal distribution of leave within couples, with a difference in leave requests between fathers and mothers [39]. Uptake by fathers is 20% [39] and a key reason being that parental leave is poorly paid (only 30% despite the recommendation of the EU Directive that payment of parental leave should be "adequate") [40, 41]. Providing a well-paid parental leave could encourage fathers to take more of it [42]. Due to the gender wage gap, where men typically earn more than women, poorly paid or unpaid parental leave can reinforce social and economic pressures that hinder gender equality. If leave doesn't compensate a significant portion of fathers' income, families often face a greater financial burden when fathers take time off compared to mothers [43]. This is in line with our results, which indicate that most fathers and mothers agreed that mothers need more leave than fathers due to the mother-baby dyad's needs, including breastfeeding. A small proportion endorsed the stereotype that mothers should stay home for child-rearing and housekeeping while fathers provide the main income. Although the role of the mother is crucial, these findings show that reconciling work and family life in our country could be still perceived as being primarily a women's responsibility. This situation was not affected by the pandemic. In fact, in 2020, the number of requests for leave from both mothers and fathers increased, but with a much more pronounced rise among mothers [40].

As for parental leave, some mothers and fathers agreed that mothers should use the leave, especially during the first few months of the child's life. The INPS data indicate that mothers use parental leave most frequently during the first 3 years of a child's life, with the gender gap being particularly wide up to this age and decreasing over time [40].

Both fathers and mothers agreed that extending paternity and parental leave could be a solution, but they (and in particular, fathers) would face challenges and resistance at work. Consistent with these beliefs, the INPS data show that working in fixed-term jobs negatively and significantly affects the likelihood of requesting parental leave, whereas fathers working full time with stable contracts are more likely to take leave [40]. This is likely due to fathers' fear of their employment contracts not being renewed because of absence from the workplace.

Lastly, some results of our regression model are confirmed by the INPS model, which shows that fathers living in central and northern regions are more likely to take leave [40]. Given the documented benefits of a father's presence, once again, as already highlighted by health surveillance on Italian children [44, 45], the parents' educational level and the region of birth contribute to disadvantages and create social and health inequalities, with consequences for future generations.

Our findings suggest an association between paternity leave and fathers' involvement in parenting. However, as noted in the literature, this relationship is likely mediated by socio-economic characteristics and pre-existing attitudes towards caregiving. Studies have shown that fathers who take leave often belong to higher socio-

economic groups or have partners who support shared parenting [1, 13]. Consequently, it is challenging to disentangle the causal impact of paternity leave from the characteristics of the fathers who take it. Future research should aim to isolate these effects, for example, by using experimental or longitudinal designs that limit selection bias.

Insights from qualitative analysis, highlighted that the low uptake of paternity and parental leave by fathers is not solely a policy issue but is deeply rooted in a cultural perception where some fathers still do not feel fully responsible for early childcare. This societal barrier, coupled with inadequate financial compensation (e.g., the reported 30% of salary, which was deemed insufficient to even "*buy diapers*"), employers' pressures, not only disincentivizes leave-taking, but also perpetuates gender inequality by reinforcing the traditional mothers/fathers' roles. As a result, the expectation that mothers should carry the main responsibility for childcare persists, hindering their return to the workforce and contributing to the gender pay gap.

Our results are consistent with previous studies that highlight structural and cultural barriers to leave uptake in Italy. Naldini and Saraceno [26] and Saraceno and Keck [27] emphasized how family policies have historically reinforced gender roles, while Cannito [28] and Dottori *et al*. [29] showed that insufficient financial support and cultural factors significantly limit fathers' engagement in caregiving. By addressing these barriers, more inclusive policies could foster greater gender equity and shared parenting responsibilities. Moreover, the involvement and presence of father are important, as stated in the Nurturing Care Framework [7] and the 2030 Agenda for Sustainable Development [46].

LIMITATIONS

Our study has some limitations. We do not have a probabilistic sample because the online questionnaire was disseminated through project networks, which may have attracted more motivated respondents. This approach, while effective in reaching a wide audience, may have introduced selection bias, as individuals with higher education levels and those residing in Northern Italy might have been more likely to encounter and complete the survey. A key limitation of this study is the voluntary nature of participation, which may have introduced selection bias. Fathers who have taken paternity leave are more likely to respond to the survey, leading to an overrepresentation of those who are already engaged in caregiving. Additionally, there is a disproportion between the number of questionnaires completed by mothers compared to fathers and consequently a women overrepresentation. One reason is that, in general, women tend to respond more frequently to questionnaire surveys [47]. Lastly, some socio-demographic variables are missing, such as age and profession. These aspects should be considered when interpreting the findings. Future studies should aim to employ probabilistic sampling methods or targeted outreach to underrepresented groups to ensure a more balanced and generalizable dataset. Additionally, the qualitative component of the study was exploratory in nature. While it provided useful contextual insights, the heterogeneity and brevity of many open-ended responses limited the possibility of performing a more structured thematic analysis or drawing generalizable conclusions.

CONCLUSIONS

To conclude, we consider our study a pilot investigation into a relatively unexplored topic that highlights strong awareness among mothers and fathers regarding the importance of paternity and parental leave for fathers, resistance from company management, and scepticism from parents about the political capacity to address their needs. Moreover, our findings complement and expand existing models by highlighting dimensions that administrative data cannot capture. For example, while the INPS model identifies regional disparities in leave uptake, our survey data reveal the underlying reasons, such as workplace culture and financial barriers, that contribute to these disparities. This approach underscores the need of integrating qualitative insights with quantitative data in further studies, in order to inform more effective and inclusive policy interventions. It is important to ensure equitable access to these tools through inclusive policies that promote active father involvement in childcare, considering the health benefits of this involvement in the early years of life. The survey confirms the need for a change in work-related and society culture, and organisational models according to which the care is a secondary role for fathers. This change can support engaged and responsive parenting by both male and female workers.

Fundings

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The Authors declare no conflict of interest.

Authors' contributions

FZ wrote the original draft and contributed to conceptualization, methodology, quantitative formal analysis, and data curation; VDS contributed to methodology, qualitative formal analysis, data curation, and manuscript review and editing; AG supported conceptualization, methodology, and manuscript review and editing; AL and GT participated in data curation, conceptualization, methodology, and manuscript review and editing; MC and MP contributed to conceptualization, data curation, and manuscript review and editing; BV and AV supported conceptualization and manuscript review and editing; ADN, MM, EMC, FS, GT and PS collaborated in the review and editing of the manuscript. All Authors have read, agreed to, and approved the final version of the manuscript.

The members of the 4E-PARENT Working Group are:

Eva Benelli (Zadig Srl, Milan, Italy), Micol Biscotto (Deep Blue, Rome, Italy), Marco Deriu (Dipartimen-

to di Discipline Umanistiche, Sociali e delle Imprese Culturali, Università di Parma, Parma, Italy; Associazione nazionale Maschile Plurale, Rome, Italy), Susanna Lana (Centro Nazionale per la Prevenzione delle Malattie e la Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy), Stefania Manetti (Associazione Culturale Pediatri, ACP, Narbolia, Italy), Andrea Santoro (Associazione Cerchio degli Uomini APS, Turin, Italy), Emilie Sartorelli (Zadig Srl, Milan, Italy), Stefania Solare (Comitato Italiano per l'UNICEF Fondazione ETS, Rome, Italy), Paola Tomasello (Deep Blue, Rome, Italy), Maria Rosa Valetto (Zadig Srl, Milan, Italy), Monica Valli (Centro Nazionale per la Prevenzione delle Malattie e la Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy).

Received on 24 February 2025.
Accepted on 25 June 2025.

REFERENCES

1. International Labour Organization. Maternity and paternity at work: Law and practice across the world. Geneva: ILO; 2014. Available from: https://www.ilo.org/publications/maternity-and-paternity-work-law-and-practice-across-world.
2. Deven F, Moss P, Petrie P. State of the art review on the reconciliation of work and family life for men and women and the quality of care services. European Commission DG V; 1999.
3. Rocha M. Promoting gender equality through regulation: the case of parental leave. Theory Pract Legislat. 2020;9(1):35-57. doi: 10.1080/20508840.2020.1830565
4. Doucet A, McKay L. Fathering, parental leave, impacts, and gender equality: what/how are we measuring? Int J Sociol Social Policy. 2020;40(5/6):441-63. doi: 10.1108/IJSSP-04-2019-0086
5. de Laat K, Doucet A, Gerhardt A. More than employment policies? Parental leaves, flexible work and fathers' participation in unpaid care work. Commun Work Family 2023;26:562-84. doi: 10.1080/13668803.2023.2271646
6. Dahl GB, Lochner L. The impact of family income on child achievement: evidence from the earned income tax credit. Am Econ Rev. 2012;102:1927-56.
7. World Health Organization, United Nations Children's Fund, World Bank Group. Nurturing care for early childhood development: a framework for helping children survive and thrive to transform health and human potential. Geneva: WHO; 2018.
8. Huerta MC, Adema W, Baxter J, Han WJ et al. Fathers' leave and fathers' involvement: evidence from four OECD countries. Eur J Soc Secur. 2014;16:308-46. doi: 10.1177/138826271401600403
9. Petts RJ, Knoester C, Waldfogel J. Fathers' paternity leave-taking and children's perceptions of father-child relationships in the United States. Sex Roles. 2020;82(3-4):173-88. doi: 10.1007/s11199-019-01050-y
10. Kvande E. Individual parental leave for fathers: promoting gender equality in Norway. In: Grau Grau M, las Heras Maestro M, Riley Bowles H (Eds). Engaged fatherhood for men, families and gender equality. Cham, CH: Springer; 2022. p. 153-63
11. O'Brien M. Fathers, parental leave policies, and infant quality of life: international perspectives and policy impact. Annals of the American Academy of Political and Social Science. 2009;624(1):190-213. doi: 10.1177/0002716209334349
12. Doucet A, McKay L. Fathering, parental leave, impacts, and gender equality: What/how are we measuring? Int J Sociol Soc Policy. 2020;40(5/6):441-63. doi: 10.1108/IJSSP-04-2019-0086
13. Haas L, Hwang CP. The impact of taking parental leave on fathers' participation in childcare and relationships with children: lessons from Sweden. Commun Work Family. 2008;11(1):85-104. doi: 10.1080/13668800701785346
14. Allen SM, Daly KJ. The effects of father involvement: an updated research summary of the evidence. Canada: Centre for Families, Work & Well-Being, University of Guelph; 2007.
15. Abraham E, Hendler T, Shapira-Lichter I, Kanat-Maymon Y. Father's brain is sensitive to childcare experiences. Proc Natl Acad Sci USA. 2014;111:9792-7. doi: 10.1073/pnas.1402569111
16. Diniz E, Brandão T, Monteiro L, Veríssimo M. Father involvement during early childhood: a systematic review of the literature. J Fam Theory Rev. 2021;13:77-99. doi: 10.1111/jftr.12410
17. Tugrul H, Stuckler D, Aassve A. Long-term impact of parenting-related leave policies on adolescents' well-being: a systematic review of quasi-experiments. Eur J Public Health. 2024;34:272-82. doi: 10.1093/eurpub/ckad228
18. Sarkadi A, Kristiansson R, Oberklaid F, Bremberg S. Fathers' involvement and children's developmental outcomes: a systematic review of longitudinal studies. Acta Paediatr. 2008;97(2):153-8. doi: 10.1111/j.1651-2227.2007.00572.x
19. Chan KL, Emery CR, Fulu E, Tolman RM, et al. Association Among Father Involvement, Partner Violence, and Paternal Health: UN multi-country cross-sectional study on men and violence. Am J Prev. Med. 2017;52(5):671-79.
20. Bolton TA, Chow T, Benton PA, Olson BH. Characteristics associated with longer breastfeeding duration: an analysis of a peer counseling support program. J Hum Lact. 2009;25(1):18-27. doi: 10.1177/0890334408325985
21. Cernigliaro A, Palmeri S, Casuccio A, Scondotto S, Restivo V; In Primis Working Group. Association of the Individual and Context Inequalities on the Breastfeeding: a study from the Sicily Region. Int J Environ Res Public Health. 2019;16(19):3514. doi: 10.3390/ijerph16193514
22. Colaceci S, Chapin EM, Zambri F, Reali L, Cedrone L, Del Brocco A, Masi M, Mohamed A, Dellafiore F, Nichinonni S, Giusti A. Verba volant, scripta manent: breastfeeding information and health messages provided to parents in the neonatal discharge summary in the Lazio Region, Italy. Ann Ist Super Sanità. 2020;56(2):142-9. doi: 10.4415/ANN_20_02_03
23. Abbass-Dick J, Brown HK, Jackson KT, Rempel L, Dennis CL. Perinatal breastfeeding interventions including fathers/partners: a systematic review of the literature. Midwifery. 2019;75:41-51. doi: 10.1016/j.midw.2019.04.001
24. Agrawal J, Chakole S, Sachdev C. The role of fathers in promoting exclusive breastfeeding. Cureus. 2022;14(10):e30363. doi: 10.7759/cureus.30363
25. Blum S, Dobrotić I, Kaufman G, Koslowski A, et al. International review of leave policies and research 2023.

Available from: http://www.leavenetwork.org/lp_and_r_reports/. Last accessed 22 February 2025.
26. Naldini M, Saraceno C. Social and family policies in Italy: Not totally frozen but far from structural reforms. Social Policy Admin. 2008;42(7):733-48. doi: 10.1111/j.1467-9515.2008.00638.x
27. Saraceno C, Keck W. Towards an integrated approach for the analysis of gender equity in policies supporting paid work and care responsibilities. Demographic Research. 2011;25(11):371-406.
28. Cannito M. Fathers and parental leave in Italy: Motivations, barriers, and gender roles. Int J Sociol. 2020;50(3):234-53. doi:10.1080/00207659.2020.1781786
29. Dottori D, Ferri E, Rossi S. Determinants of parental leave uptake in Italy: regional, cultural, and economic factors. European J Social Policy. 2024;34(1):45-62.
30. Italia. Decreto legislativo 26 marzo 2001, n. 151. Testo unico delle disposizioni legislative in materia di tutela e sostegno della maternità e della paternità, a norma dell'articolo 15 della legge 8 marzo 2000, n. 53. Gazzetta Ufficiale – Serie Generale n. 96, 26 aprile 2001. Available from: https://www.gazzettaufficiale.it/eli/id/2001/04/26/001G0200/sg.
31. Italia. Decreto legislativo 30 giugno 2022, n. 105. Attuazione della direttiva (UE) 2019/1158 del Parlamento europeo e del Consiglio, del 20 giugno 2019, relativa all'equilibrio tra attività professionale e vita familiare per i genitori e i prestatori di assistenza e che abroga la direttiva 2010/18/UE del Consiglio. (22G00114). Gazzetta Ufficiale – Serie Generale n. 176, 29 luglio 2022. Available from: https://www.gazzettaufficiale.it/eli/id/2022/07/29/22G00114/sg.
32. Istituto Nazionale della Previdenza Sociale. Circolare n. 45, 16 maggio 2023. Articolo 1, comma 359, della legge 29 dicembre 2022, n. 197 (legge di Bilancio 2023). Elevazione dell'indennità di congedo parentale dal 30% all'80% della retribuzione per la durata massima di un mese di congedo e fino al sesto anno di vita del bambino. Istruzioni operative e contabili. Variazione al piano dei conti. INPS: 2023. Available from: https://www.inps.it/it/it/inps-comunica/atti/circolari-messaggi-e-normativa/dettaglio.circolari-e-messaggi.2023.05.circolare-numero-45-del-16-05-2023_14158.html.
33. Zambri F, Santoro A, Lubbock A, Volta A, et al. Training of health professionals to promote active fatherhood during the pre and post-natal care to prevent violence against women. Sustainability. 2022;14(15):9341. doi: 10.3390/su14159341
34. Pope C, Ziebland S, Mays N. Qualitative research in health care. Analysing qualitative data. BMJ. 2000; 320(7227):114-6.
35. Pizarro J, Gartzia L. Paternity leave: a systematic review and directions for research. Human Resource Management Review. 2024;34(1):101001. doi: 10.1016/j.hrmr.2023.101001
36. Lanjekar PD, Joshi SH, Lanjekar PD, Wagh V. The effect of parenting and the parent-child relationship on a child's cognitive development: a literature review. Cureus. 2022;14:e30574. doi: 10.7759/cureus.30574
37. OECD. Paternity leave indicators. In: OECD Family Database. OECD; 2019. Available from: https://www.oecd.org/els/family/database.htm.
38. Istituto Nazionale della Previdenza Sociale. Indennità di maternità/paternità per lavoratrici e lavoratori autonomi. Roma: INPS; 2017. Available from: https://www.inps.it/it/it/dettaglio-scheda.it.schede-servizio-strumento.schede-servizi.indennit-di-maternit-paternit-per-lavoratrici-e-lavoratori-autonomi-50585.indennit-di-maternit-paternit-per-lavoratrici-e-lavoratori-autonomi.html.
39. Istituto Nazionale della Previdenza Sociale. Analisi dei divari di genere nel mercato del lavoro e nel sistema previdenziale attraverso i dati INPS. Available from: https://www.inps.it/content/dam/inps-site/pdf/dati-analisi-bilanci/attivita-ricerca/Analisi_generi_web.pdf.
40. Eurofound, Parental and paternity leave – Uptake by fathers. Luxembourg: Publications Office of the European Union; 2019.
41. European Union. Directive (EU) 2019/1158 of the European Parliament and of the Council on work-life balance for parents and carers and repealing Council Directive 2010/18/EU. Official Journal of the European Union L 188/79, 12 July 2019. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32019L1158.
42. Kvande E, Brandth B. Designing parental leave for fathers – promoting gender equality in working life. Int J Sociol Social Policy. 2020;40:465-77.
43. Ray R, Gornick JC, Schmitt J. Who cares? Assessing generosity and gender equality in parental leave policy designs in 21 countries. J Euro Social Policy. 2010;20:196-216. doi: 10.1177/0958928710364434
44. Istituto Superiore di Sanità. Sorveglianza Bambini 0-2 anni. Sintesi dei risultati. Edizione 2022. Roma: ISS; 2022. Available from: https://www.epicentro.iss.it/sorveglianza02anni/pdf/Sintesi_CONVEGNO-O_2__Versione%20STAMPA_23_Marzo_2023.pdf.
45. Istituto Superiore di Sanità. Okkio alla Salute. Indagine 2023. Roma: ISS. Available from: https://www.epicentro.iss.it/okkioallasalute/indagine-2023.
46. United Nations. The 2030 Agenda for sustainable development. Available from: https://sdgs.un.org/2030agenda. Last accessed 22 February 2025.
47. Wu MJ, Zhao K, Fils-Aime F. Response rates of online surveys in published research: a meta-analysis. Computers Human Behav Rep. 2022;7:100206. doi: 10.1016/j.chbr.2022.100206

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 209-214
DOI: 10.4415/ANN_25_03_07

Does exceeding maximum waiting times of total hip replacement patients affect resource consumption? Evidence from a highly specialized orthopedic Italian hospital

Marco Nigro[1], Stanislav Russo[2], Maja Macan[3], Virginia Gulino[1], Beatrice Ricci[4], Edoardo Gallerani[1], Elena Lombardo[3], Peter Perger[5], Emanuele Padovani[2], Anselmo Campagna[6] and Matteo Buccioli[7]

[1]*Gestione Operativa Research Fellow, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy*
[2]*Dipartimento di Scienze Aziendali, Università di Bologna, Bologna, Italy*
[3]*Università di Bologna, Bologna, Italy*
[4]*Direzione Sanitaria, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy*
[5]*UMIT Tirol, Private University for Health Sciences, Medical Informatics and Technology, Hall in Tirol, Austria*
[6]*IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy*
[7]*Struttura Semplice Dipartimentale, Accesso ai Servizi e all'Attività Libero-Professionale, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy*

ABSTRACT

Background. Long waiting times for elective surgeries are a common issue in publicly funded healthcare systems, raising concerns about their impact on patient outcomes. In Italy, the National Health System assigns priority classes to regulate waiting times, with class C patients expected to undergo surgery within 180 days. This study investigates whether exceeding this threshold affects surgical and hospitalization outcomes for patients undergoing total hip replacement (THR).

Methods. We conducted a retrospective observational study on 1,872 class C patients who underwent THR between 2019 and 2022 at the Rizzoli Orthopedic Institute and affiliated centers. Patients were categorized based on adherence to the 180-day waiting threshold. The study analyzed differences in surgical time, length of hospital stays and touch time. Additional analyses considered patient characteristics such as the American Society of Anesthesiologists (ASA) classification and Body Mass Index (BMI). Independent t-tests were used to assess statistical significance.

Results. Patients exceeding the 180-day waiting limit did not show significantly longer hospital stays or surgical times compared to those operated on time ($p>0.05$). However, ASA classification and BMI influenced hospital stay duration, with high ASA (3-4) patients staying 1.7 days longer on average and obese patients (BMI ≥30) staying 0.4 days longer.

Conclusions. The findings suggest that exceeding the maximum waiting time does not negatively impact surgical outcomes or hospital stay duration. However, clinical characteristics such as ASA and BMI play a significant role in postoperative recovery. Further research is needed to refine prioritization criteria to ensure optimal patient outcomes.

Key words
- waiting times
- total hip replacement
- length of stay
- surgical time
- public health

INTRODUCTION

The increasing pressure on healthcare systems highlights the need to move away from linear models and respond flexibly to emerging challenges [1]. Growing demand, driven by an aging population and advances in medical technology [2], has outpaced supply, creating a gap between needed services and available resources.

Address for correspondence: Stanislav Russo, Dipartimento di Scienze Aziendali, Università di Bologna, Via Capo di Lucca 34, 40126 Bologna, Italy. E-mail: stanislav.russo2@unibo.it.

This imbalance results in worse access, longer waiting times, and larger waiting lists. Addressing long wait times is a priority for Italy's National Health System to ensure timely, quality care for all patients [3].

Hospitalization days and operating room time are key indicators of hospital efficiency [4], with prolonged durations signalling worsening patient conditions [5-7]. In elective cases, non-urgent patients are expected to remain stable while waiting, but excessive delays can worsen clinical outcomes. Long waiting times, common in publicly funded healthcare systems, are influenced by factors like system capacity, patient volume, and emergency arrivals, creating a complex interplay of demand and supply.

In elective treatments, maximum waiting times are commonly used to align healthcare supply with demand. Governments set these limits to establish targets or guarantees for treatment within a certain timeframe [8]. If not met, providers may face penalties or patients can seek care elsewhere. In Italy, the National Health System classifies waiting times by pathology priority, introduced in the 2006 National Plan for the containment of waiting times. This plan established four priority classes for elective surgeries and admissions, with specific waiting time guarantees for each class:

- A-hospitalization within 30 days;
- B-hospitalization within 60 days;
- C-hospitalization within 180 days;
- D-hospitalization without the maximum defined wait, at least within 12 months.

The purpose of the study is to investigate whether there is a difference in operating on time or out of maximum time, allowed by current regulations, patients placed on the class C waiting list for total hip replacement (THR) surgery, in terms of surgical time and hospitalization time.

For the research, the American Society of Anesthesiologists (ASA) classification and Body Mass Index (BMI) were considered as clinical parameters to be considered in defining variation in consuming the surgery resources.

In particular: "The ASA physical status classification system was introduced in 1941 to provide perioperative clinicians with a standardized method to evaluate a patient's medical comorbidities and help predict perioperative risk" [9].

For what concern BMI, defined as body weight in kilograms divided by the square of height in meters (kg/m^2), is a simple and widely used proxy for body fatness in adults" [10].

For descriptive completeness, THR is a routine major orthopaedic surgery performed to replace a damaged hip joint with an artificial implant. It is primarily indicated to relieve hip pain and stiffness caused by hip arthritis. This procedure may also be used in the treatment of injuries such as hip fractures, improperly developing hips, and other degenerative conditions of the joint [11, 12].

MATERIALS AND METHODS

The starting sample consisted of all scheduled surgical patients, of priority class C, that presenting minimal pain, dysfunction, or disability, and do not show a tendency to worsen nor can cause serious damage to the prognosis, subjected to THR surgery in the Rizzoli Orthopedic Institute (ROI) and its external platforms. It numbered 3,205 patients operated from 2019-2022. BMI and ASA grades were extracted from ROI workflow software used to manage and document all aspects of clinical care. Exclusion criteria are reported as follows. Ten patients whose operating time was less than 30 minutes were excluded from the sample as it was considered a mistake made while reporting the time. The patients operated at external accredited hospitals, in 2019, also had to be excluded from the sample, as the production tool was not available, therefore it was not possible to access the operating room time. Concerning BMI and ASA, it was apparent that there was no corresponding data for all patients, so those who did not have data on BMI and ASA did not make part of the research, which significantly reduced the sample size to 1,882 patients.

It was subsequently decided to exclude 10 patients whose main diagnoses were – tumor and special joint disorders – as their worse outcomes could be due to the severity of the disease and not the factors considered in this study, which could make the result of the analysis biased.

This made a final sample number, 1,872 patients of waiting who satisfied all the criteria and had all the necessary data for the analysis. Patients included have been operated on between 2019-2022 and have the following characteristics:

- main intervention: THR;
- priority class: C;
- main diagnosis: primary, secondary, and post-traumatic arthrosis; aseptic necrosis of the head and the neck of the femur; other mechanical complications of the joint prosthesis implantation.

The statistical analysis started with dividing the sample into 2 groups based on their waiting time. Patients who waited more than 180 days – expired, and the patients who waited less or equal to 180 days – non-expired. The means were calculated of each groups' length of stay (LOS), surgical and touch time. Then, descriptive statistics were provided.

The mean or average value is a measure of central tendency used to describe the average or typical value of a set of numbers or data points. To calculate the mean value, all values in a dataset are added up and then divided by the number of values.

Next, the same sample was divided in 4 different groups depending on patients' level of ASA and BMI as follows:

- low ASA (1, 2) and high ASA (3, 4);
- obese patients (BMI ≥30) and non-obese patients (BMI <30).

The means of all the outcome variables were calculated for each of these groups.

In the end the t-tests were performed to understand if there are statistically significant differences in means.

RESULTS

The research hypothesis is to question the fact that patients undergoing THR over 180 days, although these

are cases in which the pathological and general health condition should not worsen while waiting, have longer hospitalization and intervention times. To examine this, first the sample were separated in 2 groups – patients operated before 180 days (≤180) and patients operated after 180 days – a dummy variable "threshold" was created, representing a value of 1 for the patients who exceeded the 180 days threshold of maximum waiting, and 0 for patients who did not.

Out of a total of 1,872, 906 (48.4%) were called on time and did not exceed the threshold of 180 days, while 966 (51.6%) patients waited longer than predicted for their priority class.

From this threshold, the results of the analysis are reported in relation to the outcome and clinical parameters as follows below.

Waiting time

It is the time spent on the waiting list until the procedure is performed. The unit of measurement is days, and they are calculated from the date of insertion in the waiting list until the day of the intervention. In the study, a likewise distribution was found with a mean waiting time for patients being 243.8 days and a median of 187 days.

95% of patients received the treatment in 579.2 days, 75% in 339.8 days and 50% of them in 187 days. The 50th percentile is the median value, and it presents the point where half of the waiting times are less than or equal to that value, and the other half are greater.

This variable is used to make a division between patients who waited more and less than a maximum waiting time.

Next, the hospitalization days variable is described with the descriptive statistics of the hospitalization days with respect to the 180-day threshold. The same is done for the variables used to measure time in the OR-surgical time and touch time.

Length of stay in the hospital

LOS, also called days of hospitalization or hospitalization days, is a measure of the length of time a patient requires in-hospital care, so they refer to the number of days a patient spends in a hospital as an inpatient for medical treatment, in this study THR surgery. These days include both the day of admission and the day of discharge. The mean of the LOS in the sample is 7.7 days, which tells us that the patients in the study undergoing THR surgery on average stay 7.7 days in the hospital until their discharge. This period does not consider their outpatient recovery. The median value is quite similar to 7.4 days. The standard deviation is 2.9 showing us that data points are relatively close to the mean. The minimum value in the sample is 1.8 and the maximum is 30.5, representing the minimum and the maximum number of days a patient stayed in the hospital.

Next it is calculated the distribution of the LOS over binary variable threshold, which represents patients who exceeded the threshold of maximum waiting time of 180 days (threshold=1), and those who were operated in time(threshold=0). The distribution of the 2 groups seemed not to differ largely. Standard deviation is larger for the expired patients 3.9 and with respect to 2.7 and it also has a bigger maximum value of 30.5 days. However, this does not seem to significantly influence the means of the two groups since both are close to the mean of the entire sample -7.7.

Surgical time

Surgical time is calculated as the difference between the event of the end of the surgical procedure, the last suture, and the beginning of the surgical procedure, the beginning of the surgical incision. Our Descriptive statistics analysis of Surgical time variable (min) showed that the sample, the mean value, or the average time for performing the surgery is 77.3 minutes, the median was 73 minutes. The standard deviation that measures variability or spread from the mean and had the same unit as the data, was 25.5 min. The minimum in the sample was 31 min and the maximum was 275 min. The remaining descriptive statistics were later summarized.

Surgical time of the patients who exceeded the threshold waiting time has been analyzed and those who did not. From our results, the mean surgical time of patients admitted in time was 78 minutes, while patients who exceeded the threshold had on average a shorter surgical time, 76.7 minutes. Thus, patients who waited longer for the surgery on average did not have longer surgical time. The analysis shows quite the opposite, longer surgical time for non-expired patients. This difference, however, is less than 2 minutes.

ASA

ASA classification is represented by a grade, from 1 to 5 or 6, in this sample it ranges from 1 to 4. Proportions estimation was reported as a proportion or percentage of a categorical variable that belongs to each group (1-4). We found 25.34% of patients with grade ASA 1; 55.10% of them had ASA 2; 19.23% with ASA 3 and only 0.26% of patients with ASA 4. This is because, for the purpose of the analysis, only patients whose health should not deteriorate over time were included, so multimorbid patients with severe conditions are not present in the sample. There are only 5 patients with ASA 4.

For further analysis, we defined 1,2 as a low level of ASA and 3,4 as a high level of ASA and created dummy variables levelasa=0 for the low level of ASA and levelasa=1 for a high level of ASA.

It is possible to see the proportion of patients with high ASA and low ASA in the *Table 1*, 80.5% of patients had low ASA and 19.5% had high ASA. This proportion is expected in the present sample since it contains only patients of the C category, non-urgent whose health should not deteriorate while waiting.

It has been also calculated the distribution of hospitalization days for high and low levels of ASA. The mean length of stay for the patients with low ASA was 7.3 days and for those with high levels of ASA 9.1. The assumed differences in LOS between these groups are expected as patients with high ASA could have more complications and they could need longer recovery, surveillance of the health workers, additional tests, and consequentially longer length of stay.

Table 1
Proportion estimation of high (levelasa=1) and low (levelasa=0) ASA variable

Proportion estimation — Number of obs = 1,872

	Proportion	Std. err.	Logit [95% conf.	interval]
levelasa				
0	.8050214	.0091568	.7864343	.8223561
1	.1949786	.0091568	.1776439	.2135657

ASA: American Society of Anesthesiologists; obs: observation; std err: standard error; logit: logistic regression; conf. interval: confidence interval.

As showed in *Table 2*, surgical time is calculated for patients with low ASA (levelasa=0) and patients with high ASA (levelasa=1). It is possible to see that high ASA patients do not have significantly longer surgical time (77.6 min) in respect to low ASA patients (77.2 min).

BMI

It provides a numerical value that categorizes individuals into different weight categories. From the descriptive statistics analysis the mean value was 27, which the BMI scale classifies as overweight. The median was 26.6, so that half of the dataset has BMI values below 26.6, and the other half has values above this value. Skewness and kurtosis are quite low, indicating that distribution can be close to normal.

We also calculated the summary statistics of hospitalization days for non-obese patients with dummy variable levelbmi=0 and obese patients with dummy variable levelbmi=0. From the results it can be observed that their means were slightly different, being 7.6 days for non-obese and 8 days of hospitalization for obese patients. This gave additional reason to test for the differences between these 2 groups. The groups were different in size, with 1,430 not-obese patients and 442 obese patients with BMI larger than 30.

Obese patients had on average longer surgical time (80 minutes) than non-obese patients (76.4 minutes).

In our sample, the difference between these 2 groups was 1.8 days of hospitalization. To investigate if this difference was significant, a t-test for independent samples assuming equal variances was used. In this inferential statistic, the null hypothesis states that the difference in the means between the two groups is 0. Observing the test, p-value was really close to 0 and less than the significance level of 0.05, therefore, the decision is to reject the null hypothesis and accept the alternative one. There was a difference in the days of hospitalization for patients with low and high ASA. Patients with high ASA tend to have longer hospitalization than patients with low ASA, in this sample they on average stay 1.8 days longer in the hospital.

Table 2
Summary statistics of surgical time of patients with low and high level of ASA-minutes

-> levelasa = 0

Variable	Obs	Mean	Std. dev.	Min	Max
tempochiru~n	1,507	77.25946	25.12637	31	275

-> levelasa = 1

Variable	Obs	Mean	Std. dev.	Min	Max
tempochiru~n	365	77.64658	26.98216	35	264

ASA: American Society of Anesthesiologists; obs: observation; std. dev.: standard deviation; min: minimum; max: maximum.

Once again, a significant difference in means between 2 groups, obese and non-obese patients, was confirmed. The t-test done to test this hypothesis gave the p-value of 0.02, that is smaller than the significance level (0.05), thus rejecting the null and the alternative was accepted. The obese patients have longer hospitalization than non-obese patients. The obese patients stayed on average 0.4 days longer in the hospital (9.6 hours).

It is possible to confirm that there is a significant difference in means of surgical time between 2 groups, obese and non-obese patients. The t-test done to test this hypothesis gave the p-value of 0.009, that is smaller than the significance level (0.05), thus rejecting the null and the alternative was accepted. The obese patients have longer surgical time than non-obese patients. The operation of the obese patients on average lasted 4 minutes more.

The t-test was applied for each of the investigated hypotheses. In particular, a standard student t-test was performed, and an inferential statistic was used to determine if there was a statistically significant difference between the means of 2 groups.

More in detail, statistical analysis investigated:

- differences in hospitalization days between patients who expired and those who did not expire from the waiting list;
- differences in surgical time between patients who expired and did not expire from the waiting list;
- differences in hospitalization days between patients with low and high ASA;
- differences of hospitalization days between obese and non-obese patients;
- differences in surgical time between obese and non-obese patients.

Only two results highlighted a significant difference in terms of resources consumed. In particular:

- the differences in hospitalization days between patients with low and with high ASA;
- the differences of hospitalization days between obese and non-obese patients.

1) "Null hypothesis": there is no difference in hospitalization days between patients with low and with high ASA.

"Alternative hypothesis": there is difference in days of hospitalization between patients with low and with high ASA.

Here, we questioned if there was a significant difference in means between patients with high and low ASA grades. In our sample, the difference between these 2 groups was 1.8 days of hospitalization. To investigate if this difference was significant, a t-test for indepen-

dent samples assuming equal variances was used. In this inferential statistic, the null hypothesis states that the difference in the means between the 2 groups is 0. Observing the test, the p-value was really close to 0 and less than the significance level of 0.05, therefore, the decision was to reject the null hypothesis and accept the alternative one. There was a difference in the days of hospitalization for patients with low and high ASA. Patients with high ASA tend to have longer hospitalization than patients with low ASA, in this sample they on average stay 1.8 days longer in the *Table 3*.

2) "Null hypothesis": there is no difference in hospitalization days for obese than non-obese patients.

"Alternative hypothesis": there is a difference in hospitalization days for obese than non-obese patients.

Here, a significant difference in means between 2 groups, obese and non-obese patients, is again confirmed. The t-test done to test this hypothesis gave the p-value of 0.02 that is smaller than the significance level (0.05), thus we rejected the null and accepted the alternative. The obese patients have longer hospitalization than non-obese patients. The obese patients stayed on average 0.4 days longer in the hospital (9.6 hours, as showed in *Table 4*.

DISCUSSION

Patient prioritization represents a crucial tool for assuring timely and fair access to health care services. Maximum waiting times can be understood as a form of guarantee or agreement made between the health provider and the patient that assures that treatment will be provided and that this will happen within a specified timeframe.

After performing the t-tests to determine if there is a statistically significant difference between the means of the two groups – patients who exceeded the threshold waiting time and patients who did not – it can be concluded that being operated on after the time limit of 180 days does not result in having worse outcomes, i.e., longer length of stay and surgical time.

All two t-tests showed that the difference in means is irrelevant. Two groups of non-expired and expired patients and similar in size. There are 906 non-expired patients and 966 expired ones in the sample, therefore we do not assume that the difference in the size of the sample could influence the outcomes of the t-tests. The size of the sample is large enough to perform this type of analysis, however, a larger sample size could make the analysis more relevant and precise.

Table 3
T-test assuming equal variances of the hospitalization days variable with respect to patients with low ASA and high ASA grade

Two-sample t test with equal variances

Group	Obs	Mean	Std. err.	Std. dev.	[95% conf.	interval]
0	1,507	7.359604	.065006	2.523539	7.232092	7.487116
1	365	9.10941	.2008468	3.837172	8.714445	9.504376
Combined	1,872	7.700779	.06727	2.910544	7.568847	7.832711
diff		-1.749806	.1649494		-2.07331	-1.426302

diff = mean(0) - mean(1) t = -10.6081
H0: diff = 0 Degrees of freedom = 1870

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0
Pr(T < t) = 0.0000 Pr(|T| > |t|) = 0.0000 Pr(T > t) = 1.0000

ASA: American Society of Anesthesiologists; obs: observation; std err: standard error; std. dev.: standard deviation; conf. interval: confidence interval.

Table 4
T-test assuming equal variances of the hospitalization days variable with for obese and non-obese patients

Two-sample t test with equal variances

Group	Obs	Mean	Std. err.	Std. dev.	[95% conf.	interval]
0	1,430	7.606065	.0750941	2.839709	7.458759	7.753372
1	442	8.007205	.1480427	3.112419	7.716248	8.298162
Combined	1,872	7.700779	.06727	2.910544	7.568847	7.832711
diff		-.4011398	.1581679		-.711344	-.0909355

diff = mean(0) - mean(1) t = -2.5362
H0: diff = 0 Degrees of freedom = 1870

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0
Pr(T < t) = 0.0056 Pr(|T| > |t|) = 0.0113 Pr(T > t) = 0.9944

Obs: observation; std err: standard error; std. dev.: standard deviation; conf. interval: confidence interval.

The second research question regarded patients' characteristics that, if high, can define individuals as at-risk patients, ASA and BMI. It was evident that patients with high ASA spent 1.7 days more time in the hospital than patients with low ASA. The same is shown for obese patients who had 0.4 days or 9.6 hours longer stay in the hospital than non-obese patients.

All these differences were significant in the tests with a p-value smaller than the significance level chosen for this analysis (0.05).

T-tests performed in this analysis confirmed that there is a statistical difference in means between the two groups, but it doesn't determine whether one variable causes the difference in means or if there are other factors at play.

It is evident that the distribution of these variables is proportional in the two groups, patients who exceeded the 180-day waiting limit have on average a very similar BMI (≈27) and ASA (≈1.9) to patients who were surgically treated on time. The groups are balanced; therefore, even if they are aggravating factors, these variables did not cause bias in the results of the analysis of tests done on the impact of waiting time on the outcomes.

Finally, although at-risk patients do have longer LOS, based on our initial analysis, which indicated that adhering to the 180-day threshold does not influence the outcomes, we can assume the same for the at-risk groups, as the variables (age, ASA; BMI) are evenly distributed across both groups. There is no presumption that exceeding maximum waiting times worsens the outcomes: length of stay and surgical time, even for at-risk patients. However, further analysis should be done on the issue.

T-tests, as mentioned before, do not establish causation or explain why that difference exists. To investigate the impact of one variable on another and establish causation it is needed to conduct more complex analyses, such as regression analysis or experimental design. Regression analysis allows us to assess the relationship between variables and can help identify whether changes

in one variable are associated with changes in another. However, even correlation or regression analyses cannot definitively establish causation; they can only provide evidence of an association or relationship.

At first glance, the results of the analysis can put into question the accuracy of the patient prioritization methods and adherence to the maximum waiting times, given that the patients waiting more than six months do not show worse outcomes in terms of longer hospital stay and longer surgical time. This conclusion holds true for both the overall patient population and at-risk groups defined by ASA, BMI. However, the benefits of adherence to maximum waiting times go beyond the avoidance of further deterioration of patients' health and surgical outcomes.

CONCLUSIONS

In conclusion, the maximum waiting times are the most prevalent approach to deal with the long waiting times and are an indispensable part of regulations and guidelines for the management of the waiting list implemented by the hospitals, including ROI.

According to the literature, for patients undergoing THR, receiving care on time reduces the burden of living with pain or dysfunction that impacts the quality of life.

However, it remains important to state that health care institutions, for organizational reasons and in order to be able to respond efficiently to the health demand of citizens represented by waiting lists, should still consider in organizational planning not only waiting times but also factors such as ASA and BMI, because they could influence the scheduling of interventions and the management of productive resources allocated to planned surgical activity.

It's important to note that while statistical differences were identified, the study does not establish causation. It indicates that certain patient characteristics are associated with longer lengths of stay but it doesn't determine whether these characteristics directly cause the differences. The study acknowledges the need for further analysis to delve deeper into the relationship between these variables.

Authors' contributions

All Authors have contributed significantly to the work and approved the final version.

Conflict of interest statement

There are no competing interests to declare.

Received on 5 February 2025.
Accepted on 26 June 2025.

REFERENCES

1. Plsek PE, Greenhalgh T. Complexity science: The challenge of complexity in health care. BMJ. 2001;15;323(7313):625-8. doi: 10.1136/bmj.323.7313.625
2. Frankel S, Ebrahim S, Davey Smith G. The limits to demand for health care. BMJ. 2000;321(7252):40-5. doi: 10.1136/bmj.321.7252.40. PMID: 10875836
3. De Rosis S, Guidotti E, Zuccarino S, Venturi G, Ferrè F. Waiting time information in the Italian NHS: A citizen perspective. Health Policy. 2020;124(8):796-804. doi: 10.1016/j.healthpol.2020.05.012
4. Baek H, Cho M, Kim S, Hwang H, Song M, Yoo S. Analysis of length of hospital stay using electronic health records: A statistical and data mining approach. PLoS One. 2018;13(4):e0195901. doi: 10.1371/journal.pone.0195901
5. Nikolova S, Sinko A, Sutton M. Do maximum waiting times guarantees change clinical priorities for elective treatment? Evidence from Scotland. J Health Econ. 2015;41:72-88. doi: 10.1016/j.jhealeco.2015.02.001
6. The Lancet Rheumatology. Too long to wait: The impact of COVID-19 on elective surgery. Lancet Rheumatol. 2021;3(2):e83. doi: 10.1016/S2665-9913(21)00221-5
7. Sobolev BG, Fradet G, Hayden R, Kuramoto L, Levy AR, FitzGerald MJ. Delay in admission for elective coronary-artery bypass grafting is associated with increased in-hospital mortality. BMC Health Serv Res. 2008;8:185. doi: 10.1186/1472-6963-8-185
8. Organisation for Economic Co-operation and Development. Waiting times for health services: Next in line. Paris: OECD Publishing; 2020. doi: 10.1787/242e3c8c-en
9. Hendrix JM, Garmon EH. American Society of Anesthesiologists Physical Status Classification System. Treasure Island (FL): StatPearls Publishing; 2025.
10. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894(i-xii):1-253.
11. American Academy of Orthopaedic Surgeons. Total hip replacement. Rosemont (IL): AAOS; 2023. Available from: https://orthoinfo.aaos.org/en/treatment/total-hip-replacement.
12. Johns Hopkins Medicine. Hip replacement surgery. Baltimore (MD): Johns Hopkins University; 2023. Available from: https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/hip-replacement-surgery.

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 215-225
DOI: 10.4415/ANN_25_03_08

Healthcare professionals' perceptions of caesarean section decision-making and the implementation of Audit&Feedback strategies in the Calabria Region: a qualitative study

Vincenza Di Stefano[1,2*], Jessica Preziosi[3*], Francesca Zambri[1], Gabriella Tambascia[1,2], Paola Scardetta[1], Edoardo Corsi Decenti[1], Flavia Splendore[1,2], Alice Maraschini[4], Daniela Lico[5], Erika Rania[5], Deborah Considerato[5], Roberta Venturella[6], Serena Donati[1], Anna Domenica Mignuoli[7], Angela Giusti[1] and the EASY-NET Working Group[**]

[1]*Centro Nazionale per la Prevenzione delle Malattie e la Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy*
[2]*Dipartimento di Biomedicina e Prevenzione, Università degli Studi di Roma "Tor Vergata", Rome, Italy*
[3]*Dipartimento di Scienze della Salute della Donna, del Bambino e di Sanità Pubblica, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy*
[4]*Servizio di Statistica, Istituto Superiore di Sanità, Rome, Italy*
[5]*Ospedale"Pugliese-Ciaccio", Catanzaro, Italy*
[6]*Dipartimento di Medicina Sperimentale e Clinica, Università degli Studi "Magna Grecia" di Catanzaro, Catanzaro, Italy*
[7]*Dipartimento Salute e Walfare, Regione Calabria, Catanzaro, Italy*
**These Authors share first authorship*
***The members of the EASY-NET Working Group are listed before the references*

Abstract

Introduction. Calabria Region has one of the highest caesarean section (CS) rate in Italy. To encourage the implementation of Audit&Feedback strategies, this study aimed to explore factors influencing CS decision-making from healthcare professionals' perspectives.

Method. A descriptive qualitative study was conducted through focus groups (FGs) with healthcare professionals (HPs) from 11 Maternity Units and 3 Community Health Services for Families of Calabria, from February to April 2021.

Results. Six FGs were carried out, involving 92 HPs. Main determinants influencing high CS rates included medicalization of birth, reported women's fear of childbirth, family pressure, cultural beliefs, organizational issues, and medico-legal concerns. HPs emphasized teamwork, midwifery-led low-risk pathways, training, and audits to reduce CS rates and improve quality of care.

Conclusions. This study identified determinants influencing CS decision-making in Calabria highlighting opportunities to reduce CS through empowering education, shared protocols, and women's active involvement in decision-making process. Audit&Feedback strategies could improve health outcomes.

Key words
- caesarean section
- audit and feedback
- qualitative study

INTRODUCTION

In the last decades, caesarean section (CS) rates have increased steadily worldwide [1], and these trends are expected to continue [2]. The ideal CS rate was stated to be around 10-15% by the World Health Organization (WHO) [3], with a rate over 19% not associated with benefits in reducing maternal and neonatal morbidity [4].

Address for correspondence: Francesca Zambri, Centro Nazionale per la Prevenzione delle Malattie e la Promozione della Salute, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: francesca.zambri@iss.it.

In 2019, in Europe, the median CS rate was 26%, showing stability or even a decrease in some countries [5]. In Italy, although the CS rate gradually decreased from 38.0% in 2009 to 30.3% in 2023 [6], it remains one of the highest in Europe [7], with significant regional variations, ranging from 17.0% in Tuscany to 46.5% in Campania [6]. Substantial differences also exist within the same regions, as highlighted by the Italian National Outcomes Evaluation Program (Programma Nazionale Esiti, PNE) [8]. In 2023, Calabria reported a CS rate of 35.8% [6], and despite its reduction over the years, the Region still shows high rates of both primary CS [9].

An increased CS rate is often observed when the procedure is performed without clear clinical indications, driven by multiple factors [10]. Health professionals' (HPs) attitudes play a key role in CS decision-making with frequent ambiguity regarding what they consider clinical indications [11]. Gaining a deeper understanding of HPs' views, values, and concerns is crucial for effective change management [11]. Exploring their perceptions of the factors influencing the decision to perform CS provides valuable insights into the decision-making process. A qualitative approach is commonly used to investigate these aspects, allowing researchers to examine the *what*, *why*, *how* and *where* of the factors influencing CS decision-making [12-14].

In 2019, the Calabria Region joined the EASY-NET program (NET-2016-02364191-6), a project funded by the Italian National Ministry of Health and the participating regions (https://easy-net.info/about/) and focused on implementing Audit&Feedback (A&F) strategies to improve the quality of care. As part of this initiative, the Work Package 6 in the Calabria Region aimed to evaluate the appropriateness of CS and healthcare practices in different clinical and organizational settings and to assess the effectiveness of A&F strategies in modifying professional behaviour and improving adherence to evidence-based practices in CS decision-making [15, 16]. The Work Package 6 specifically focused on engaging HPs, evaluating their perceptions and attitudes, and identifying potential barriers and facilitators to the adoption of A&F strategies in CS reduction [17]. Given the concerns about rising CS rates and the lack of clarity regarding the factors influencing CS decision-making, understanding the perspectives of those directly involved in these decisions is essential.

The aim of this study is to explore the factors influencing CS decision-making from the perspectives of HPs in Calabria Region, within the EASY-NET program, to support the implementation of A&F strategies in the Region.

METHODS

Design

A descriptive qualitative design was selected to gain a deeper understanding of the factors influencing the decision-making process in the context of CS [14, 18]. This research design aligns with a constructivist paradigm, guiding appropriate actions based on the findings [19].

Six focus groups (FGs) were conducted to explore HPs' perceptions of the determinants related to CS decision-making [20, 21]. The study was designed and reported following the Standards for Reporting Qualitative Research (SRQR) checklist [22].

Healthcare setting

In Calabria and across Italy, maternal and child public healthcare services is free of charge for all women. The Italian National Health System (NHS) follows a *Hub and Spoke* model, where *Hubs* handle high-complexity cases and *Spokes* manage low- to medium-complexity ones, referring high-risk patients when needed. The Maternity Units network in Calabria consists of three *Hub* hospitals and eight *Spoke* hospitals, including one private facility. The Calabria Region has also implemented dedicated pathways for managing low-risk pregnancies, ensuring integration between hospitals and territorial services. The Community Health Services for Families are primary care services dedicated to family and women's health, ensuring access in both urban and rural areas. They play a key role in promoting maternal health strategies, offering antenatal and postnatal care, antenatal group meetings, and structured specific support for low-risk pregnancies.

Participants

All 11 Maternity Units were invited to participate. Furthermore, the three Community Health Services for Families involved in the low-risk care pathway were also included in the study. Participants were recruited through purposeful, theoretically driven sampling, selecting HPs actively involved in maternity and neonatal care at the time of the study. They were contacted via email and invited to participate in the study. Specifically, the sample included a diverse mix of professionals involved in the birth pathway (obstetricians, midwives, anaesthesiologists, and paediatricians), working in various healthcare settings, including both hospital and community-based. Participants held different roles and levels of experience, reflecting the diversity of healthcare professionals involved in maternity care across the Calabria Region, as well as the structure and composition of local healthcare teams.

Data collection and analysis

Socio-demographic data were collected anonymously through a structured online form, shared with participants the day before the FGs, alongside an informed consent form to authorize audio recording and anonymous transcription of discussions. FGs were conducted online, in compliance with COVID-19 regulations, and facilitated by expert researchers from the Italian National Institute of Health (Istituto Superiore di Sanità, ISS). A semi-structured interview guide *(available online as Supplementary material)* was used, developed collaboratively by the research team, in conjunction with expert HPs and local specialists. An observer from the research team attended each FG, lasting 60 to 90 minutes. Full transcripts were independently read and coded by two researchers, who then discussed the themes and categories to define the coding tree. In case of disagreement, a third researcher was consulted. A categorical data analysis approach was applied, combining deductive and inductive approach [19]. Deductive cat-

egories were pre-defined based on the primary research questions, while inductive categories emerged during the coding process. The analysis was conducted using NVivo 12 Plus software. Data saturation was reached when no new categories emerged.

Ethical approval and data protection

Ethical approval was granted by the Research Ethics Committee of "Pugliese Ciaccio" Hospital in Catanzaro, which served as the coordinating centre for the project (Record 55, CdA-INIH of 30.03.2022). Informed consent was obtained from all participants before the focus group interviews. Anonymity was ensured, and recordings were transcribed using assigned codes and general professional roles (e.g., midwife, obstetrician) for confidentiality.

RESULTS

Six FGs were conducted from February to April 2021, involving a total of 92 participants, with a mean age of 44.8 years (SD±10.9). The participants were HPs from 10 out of 11 Maternity Units and three of the Community Health Services for Families of Calabria Region. The represented professions were midwives (45%), obstetricians (35%), anaesthesiologists (11%) and paediatricians (9%). The main socio-demographics characteristics are shown in *Table 1*.

The themes and categories emerging from the deductive and inductive categorial qualitative data analysis are described below and presented in *Table 2*.

Theme 1. Determinants of CS perceived by HPs

The first theme explores HPs' perceptions of the key determinants influencing CS rates, categorized into external influences, organizational factors of the healthcare system and HPs' personal influences.

1.1 External influences on HPs

External determinants arise mainly from women's belief and their social context, which professionals perceive as influencing the choice of delivery mode.

Table 1
Socio-demographic characteristics of participants (N=92)

Participants' data	N (%)
Mean age in years	44.8 (SD±*10.9*)
Women	74 (80.4)
Men	18 (19.6)
Professions	
Obstetrician	29 (31.5)
Obstetrician resident	4 (4.4)
Midwife	35 (38)
Midwife coordinator	6 (6.5)
Anaesthesiologist	10 (10.9)
Paediatrician	8 (8.7)
Working experience in childbirth care	
Mean working years (±*SD*)	18 (SD±11.3)
Working place	
Maternity Unit	85 (92.3)
Community Health Services for Families	7 (7.6)

SD: standard deviation

- *General perspectives on CS rate*

HPs recognized the high CS rate as a global issue, not limited to Calabria, as well as the need for change in current clinical practice.

Obstetrician: *"It is widely acknowledged that the CS rate is too high".*

Paediatrician/Anaesthesiologist: *"We know this is a shared problem, not just in Calabria".*

- *Beliefs about normal birth*

HPs reported a cultural shift has led many women to view childbirth as a medicalized event rather than a physiological process. The misconception that CS is safer and more convenient than vaginal birth (VB) reflects a lack of awareness about associated risks and benefits:

Midwife: *"…Women believe that, with new techniques, a planned CS is safer than VB and therefore they have fewer medical complications".*

Although most HPs supported CS only when medically necessary, some perceived it as a safer option, especially for advanced maternal age or Assisted Reproductive Technology pregnancies conceived.

- *Women's request for CS*

HPs noted that some women request a CS early in pregnancy, primarily due to fear of labour:

Obstetrician/Midwife: *"There are not a few women who, from the moment they see the first foetal heartbeat, ask for a CS due to fear of labour".*

During labour, requests for CS often stem from pain, fatigue, or fear. While some HPs acknowledge these requests, many believe that self-determination in birth mode should not be an option without medical indication:

Obstetrician: *"Self-determination during labour should not exist because 99% of women in labour would ask for a CS".*

However, in non-emergency cases, HPs sometimes consider women's persistent requests, which may influence final decisions:

Obstetrician: *"Certainly, if the woman repeats continuously in the ears, "I want CS, I want CS" it often comes to that in the end. But I do not agree with the woman's self-determination".*

- *Women's expectation and preparedness for childbirth*

A cross-cutting concern in all FGs was women expectations and preparation to childbirth. HPs emphasized the importance of prenatal information to set realistic expectations and reduce fear.

Midwives, in particular, stressed the role of preparation in birth outcomes, advocating for antenatal group meetings to help women manage labour fears and build confidence. However, HPs noted challenges in organizing such meetings, particularly in Calabria's remote areas, where attendance is low due to cultural resistance and logistical barriers. As a result, birth experiences shared by family members or peers can strongly influence women's perception of childbirth.

Obstetrician: *"We know that in certain remote areas, there is resistance to physiological birth pathways. Antenatal*

Table 2
Themes, categories, nodes

Themes	Categories	Nodes
1. Determinants of CS perceived by HPs	1.1 External influences on HPs	• General perspectives on CS rate • Beliefs about normal birth • Women's request for CS • Women's expectations and preparedness for childbirth • Fear of childbirth • Pressure from relative
	1.2 Organizational influences of the healthcare system	• Insufficient staffing and working alone during shifts • Challenges in emergency transfers • Influence of private healthcare • Fragmented care pathway • Clinical shared protocols, standardized language, and procedures • Vaginal Birth After Caesarean • Bureaucratic burden • Impact of COVID-19 on healthcare organization • Sense of abandonment by institutions
	1.3 HPs' personal influences	• Adherence to delivery's physiological timing • Clinicians' experience • Fear of legal consequences
2. Enablers of quality birth care	2.1 Staff commitment 2.2 Teamwork 2.3 Midwifery-led pathways 2.4 Audit&Feedback	
Suggestions for continuity of care improvement	• Simulated training courses on obstetric topics • Periodic clinical audits • Development, sharing, and regular updating of clinical protocols • Cultivating a climate of trust within the team, supporting low-risk labor and delivery under midwifery-led care • Promoting continuous professional development • Facilitating effective networking between hospital and community services • Utilizing management units and regional data streams • Implementing the Audit&Feedback strategy	

CS: Cesarean section; HP: Healthcare professional.

group meetings are not part of the cultural background, but they could be a good starting point!"

Midwife: *"During labour we understand if women have attended antenatal group meetings because they bear the pain better, they are stronger and more confident".*

Obstetrician: *"When there is no proper education about pregnancy, women often rely more on family members or neighbours' experience than on professionals, unfortunately, making counselling more difficult".*

• *Fear of childbirth*

Closely linked to self-confidence and preparedness, HPs identified fear of labour pain as a major factor influencing women's preference for CS:

Obstetrician: *"We are seeing increasing difficulty among women in their approach to labour and pain… many ask for a CS because they are often afraid of pain, they can't handle pain, so it is the main cause".*

Limited access to epidural analgesia in some hospitals, further exacerbates this fear, influencing women's birth choices:

Anaesthesiologist: *"Pain management has now entered woman's mindset…analgesia plays an important role in the childbirth experience".*

Obstetrician: *"When labour is so long and it lasts many hours, women could be helped by analgesia".*

• *Pressure from relatives*

The social perception that CS is safer than VB extends beyond women, influencing family members, who often exert strong pressure on the decision-making process, in addition to cultural beliefs.

Anaesthesiologist: *"…relatives are often behind the door, and the pressure is very strong".*

Obstetrician: *"Culturally, you have 30-40 people waiting outside the delivery block and they ask you 'And when is the baby going to born?', 'Why hasn't the baby been born yet?', 'Why don't you just do a CS?'…so in the end it becomes an instrumental delivery or a CS".*

1.2 Organizational influences of the healthcare system

The second category of *Determinants of CS perceived by HPs* theme focuses on how the organization of the healthcare system influences CS decision-making.

• *Insufficient staffing and working alone during shifts*

Staff shortages emerged as a recurring concern across all FGs, particularly related to shift scheduling. HPs expressed concern about being required to work in multiple settings simultaneously, which can compromise the quality of care:

Midwife: *"We are few, with no dedicated schedule, especially in the morning... at the same time, a midwife, who*

has to follow labour, has to take care of the CS surgery. We do it with great effort, because there are no staff, not just the midwives, all the staff".

Professionals recognized that staff shortages are not unique to Calabria but represent a broader issue within Italy's public NHS:

Obstetrician: *"It's a common problem, not just in Calabria, but probably across Italy. You can't provide good care if professionals keep decreasing instead of increasing".*

The reorganization of the NHS has exacerbated staff shortages, particularly after the closure of smaller Maternity Units performing fewer than 500 deliveries per year. A neonatologist noted:

Paediatrician: *"Since the NHS reorganization and the closure of smaller Maternity Units, births have increased in larger centres, but with the same number of staff".*

HPs emphasized the importance of increasing personnel to provide high-quality care:

Midwife: *"You need to have staff; you need to have midwives".*

Staff shortage and working alone during shifts were critical factors that led HPs to make quicker decisions in situations where labour safety was in question, often opting for a CS pre-emptively to avoid complications:

Obstetrician: *"I wouldn't say it's the main reason, but it definitely plays a role in deciding to do a CS half an hour earlier rather than later. Personally, it does".*

Obstetricians expressed frustration over having no colleagues to discuss clinical cases with during solo shifts:

Obstetrician: *"What do I do? Send the CTG (cardiotocography) to my colleague? If something is wrong, like an abnormal CTG or prolonged dilation, you're alone. In the end, probably the simplest decision is to decide for a CS".*

In urgent cases, on-call colleagues could be contacted, but it's perceived that they were called primarily to perform a CS, rather than for collaborative decision-making:

Obstetrician: *"If the doctor is alone on shift, they have to call the on-call doctor, who usually responds, "You called me to avoid legal problems, let's just do the CS".*

- *Challenges in emergency transfers*

The connection between *Spoke* and *Hub* hospitals was highlighted as a concern in urgent or emergency situations, particularly regarding the availability of blood bags, and the timing of patient transfers to Neonatal Intensive Care Units (NICU).

- *Influence of private healthcare*

Many women preferred private obstetric care, relying on a private obstetrician, who determined the mode of birth, rather than using public antenatal healthcare services:

Midwife: *"Many women are followed privately, and in the end, the doctor decides the mode of birth".*

Some professionals raised concerns about other medical specialists certifying that women were unable to handle labour for VB due to non-obstetric health problems, a practice with potential legal implications. Additionally, HPs criticized the previous system, where private maternity care facilities performed excessive CS procedures due to financial incentives, with the subsequent increase in repeat C-section as well:

Obstetrician: *"In the past, private hospitals performed a lot of CS to receive higher reimbursements. Now, we are dealing with more repeat CS cases".*

- *Fragmented care pathway*

HPs reported low levels of integration within the birth care pathway, as well as a lack of collaboration and trust between different healthcare providers, including Community Health Services for Families, Hospital-based professionals, freelance obstetricians and midwives, general practitioners (GPs) and family paediatricians. In some areas, the integration process for managing low-risk pregnancies was still in its early stages, facing many challenges. Resistance to new care modalities and fluid collaboration between hospital and community services were noted, with the reorganization of work and the creation of integrated clinical tools seen as essential for progress:

Midwife: *"Improving communication would help us achieve better outcomes".*

- *Clinical shared protocols, standardized language, and procedures*

Only few centres reported having defined, regularly updated protocols. In contrast, in centres without standardized protocols, HPs frequently raised concerns about the lack of consistency in clinical management.

Obstetrician resident: *"We have protocols that we all follow, and we update them monthly, discussing our clinical cases in light of these protocols".*

Obstetrician: *"If we had shared protocols on induction timing and criteria, we might wait the proper time than inducing labour a week early. That could help reduce the primary CS rate and working better".*

HPs reported a substantial variation in timing of birth, depending on the clinician, so the implementation of shared protocols could uniform the management (e.g., *a uniform approach to CTG interpretation*) and reduce primary CS.

Midwife: *"For minor decelerations, guidelines suggest trying maternal position changes first. If we followed protocols instead of rushing decisions, we could prevent some early CS procedures".*

- *Vaginal birth after caesarean*

The planned elective repeat CS was another cross-cutting topic. HPs were aware that the low rate of Vaginal Birth After Caesarean (VBAC) contribute to the high overall CS rate. Factors limiting VBAC include lack of women's and relatives' awareness, limited support from HPs, insufficient staff and protocols, structural barriers (e.g., *no blood bank in some Spoke hospitals*):

Midwife: *"We perform repeat CS often, and that increases the total CS rate".*

Obstetrician: *"Women assume that after one CS, they will automatically need another CS because obstetricians don't support VBAC. We simply don't have the structures to manage these cases".*

Obstetrician: *"The absence of a second doctor and a blood transfusion centre makes VBAC even more difficult".*

• *Bureaucratic burden*

Some HPs complained about excessive bureaucracy and the lack of an integrated IT system to facilitate lab test requests, specialist referrals, and medical record sharing:

Obstetrician: *"Everything is still done on paper, there's no software system to quickly view test results or submit requests electronically. Documents are still physically carried between departments!"*

• *Impact of COVID-19 on healthcare organization*

The COVID-19 pandemic severely disrupted maternal care services, particularly the suspension of antenatal group meetings and the absence of a person of woman's choice to support her during pre-natal and postnatal visits. COVID restrictions also affected organisation, leading to the sudden suspension of periodic audits and meetings where clinicians discussed clinical cases and protocols.

Obstetrician: *"Women preparation has worsened, probably because antenatal group meetings were no longer usable, due to the COVID-19 emergency".*

Midwife: *"The absence of fathers or a support person during childbirth had a huge impact. Women were frightened".*

• *Sense of abandonment by institutions*

Some HPs felt that the CS rate couldn't be reduced without the help of healthcare institutions, and felt unsupported, especially when requesting additional staff or resources.

Obstetrician: *"We are alone. We've never received answers from the institutions".*

1.3 HPs' personal influences

The third category focuses on internal factors influencing HPs in CS decision-making.

• *Adherence to delivery's physiological timing*

When discussing excellence in maternity care, obstetricians highlighted the autonomy of midwives as a key factor in ensuring quality care.

Obstetrician: *"Midwives guide physiological childbirth!"*

Although midwives were recognized for their crucial role in promoting VB, HPs reported the system's strong focus on medicalised care, prioritising pathology pathways over the natural timing of childbirth, impacting both labour management and CS rates.

Obstetrician: *"Perhaps we need to have more confidence in our midwifery team".*

Obstetrician: *"We should probably leave more space for midwives".*

Obstetricians acknowledged that their presence in the delivery room, even during uncomplicated labours, could put pressure on midwives.

Obstetrician: *"Obstetricians often intervene even during physiological labour; their constant presence in the delivery room isn't helpful".*

Midwives also highlighted inappropriate birth practices, such as not respecting the physiological timing of labour or neglecting to encourage women to adopt comfortable birthing positions.

Midwife: *"We do not respect the time of labour times, the physiological time!"*

Midwife: *"During labour, we should respect the transition period instead of treating it as a stage where contractions stop and oxytocin must be administered".*

• *Clinicians' experience*

Experience significantly influenced decision-making. Less experienced obstetricians and midwives tended to opt for CS earlier than their more experienced colleagues:

Obstetrician: *"Younger midwives, even more than younger doctors, fear reaching the so-called 'point of no return".*

The tendency to act pre-emptively was also noted by neonatologists, who shared the concern of avoiding potential complication:

Paediatrician: *"Sometimes, performing a CS is a way to resolve a situation before it takes a negative turn".*

• *Fear of legal consequences*

The fear of legal repercussions was another cross-cutting issue across all FGs, affecting all's HPs, particularly among obstetricians, and strongly influencing their clinical decision with a significant role in the high CS rate:

Obstetrician/Midwife: *"Another factor is defensive medicine. Unfortunately, with the increasing risk of legal complaints, our approach is inevitably influenced".*

Theme 2. Enablers of quality birth care

The second theme focuses on perceived facilitating factors in maternity care, as dedication of staff to their work, teamwork, and midwifery-led pathways.

2.1 Staff commitment

In all FGs, HPs dedication to their work was evident, with participants describing their passion for their profession as their greatest strength:

Paediatrician: *"Our strength is definitely us, the whole team! We often work with limited staff, juggling multiple responsibilities, yet we manage to make things work thanks to our dedication as doctors, midwives, and nurses".*

Obstetricians particularly acknowledged midwives' commitment:

Obstetrician: *"They are truly exceptional. They don't watch the clock, and they work beyond their shifts when needed".*

2.2 Teamwork

Teamwork and interprofessional collaboration were consistently mentioned in all FGs as key factors for success.

Obstetrician: *"In difficult moments, communication is as simple as looking each other in the eye".*

Despite staff shortages, professionals described their teamwork as "one big family" dedicated to providing the best care:

Midwife/Obstetrician: *"If the obstetrician and midwife work in harmony, the birth will be fine".*

This collaborative approach was reflected in case discussions. While obstetricians made the final decision, midwives played a key role in the decision-making process.

Obstetrician: *"In the delivery room, a simple glance, a piece of advice, or a word exchanged between the midwife and obstetrician can be decisive. If I have to choose between vacuum extraction or a CS, I need the full support of the midwife".*

The generational shift among obstetric staff was seen as beneficial, balancing senior experience with the skills of younger colleagues.

2.3 Midwifery-led pathways

Midwives highlighted the growing implementation of dedicated antenatal care services for low-risk pregnancies, managed exclusively by midwives in Community Health Services for Families or Birth Centres (*BRO Pathway – Basso Rischio Ostetrico* – Midwifery-Led Obstetric Low-Risk Pathway).

HPs perceived this model as highly effective, noting its continuity of care, allowing midwives to support women both before and after birth. Some midwives reported that although this model is still relatively new, demand is growing rapidly.

Midwife: *"Initially, we thought there wouldn't be enough women interested, but word of mouth has filled these clinics, and we are still expanding".*

Their work was widely appreciated by both women and other HPs. Obstetricians noted that women were highly satisfied with the care received.

Obstetrician: *"No woman who has gone through the BRO pathway has ever said she was dissatisfied or uncared for. This encourages us to refer women to this model before and after birth, reinforcing the continuity of care".*

Although collaboration between Community Health Services for Families and other territorial services (such as GPs and freelance obstetricians) still needs improvement, participants acknowledged progress.

Midwife: *"A dialogue is emerging between community services, professionals working at community level, and the hospital. This must become a cornerstone of cooperation".*

One of the strongest takeaways from the FGs was the collective awareness among HPs that improving care for women is a shared goal.

Obstetrician: *"All the professionals involved in this project have a strong desire to improve and grow. You can feel it; there's a willingness to embrace new challenges and collaborations".*

2.4 Audit&Feedback

The exploration of HPs' knowledge and opinions on the A&F intervention and the use of data collection in clinical practice revealed that, although A&F strategies were not yet implemented in any Maternity Unit, some centres regularly conducted clinical audits as a structured tool.

Obstetrician: *"We conduct audits weekly. All of us, obstetricians and midwives, participate, especially when dealing with complex cases. The goal is to analyse them together and find ways to improve management".*

Professionals were familiar with clinical audits, though most were not well-acquainted with A&F. Clinical audits were viewed positively, as opportunities for learning and improvement and, in some centres, as an opportunity to update protocols. However, in a few cases, case discussions were seen negatively, reflecting a lack of open communication in some settings.

Obstetrician: *"Unfortunately, in our reality, there is no real professional dialogue".*

Midwife: *"Sometimes, these meetings lead us to revise and improve some clinical protocols".*

Participants reported difficulties accessing data at both hospital and regional levels, such as the Hospital discharge records (Schede di dimissione ospedaliera, SDO) and the Birth certifications (Certificato di Assistenza al Parto, CeDAP). Only one centre used the Robson Classification to monitor CS rates. Despite these challenges, all professionals recognised the value of data-driven approaches and saw A&F as a potential tool for improvement.

Suggestions for continuity of care improvement

During FGs, several suggestions for improving continuous care were raised. HPs proposed improving their work and reducing CS rates through enhanced training and professional development focusing on team-based courses covering obstetric emergencies, labour induction, and CTG interpretation to ensure shared best practices. The importance of periodic clinical audits was widely acknowledged, along with the need to develop, share, and update clinical protocols for standardised care. Professionals highlighted fostering a culture of trust to support low-risk labour in midwifery-led care models, allowing midwives greater autonomy in physiological births. Strengthening hospital-community collaboration was a priority, with joint protocols integrating maternity care levels to align decisions and interventions. Additionally, regional data streams were seen as essential for monitoring trends and adapting practices, implementing an A&F strategy was considered key to improving clinical outcomes through structured reflection and continuous improvement.

DISCUSSION

One of the main objectives of the EASY-NET program was to reduce the CS rate in the Calabria Region. This qualitative study explored the perspectives of HPs on the determinants of CS and the potential opportunities for optimising decision-making.

The findings highlight a complex interplay of cultural, social, and clinical factors influencing CS rates, aligning closely with the multifaceted framework outlined in *The Lancet Series on Optimising Caesarean Use* [11], which emphasizes the need to consider clinical, organizational, and sociocultural drivers.

The optimal CS rate remains a topic of debate among HPs [23]. In our study, HPs acknowledged the elevated CS rate and recognised the reduction of unnecessary CS as a global concern.

Regarding cultural and social beliefs, HPs observed that CS has become "normalized", altering perceptions of what constitutes a *normal (vaginal) birth*. Although the relative risks of complications in case of CS are higher than VB, recent studies have shown that perceiving CS as a standard, safe mode of delivery contributes to its prevalence [24, 25]. Women reported that it was no longer necessary to suffer the *double pain* of labour,

and the perception of CS as a safe or even safer alternative to labour and VB aligns with findings from other studies [26]. However, in contrast, two Italian surveys conducted in 2003 and 2013 showed that over 80% of women preferred VB [27, 28].

From a social context perspective, family pressure plays a role in influencing decision-making, and our study confirms previous findings that it can increase the risk of CS [29]. Given the critical role of HPs in decision-making processes, fostering a shared philosophy around normal birth, embraced by professionals, women, and their families, could reduce CS rates [25, 28]. In our study, HPs also identified CS on maternal request as a significant concern. Among the reasons why women request CS, HPs reported a lack of preparation for childbirth, fear of pain and previous negative experiences, in line with preview studies [25, 30]. From HP's perspective, many clinicians opposed self-determination, particularly during labour, though some were more accepting, as reported also in the literature [10]. Furthermore, private healthcare influenced birth timing and planning, with the perception that private obstetricians often contributing to higher CS rates compared to public care, as reported in other studies [31] and confirmed by the higher CS rates observed in accredited private maternity units compared to public ones in Italy [8]. HPs noted that other specialists sometimes certified women as unable to undergo labour, leading to CS authorization.

A shared, informed care plan between women and HPs could enhance awareness, trust in normal birth, and supporting women fearing of childbirth to manage anxieties and transition into motherhood, as supported by the literature [32]. HPs recognized the need to encourage women and partners to attend antenatal group meetings to increase couple's awareness and women's preference for spontaneous labour and VB. It confirms that participation in the antenatal group meetings is associated with better health outcomes during pregnancy, childbirth and postpartum [33, 34].

Most participants, particularly midwives, emphasized the lack of respect for physiological delivery timing and the overuse of labour induction. HPs reported non-evidence-based inductions, without respecting childbirth timelines as key factors transforming physiological labour into a non-physiological process, increasing CS rates, consistent with literature findings [35]. The lack of shared clinical protocols, as reported in this study, also contributes to unnecessary interventions during labour [35]. In response to this, following this study, the EASY-NET WORKING GROUP collaborated with representatives of all Maternity Units of Obstetrics and Gynecology in Calabria to develop shared guidance on labour induction, adopted across the Region to promote evidence-based practices [36].

HPs highlighted the impact of legal concerns on CS decision-making, with defensive medicine driving the preference for CS to avoid litigation risks associated to VB. This aligns with literature, which connects higher medical liability judgments to delays or omissions in performing a CS [10, 37].

The FGs showed that obstetricians' decision-making was influenced by age, experience, confidence, and skills in managing complex VBs, often linked to fear of legal consequences. Limited expertise in operative vaginal delivery may lead to a preference for CS in urgent cases, as seen in other obstetric units [38]. HPs suggested that improving junior staff education could help address this issue, as noted in a recent Irish study [25]. While younger obstetricians may have higher CS rates, HPs noted that generational staff changes have strengthened team collaboration. Consistent with literature, CS decision-making was a shared process, with obstetricians as the final decision-makers [10], supported by experienced midwives.

Healthcare system organization also emerged as a key factor, with a common issue being staff shortages across all HPs, limiting the provision of professional support and continuous, one-to-one intrapartum care, a recognized measure in reducing CS rates [39-41]. Furthermore, HPs consistently highlighted that insufficient staff availability for emergency CS often led to performing the procedure prematurely, rather than waiting for the optimal moment [10]. In addition, the presence of Blood Transfusion Centres and NICUs within the Maternity Units was perceived as enhancing HPs' sense of security during childbirth.

Moreover, the absence of a companion of the woman's choice during labour, as was the case during the FGs due to COVID-19 pandemic restrictions [42], was identified as a significant factor influencing mothers' requests for CS. The right to have a chosen companion during childbirth is endorsed by WHO recommendations [41] and is widely recognized in the literature as a positive determinant of health outcomes [39].

Previous CS is a prominent driver of CS use, as recently highlighted by a recent systematic review [43]. Despite VBAC being recommended by guidelines, only 16,6% of women in Italy and 6.2% in Calabria, had it in 2023 [6]. The high contribution of previous CS (Robson group 5) to overall European CS rates, particularly in Southern Europe (up to 95.0%), raises concerns about what some authors call the "domino effect" of primary CS [43]. This highlights how total CS rates are also strongly influenced by the increasing number of primary CS, underlining the critical importance of implementing strategies to reduce them. Meanwhile, the overall CS rate in Calabria decreased from 38.5% in 2021 to 35.8% in 2023 [6], with the greatest reduction observed in Robson group 2a (nulliparous with induced labour) and group 3 (multiparous without previous CS, spontaneous labour), aligning with the A&F meetings and training courses organizing by EASY-NET program, focused primarily on the appropriateness of labour induction and physiological pregnancy management [16].

In this study, the effect of labour analgesia on pain management and delivery mode was debated among HPs during FGs. A recent Cochrane review confirmed no differences in CS rate between women with or without epidural analgesia; an increased risk of instrumental VB has also been reported but with limitations [44]. The WHO recommendations *for a positive childbirth experience* state that epidural analgesia is recommended for healthy pregnant women requesting pain relief during labour, according to the woman's preferences [41].

Teamwork and continuity of care result from a joint effort in which all HPs are involved, along with women and couples, in a shared care plan. An important step forward in maternity care is the recent implementation of the Midwifery-Led Obstetric Low-Risk Pathway in the Calabria Region [45]. This care pathway provides midwives with a framework for managing pregnancy within Community Health Services for Families and Birth Centres, in accordance with the guidelines set by the Ministry of Health's Birth Pathway Committee [46]. Additionally, in a context where maternity care is strongly led by private obstetricians, the introduction of the Midwifery-Led Obstetric Low-Risk Pathway represents a shift toward a more generalised adoption of midwifery-led care, ensuring broader access to evidence-based maternity services.

HPs demonstrated familiarity with clinical audits, which were regularly conducted in some Maternity Units. However, A&F strategies had not yet been implemented, and most professionals were unaware of their potential benefits. This challenge was compounded by limited access to current data, particularly at hospital and regional levels (e.g., SDOs and CEDAP), which emerged as another key barrier. Evidence shows that the implementation of A&F strategies, combined with clinical guidelines, could be a viable approach to improving clinical outcomes [47-49] and reducing CS rates [16, 34]. Current data allows for real-time trend identification, personalized interventions, and greater engagement from HPs. Therefore, moving from a clinical audit to A&F using current data enables timely and data-driven feedback that enhances the effectiveness of improvement strategies [48].

Therefore, the study highlighted CS determinants from HPs' perspectives, contributing to a topic for which qualitative literature is still scarce in Italy. The multidisciplinary nature of the FGs and the participatory approach played a significant role in shaping the research process, especially for designing action-oriented initiatives. Furthermore, the findings were later used to develop a quantitative study aimed at further exploring the determinants that emerged from the qualitative phase.

Among the concrete actions implemented, the findings also helped to identify learning needs, leading to the organisation of targeted training sessions aligned with HPs' expectations, as well as a structured series of A&F meetings. This structured engagement ultimately contributed to the development of shared protocols across all Maternity Units, including clinical practice recommendations for labour induction [36] and the implementation of the Midwifery-Led Obstetric Low-Risk Pathway [45]. The Calabria Region formally approved both initiatives, marking an important step toward evidence-based maternity care.

A study limitation is that it only explored the perspectives of HPs. Gathering insights from expectant mothers and couples would provide a more comprehensive understanding.

CONCLUSIONS

This study highlighted factors influencing delivery mode decisions from HPs' perspective. In the Calabria Region, the CS rate is influenced by a complex interaction of cultural, social and clinical factors. HPs highlighted key challenges, such as the normalization of CS, social and family pressures, and concerns over legal consequences. Several opportunities to reduce CS rate emerged, including HPs' enhanced education and training, implementing evidence-based clinical protocols, and promoting greater involvement of women in making informed decisions about their mode of delivery. In this context, integrating A&F could further strengthen these efforts by providing timely, current data to monitor progress and refine strategies. A&F may also help reinforce best practices, improve adherence to guidelines, and promote a culture of continuous improvement. Addressing this challenge will clearly require a multidisciplinary and collaborative approach, involving HPs, government institutions, and local communities. Only through a collective effort will it be possible to improve maternal and child health and ensure safe and evidence-based childbirth care.

The members of the EASY-NET Working Group are:

Caterina Azzarito (Former Health Protection Department of the Calabria Region, Catanzaro) Alessandro Ciciarello (Project Manager Exprivia SpA, Catanzaro); Giuseppe Battagliarin (Former Italian National Birth Pathway Commission Chair); Anna Laura Regalia (Former Department of Obstetrics and Gynaecology, San Gerardo Hospital, Monza); Federica Visconti ("Pugliese-Ciaccio" Hospital, Catanzaro); Susanna Lana (National Centre for Disease Prevention and Health Promotion, Italian National Institute of Health, Rome); Bruno Tucci, Pietro Gervasi, Maria Carmela Forte, Loredana Cistaro (Hospital of Castrovillari, Castrovillari); Gaetano Gigli, Cinzia D'Agostino (Hospital of Corigliano, Corigliano); Michele Morelli, Rosanna Mazzulla ("SS. Annunziata" Hospital, Cosenza); Giuseppe Pirillo, Domenico Galea, Serena D'Agostino ("San Giovanni di Dio" Hospital, Crotone); Raffaele Misasi ("iGreco Riuniti" Hospitals, Cosenza); Caterina Mastroianni, Salvatore Iannelli ("Giovanni Paolo II" Hospital, Lamezia Terme); Edoardo Pedullà, Bruno Palumbo (Hospital of Locric, Locri); Ilenia Cosoleto, Cristina Zappia ("Santa Maria degli Ungheresi" Hospital, Polistena); Enzo Bognoni, Lucia Porcino ("Riuniti" Hospitals, Reggio Calabria); Viviana Umbro, Vincenzo Mangialavori ("G. Jazzolino" Hospital, Vibo Valentia); Giampiero Russo (Community Health Family Service of Cosenza, Cosenza); Santina Procopio (Community Health Family Service of Catanzaro, Catanzaro); Paola Infortuna (Community Health Family Service of Melito, Reggio Calabria).

Funding

The EASY-NET program has received funding from the Italian National Ministry of Health NET-2016-02364191-6.

Conflict of interest statement

The Authors declare no conflict of interest.

Received on 22 April 2025.
Accepted on 9 July 2025.

REFERENCES

1. Boerma T, Ronsmans C, Melesse DY, Barros AJD, Barros FC, Juan L, Moller AB, Say L, Hosseinpoor AR, Yi M, de Lyra Rabello Neto D, Temmerman M. Global epidemiology of use of and disparities in caesarean sections. Lancet. 2018;392(10155):1341-8. doi: 10.1016/S0140-6736(18)31928-7
2. Betrán AP, Ye J, Moller A, Souza JP, Zhang J. Trends and projections of caesarean section rates: Global and regional estimates. BMJ Global Health. 2021;6(6):e005671. doi:10.1136/ bmjgh-2021-005671
3. World Health Organization. WHO statement on caesarean section rates. WHO; 2015. Available from: https://iris.who.int/bitstream/handle/10665/161442/WHO_RHR_15.02_eng.pdf?sequence=1.
4. Molina G, Weiser TG, Lipsitz SR, et al. Relationship between cesarean delivery rate and maternal and neonatal mortality. JAMA. 2015;314:2263. doi: https://doi.org/10.1001/jama.2015.15553
5. Euro-Peristat Network , Billy A, Lecomte A, Pastore J, Weber G. European Perinatal Health Report: Core indicators of the health and care of pregnant women and babies in Europe from 2015 to 2019. Luxembourg: Euro-Peristat; 2022. Available from: https://www.europeristat.com/images/Euro-Peristat_Fact_sheets_2022_for_upload.pdf.
6. Ministero della Salute. Certificato di assistenza al parto (CeDAP) Analisi dell'evento nascita – Anno 2023. Roma: Ministero della Salute; 2024. Available from: https://www.salute.gov.it/imgs/C_17_pubblicazioni_3524_allegato.pdf.
7. Amyx M, Philibert M, Farr A, et al. Trends in caesarean section rates in Europe from 2015 to 2019 using Robson's Ten Group Classification System: A Euro-Peristat study. BJOG. 2024;131(4):444-54. doi: 10.1111/1471-0528.17670
8. Programma Nazionale Esiti (PNE). Parti con taglio cesareo: volumi di ricovero. 2024. Available from: https://pne.agenas.it/ospedaliera/indicatori/131?tab=aree&mode=1&tval=1.
9. Programma Nazionale Esiti (PNE). Parti con taglio cesareo: Proporzione di parti con taglio cesareo primario. 2024. Available from: https://pne.agenas.it/ospedaliera/indicatori/37?tab=aree&mode=0&tval=0.
10. Panda S, Begley C, Daly D. Clinicians' views of factors influencing decision-making for caesarean section: A systematic review and metasynthesis of qualitative, quantitative and mixed methods studies. PLoS One. 2018;13(7):e0200941. doi: 10.1371/journal.pone.0200941. Erratum in: PLoS One. 2018;13(8):e0202688.
11. Betrán AP, Temmerman M, Kingdon C, Mohiddin A, Opiyo N, Torloni MR, Zhang J, Musana O, Wanyonyi SZ, Gülmezoglu AM, Downe S. Interventions to reduce unnecessary caesarean sections in healthy women and babies. Lancet. 2018;392(10155):1358-68. doi: 10.1016/S0140-6736(18)31927-5
12. Panda S, Daly D, Begley C, Karlström A, Larsson B, Bäck L, Hildingsson I. Factors influencing decision-making for caesarean section in Sweden - a qualitative study. BMC Pregnancy Childbirth. 2018;18(1):377. doi: 10.1186/s12884-018-2007-7
13. Berdzuli N, Llop-Gironés A, Farcasanu D, Butu C, Grbic M, Betran AP. From evidence to tailored decision-making: a qualitative research of barriers and facilitating factors for the implementation of non-clinical interventions to reduce unnecessary caesarean section in Romania. BMJ Open. 2024;14(2):e065004. doi: 10.1136/bmjopen-2022-065004
14. Sandelowski M. Whatever happened to qualitative description? Res Nurs Health. 2000;23(4):334-40. doi: 10.1002/1098-240x(200008)23:4<334::aid-nur9>3.0.co;2-g
15. World Health Organization. WHO recommendations non-clinical interventions to reduce unnecessary caesarean sections. Geneva: WHO; 2018. Available from: https://iris.who.int/bitstream/handle/10665/275377/9789241550338-eng.pdf.
16. Acampora A, Angelici L, Deroma L, Tullio A, Ciccone G, Pagano E, Marchesini G, Marenzi G, Bonomi A, Venturella R, Zambri F, Preziosi J, Giusti A, Maraschini A, Mignuoli AD, Bramanti P, Ciurleo R, Davoli M, Agabiti N. Il programma di rete EASY-NET: un contributo alle conoscenze sull'efficacia dell'audit&feedback. Epidemiol Prev. 2024;48(6):476-83. doi: 10.19191/EP24.6.A773.130
17. Preziosi J, Mignuoli AD, Maraschini A, Zambri F, Corsi Decenti E, Tambascia G, Venturella R, Donati S, Giusti A; Gruppo di lavoro Easy-Net della Regione Calabria. Il protocollo del progetto prospettico Easy-Net per migliorare l'appropriatezza del ricorso al taglio cesareo nella Regione Calabria. Recenti Prog Med. 2023;114(12):735-9. doi: 10.1701/4142.41391
18. Kim H, Sefcik JS, Bradway C. Characteristics of qualitative descriptive studies: a systematic review. Res Nurs Health. 2017;40:23-42. doi: https://doi.org/10.1002/nur.21768
19. Creswell JW. Research design: Qualitative, quantitative, and mixed methods approaches. 3rd ed. Sage Publications; 2009.
20. Krueger R, Morgan D. The focus group kit. London: Sage Publications; 1998.
21. Mays N, Pope C. Qualitative research in health care. Assessing quality in qualitative research BMJ. 2000;320(7226):50-2. doi: https://doi.org/10.1136/bmj.320.7226.50
22. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-51. doi: 10.1097/ACM.0000000000000388
23. Cavallaro FL, Cresswell JA, Ronsmans C. Obstetricians' opinions of the optimal caesarean rate: A global survey. PLoS One. 2016;11(3):e0152779. doi: 10.1371/journal.pone.0152779
24. Liu S, Liston RM, Joseph KS, Heaman M, Sauve R, Kramer MS; Maternal Health Study Group of the Canadian Perinatal Surveillance System. Maternal mortality and severe morbidity associated with low-risk planned cesarean delivery versus planned vaginal delivery at term. CMAJ. 2007;176(4):455-60. doi: 10.1503/cmaj.060870
25. Gallagher L, Smith V, Carroll M, Hannon K, Lawler D, Begley C. What would reduce caesarean section rates?-Views from pregnant women and clinicians in Ireland. PLoS One. 2022;17(4):e0267465. doi: 10.1371/journal.pone.0267465
26. Long Q, Kingdon C, Yang F, Renecle MD, Jahanfar S, Bohren MA, Betran AP. Prevalence of and reasons for women's, family members', and health professionals' preferences for cesarean section in China: A mixed-methods systematic review. PLoS Med. 2018;15(10):e1002672. doi: 10.1371/journal.pmed.1002672
27. Donati S, Grandolfo ME, Andreozzi S. Do Italian mothers prefer cesarean delivery? Birth. 2003;30(2):89-93. doi:

10.1046/j.1523-536x.2003.00226.x
28. Torloni MR, Betrán AP, Montilla P, Scolaro E, Seuc A, Mazzoni A, Althabe F, Merzagora F, Donzelli GP, Merialdi M. Do Italian women prefer cesarean section? Results from a survey on mode of delivery preferences. BMC Pregnancy Childbirth. 2013;13:78. doi: 10.1186/1471-2393-13-78
29. Takegata M, Smith C, Nguyen HAT, Thi HH, Thi Minh TN, Day LT, Kitamura T, Toizumi M, Dang DA, Yoshida LM. Reasons for increased caesarean section rate in Vietnam: A qualitative study among Vietnamese mothers and health care professionals. Healthcare (Basel). 2020;8(1):41. doi: 10.3390/healthcare8010041
30. Wigert H, Nilsson C, Dencker A, Begley C, Jangsten E, Sparud-Lundin C, Mollberg M, Patel H. Women's experiences of fear of childbirth: a meta-synthesis of qualitative studies. Int J Qual Stud Health Well-being. 2020;15(1):1704484. doi: 10.1080/17482631.2019.1704484
31. Turner MJ, Reynolds CME, McMahon LE, O'Malley EG, O'Connell MP, Sheehan SR. Caesarean section rates in women in the Republic of Ireland who chose to attend their obstetrician privately: a retrospective observational study. BMC Pregnancy Childbirth. 2020;20(1):548. doi: 10.1186/s12884-020-03199-x
32. O'Connell MA, Khashan AS, Leahy-Warren P, Stewart F, O'Neill SM. Interventions for fear of childbirth including tocophobia. Cochrane Database Syst Rev. 2021;7(7):CD013321. doi: 10.1002/14651858.CD013321.pub2
33. Çankaya S, Şimşek B. Effects of antenatal education on fear of birth, depression, anxiety, childbirth self-efficacy, and mode of delivery in primiparous pregnant women: A prospective randomized controlled study. Clin Nurs Res. 2021;30(6):818-29. doi: 10.1177/1054773820916984
34. Chen I, Opiyo N, Tavender E, Mortazhejri S, Rader T, Petkovic J, Yogasingam S, Taljaard M, Agarwal S, Laopaiboon M, Wasiak J, Khunpradit S, Lumbiganon P, Gruen RL, Betran AP. Non-clinical interventions for reducing unnecessary caesarean section. Cochrane Database Syst Rev. 2018;9(9):CD005528. doi: 10.1002/14651858.CD005528.pub3
35. Yazdizadeh B, Nedjat S, Mohammad K, Rashidian A, Changizi N, Majdzadeh R. Cesarean section rate in Iran, multidimensional approaches for behavioral change of providers: a qualitative study. BMC Health Serv Res. 2011;11:159. doi: 10.1186/1472-6963-11-159
36. Regione Calabria. Decreto del Commissario ad Acta n. 90 del 18/08/2022. Induzione del travaglio di parto – Linee di indirizzo. Regione Calabria; 2022. Available from: https://www.regione.calabria.it/wp-content/uploads/2022/08/allegato-a-al-dca-n.90-del-18.08.2022.pdf and Annex available from: https://www.regione.calabria.it/wp-content/uploads/2022/08/dca-n.90-del-18.08.2022.pdf.
37. Rudey EL, Leal MDC, Rego G. Defensive medicine and cesarean sections in Brazil. Medicine (Baltimore). 2021;100(1):e24176. doi: 10.1097/MD.0000000000024176
38. American College of Obstetricians and Gynecologists (College); Society for Maternal-Fetal Medicine; Caughey AB, Cahill AG, Guise JM, Rouse DJ. Safe prevention of the primary cesarean delivery. Am J Obstet Gynecol. 2014;210(3):179-93. doi: 10.1016/j.ajog.2014.01.026
39. Bohren MA, Hofmeyr GJ, Sakala C, Fukuzawa RK, Cuthbert A. Continuous support for women during childbirth. Cochrane Database Syst Rev. 2017;7(7):CD003766. doi: 10.1002/14651858.CD003766.pub6
40. Smith V, Gallagher L, Carroll M, Hannon K, Begley C. Antenatal and intrapartum interventions for reducing caesarean section, promoting vaginal birth, and reducing fear of childbirth: An overview of systematic reviews. PLoS One. 2019;14(10):e0224313. doi: 10.1371/journal.pone.0224313
41. World Health Organization. WHO recommendations: intrapartum care for a positive childbirth experience. Geneva: WHO; 2018.
42. Zambri F, Nannavecchia AM, Brescianini S, Rusconi F, Corsi Decenti E, Puglia M, Pacifici M, Buono P, Cantoira S, Gagliardi L, Ghiotti P, Leoni O, Masè C, Mazzucato M, Mondo L, Pellegrini E, Pertile R, Scoppa A, Visonà Dalla Pozza L, Giusti A. Breastfeeding and presence of the companion of woman's choice during COVID-19 pandemic in Italy: regional population-based routine data and best practices at birth. Epidemiol Prev. 2023;47(4-5):263-72. doi: 10.19191/EP23.4-5.A587.066
43. El Radaf V, Campos LN, Savona-Ventura C, Mahmood T, Zaigham M. Robson ten group classification system for Caesarean sections across Europe: A systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2025;305:178-98. doi: 10.1016/j.ejogrb.2024.11.052
44. Anim-Somuah M, Smyth RM, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. Cochrane Database Syst Rev. 2018;5(5):CD000331. doi: 10.1002/14651858.CD000331.pub4
45. Regione Calabria. Linee di indirizzo operative per la definizione ed organizzazione della presa in carico da parte dell'Ostetrica/o nel Percorso Nascita Fisiologico Territorio-Ospedale ai sensi del DPGR 28/2012. 2 (Gestione Autonoma nel percorso nascita fisiologico, Aree Funzionali nel percorso nascita fisiologico). Regione Calabria; 2023. Available from: https://www.regione.calabria.it/website/portalmedia/decreti/2023-07/ALLEGATO-215.pdf.
46. Ministero della Salute. Linee di indirizzo per la definizione e l'organizzazione dell'assistenza in autonomia da parte delle ostetriche alle gravidanze a basso rischio ostetrico (BRO). Roma: Ministero della Salute; 2017. Available from: https://www.salute.gov.it/imgs/C_17_pubblicazioni_2836_allegato.pdf.
47. Ivers N, Jamtvedt G, Flottorp S, et al. Audit and feedback: effects on professional practice and healthcare outcomes. Cochrane Database Syst Rev. 2012;(6):CD000259.
48. Di Blasio N, Acampora A, Angelici L, Pagano E, Ciccone G. Audit & Feedback: come funziona. Recenti Prog Med. 2022;113(12):733-8. doi: 10.1701/3914.38975
49. Di Blasio N, Acampora A, Bonomi A, Ciurleo R, Deroma L, Donati S, Marchesini G. A&F: gli ostacoli nell'implementare interventi nel sistema sanitario. Recenti Prog Med. 2023;114(7):432-40. doi: 10.1701/4062.40462

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 226-231
DOI: 10.4415/ANN_25_03_09

Exploring the link between cervical cancer screening and COVID-19 vaccination adherence. Evidence from a pilot study in Rome, Italy (2021-2022)

Ilaria Mussetto[1], Paolo Lombardo[1], Antonio Sciurti[1], Fabiano Grassi[1], Erika Renzi[1], Valentina Baccolini[1], Enrico Di Rosa[2] and Alessandra Sinopoli[2]

[1]*Dipartimento di Sanità Pubblica e Malattie Infettive, Sapienza Università di Roma, Rome, Italy*
[2]*Dipartimento di Prevenzione, Azienda Sanitaria Locale Roma 1, Rome, Italy*

Abstract

Introduction. Oncological screenings and vaccinations are essential preventive strategies, yet participation in both remains suboptimal and variable.

Methods. This pilot study examines the association between cervical cancer screening adherence and COVID-19 vaccination uptake among women aged 25-64 years in a large Local Health Authority in Rome, Italy, during 2021-2022. Analyzing data from 101,302 women, we identified a strong positive association between COVID-19 vaccination status and cervical screening participation, suggesting that common determinants influence both behaviors.

Results. Age and area of residence also emerged as predictors of screening adherence, with lower participation observed among younger women and those living in central districts.

Conclusions. Our findings highlight the need to foster a broader culture of prevention by integrating vaccination and screening efforts to improve public health outcomes. Enhancing health literacy and addressing shared barriers may increase participation in both programs. However, further research is needed to validate these findings, explore the underlying determinants of preventive behaviors, and develop targeted interventions to boost adherence to prevention programs.

Key words

- prevention
- oncological screening
- COVID-19 vaccination
- screening adherence
- cervical cancer screening

INTRODUCTION

Cervical cancer is a significant global health concern. The highest incidence and mortality are observed in low- and middle-income countries, particularly in sub-Saharan Africa, South America, and South-East Asia [1] where limited access to screening and preventive measures significantly reduces survival rates. To accelerate its elimination, in 2020 the World Health Organization (WHO) launched a global strategy that focuses on three initiatives: (i) vaccination of 90% of girls with the human papillomavirus (HPV) vaccine by the age of 15; (ii) screening of 70% of women by the age of 35, and again by the age of 45; and (iii) treatment of 90% of precancerous and invasive tumours [2]. Unfortunately, significant progress is still required to meet these targets, as cervical screening coverage remains highly variable across the globe and is particularly low in Africa, reaching just 14% among women aged 30-49 as of 2020 [3]. Even within the WHO European Region, screening rates exhibit substantial variation, from 78.5% in Sweden to just 3.9% in Romania in 2021 [4]. Italy falls among the countries with intermediate adherence rates, with cervical screening participation among women aged 25 to 64 years decreasing from slightly more than 40% in the pre-pandemic years to approximately 34% in 2020, with an increase to around 39% in 2021 and 40% in 2022 [4].

However, achieving the WHO's targets for cervical cancer elimination requires not only expanding global screening coverage but also integrating these efforts with robust vaccination strategies. Even though they are different health promotion interventions, with vaccination being part of primary prevention and cancer screening falling under secondary prevention, they both embody and promote the fundamental principles of prevention: maintaining health and ensuring access to early diagnosis. In Italy, these efforts are made possible through the universalistic framework of the National

Address for correspondence: Ilaria Mussetto, Dipartimento di Sanità Pubblica e Malattie Infettive, Sapienza Università di Roma, Piazzale Aldo Moro 5, 00185 Rome, Italy. E-mail: ilaria.mussetto@uniroma1.it.

Health Service (NHS), which is a public system primarily funded through general taxation and guarantees access to essential and uniform healthcare services for all citizens across the country. Both vaccines and organized oncological screenings are included in the essential levels of assistance (livelli essenziali di assistenza, LEA) [5], which represent the services and treatments that the NHS is obligated to provide to all citizens, either free of charge or for a modest fee (ticket). All regional health systems in Italy guarantee population screening programs for cervical, breast, and colorectal cancer. These organized programs include the active invitation of target populations, free testing and treatment, and quality control throughout the entire process, supported by continuous monitoring by the National Screening Monitoring Centre [6]. As for vaccinations, the provision of free vaccinations is guided by the National Vaccine Prevention Plan. Regional health authorities are responsible for implementing vaccination programs, ensuring accessibility and adherence to national guidelines [6].

Despite the extensive literature investigating adherence to either vaccination or cancer screening programs uptake, little evidence is available on their potential association. Indeed, while these two preventive interventions have distinct characteristics that can serve as barriers or facilitators to access, identifying and addressing shared factors influencing participation in both campaigns could significantly improve overall health outcomes. A few studies have begun to explore this connection: for example, Kuitto *et al*. have found that attitudinal factors were the strongest determinants of participation in both cervical screening and HPV vaccination [7], but the evidence remains limited and usually refers to a common disease (i.e., vaccination and screening for cervical cancer). Therefore, in line with the need to adopt a comprehensive approach when it comes to population health [6], we conducted a pilot study to investigate the association between adherence to cervical cancer screening uptake and vaccination, using data on COVID-19 vaccine administration during 2021 and 2022 in one of Italy's largest Local Health Authorities (LHA; in Italian ASL, Azienda Sanitaria Locale), LHA Rome 1. The aim of this study was twofold: to (i) explore potential correlations between participation in cervical cancer screening and COVID-19 vaccination programs, testing the hypothesis that these activities are interconnected and reflect the adoption of general health promotion behaviors, and (ii) identify demographic predictors of cervical cancer screening uptake at local level to guide the design of future campaigns.

METHODS

Setting

In Italy, cervical screening programs for cervical cancer are offered through the NHS. NHS is organized at three levels: national, regional, and local. At the central level, the Ministry of Health defines the fundamental principles and LEA; at the regional level, Regional Health Systems plan, organize, and manage healthcare services independently; at the local level, the actual provision of services and healthcare services is entrusted to LHA, which directly manage hospital and territorial care.

The study in question involved the LHA Rome 1, which covers Municipalities I, II, III, XIII, XIV, and XV in the city of Rome, with an approximate resident population of one million people accounting for 36% of the entire municipality's population, of whom about 53% are women [8]. The area is heterogeneous, including both the historic center and peripheral areas, with diverse social and economic characteristics, requiring accessible, integrated, and sensitive healthcare services.

Cervical cancer screening strategies for early detection are offered to all residents between 25-64 years. Specifically, women aged between 25 and 29 years are invited to undergo a cervical smear test every three years, whereas women aged between 30 and 64 years are screened with an HPV test every five years. Women who test positive in the initial screening are either invited for close follow-up or referred for a second-level examination with colposcopy. Exclusion criteria from the screening program include a prior history of cervical cancer, documented total hysterectomy, or serious medical conditions (e.g., terminal illness). Eligible individuals are invited to participate through personal letters sent directly to their home address.

As for the SARS-CoV-2 vaccine campaign, in Italy it began on December 27, 2020, and the National COVID-19 Vaccination Strategic Plan was officially adopted by decree on March 12, 2021 [9]. Initially, the vaccination campaign in Italy followed a prioritization order based on the risk of infection and severe illness from COVID-19 across different population groups. It began with healthcare workers, elderly residents, and individuals aged 80 and above, before expanding to include those with comorbidities, school staff, and law enforcement. Eventually, it became available to the entire population based on descending age groups.

Data collection

This study retrospectively analyzed women invited by LHA Rome 1 to undergo cervical screening from January 2021 to December 2022. Invitations are usually sent during two periods each year: from January to July and from September to November, while appointments are scheduled within one month of the invitation.

The outcome, adherence to cervical screening in 2021 or 2022, was defined as undergoing the first level of screening tests, either the Papanicolaou (Pap) smear or HPV test, according to the screening protocol. Vaccine status was determined by whether women had received the COVID-19 vaccination and, if applicable, the number of doses administered. Data were retrieved from the routinely collected records of the LHA Rome 1 cancer-screening platform, which provides aggregated participation data by age group and by residence district. The following baseline data were considered: age, district of residence, cervical screening uptake in 2021 or 2022, cervical cancer screening uptake in the previous round, COVID-19 vaccination status, and number of vaccine doses received.

Statistical analysis

Descriptive statistics were obtained using median and interquartile range (IQR) for continuous variables and proportions for dichotomous and categorical variables. For the purposes of this analysis, women were classified into five groups according to their ages (≤30 years, 31-40 years, 41-50 years, 51-60 years, and >60 years). Participation in the previous round of cancer screening was coded as not applicable (for newly invited women), yes, or no, while COVID-19 vaccination was categorized into four classes: none, one dose, primary cycle (according to vaccine type: two doses for Comirnaty, Spikevax and Vaxzevria, one dose for Jcovden), and booster dose. Living area was collapsed into two groups based on the district location: central (Districts I and II) and suburbs (Districts III, XIII, XIV, XV).

For the univariable analysis, the Wilcoxon rank-sum test was used to compare continuous variables with the outcome (i.e., cervical cancer screening uptake), whereas Pearson's chi-squared test was used for dichotomous and categorical variables. A multivariable log-binomial regression model was built to identify predictors of adherence to cervical cancer screening. Variables were included in the model based on expert opinion. Multicollinearity was checked using a variance inflation factor of 5 as the threshold. Given the large amount of available data, a calibration plot was used to visually evaluate the goodness of fit of the model, showing a good calibration [10]. As a result, the final model consisted of the following variables: COVID-19 vaccination (categorical), age (categorical), and living area (dichotomous). Adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) were calculated. To further investigate the role of living area as a potential effect modifier of the association between COVID-19 vaccination and cervical cancer screening adherence, we conducted a stratified analysis and built two separate models for women residing in the central area and in the suburbs, respectively, using the same covariates as the main analysis. All statistical analyses were performed using R Statistical Software (version 4.2.3; R Core Team 2023, R Foundation for Statistical Computing, Vienna, Austria). A two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 101,302 women were invited by LHA Rome 1 to participate in cervical cancer screening in 2021 and 2022, had available data on COVID-19 vaccinations, and were therefore included in this pilot study, representing 82.4% of the total number of women eligible for cervical cancer screening over the study period. Vaccination data were unavailable for the remaining women due to partially incomplete or inaccurate registry records (likely resulting from changes of residence causing delays or inconsistencies in population registry data). The median age of participants was 44.8 years (IQR: 34.1-56.0, range: 25-64) (*Table 1*). Almost two thirds of women (65.4%) had not participated in previ-

Table 1
Characteristics of LHA Rome 1 women invited to cervical cancer screening program in 2021 and 2022, by screening adherence

	Total (N=101,302)	Non-adherent women (N=92,690)	Adherent women (N=8,612)	p-value*
Age in years	44.8 (34.1-56.0)	44.7 (33.8-55.8)	46.0 (36.5-56.9)	<0.001
Age				
≤30 years	17,182 (16.8)	15,990 (17.3)	1,044 (12.1)	<0.001
31-40 years	25,116 (24.6)	22,585 (24.4)	2,227 (25.9)	
41-50 years	22,005 (21.5)	19,846 (21.4)	1,937 (22.5)	
51-60 years	28,682 (28.0)	25,999 (28.0)	2,456 (28.5)	
>60 years	9,285 (9.1)	8,270 (8.9)	948 (11.0)	
Previous participation in cancer screening program				
Not applicable	9,723 (9.6)	9,331 (10.1)	392 (4.6)	<0.001
Yes	25,303 (25.0)	21,315 (23.0)	3,988 (46.3)	
No	66,276 (65.4)	62,044 (66.9)	4,232 (49.1)	
COVID-19 vaccination				
None	27,644 (27.3)	27,153 (29.3)	491 (5.7)	<0.001
One dose	1,672 (1.7)	1,534 (1.7)	138 (1.6)	
Primary cycle	14,617 (14.4)	13,365 (14.4)	1,252 (14.5)	
Booster dose	57,369 (56.6)	50,638 (54.6)	6,731 (78.2)	
Living area				
Suburbs (Districts III, XIII, XIV and XV)	62,951 (62.1)	56,819 (61.3)	6,132 (71.2)	<0.001
Central (Districts I and II)	38,351 (37.9)	35,871 (38.7)	2,480 (28.8)	

Results are expressed as median (interquartile range), or frequency (percentage); LHA: Local Health Authority; *Wilcoxon rank-sum test for continuous variables and Pearson's chi-squared test for categorical variables.

ous round of cancer screening. The majority (72.8%) had received at least one dose of the COVID-19 vaccine, and more than half (56.6%) had also received the booster dose. Additionally, slightly less than two out of three participants were living in the LHA Rome 1 suburbs (i.e., Districts III, XIII, XIV and XV).

Adherence to the cervical cancer screening program varied by district. Specifically, Districts III (9.2%), XIII (10.5%), XIV (9.7%), and XV (9.9%) showed the highest adherence rates, while central districts (i.e., Districts I and II), reported lower rates of 7.1% and 5.9%, respectively *(Figure 1)*.

Univariable analysis showed that women who adhered to cervical cancer screening in 2021 or 2022 were older (median age: 46.0 *vs* 44.7 years; p<0.001), were more likely to have already participated in the cancer screening program (46.3% *vs* 23.0%, p<0.001), had a greater uptake of COVID-19 vaccination (booster dose: 78.2% *vs* 54.6%; no dose: 5.7% *vs* 29.3%; p<0.001), and were more likely to live in suburban districts (71.2% *vs* 61.3%; p<0.001) (*Table 1*).

In the multivariable analysis, the highest prevalence of adherence to cervical screening was found for women who had received a booster dose of COVID-19 vaccination compared to those who were not vaccinated (aPR: 6.34, 95% CI: 5.80-6.95; p<0.001) (*Table 2*). Similarly, having received either one dose or the primary vaccination cycle was positively associated with the outcome (aPR: 4.62, 95% CI: 3.83-5.52 and aPR: 4.72, 95% CI: 4.27-5.24; p<0.001). Additionally, being in a higher age range (31-40 years, 41-50 years, 51-60 years, and >60 years) was consistently associated with greater adherence to cervical cancer screening (aPR: 1.49, 95% CI: 1.39-1.60; aPR: 1.53, 95% CI: 1.43-1.65; aPR: 1.34, 95% CI: 1.25-1.44; and aPR: 1.53, 95% CI: 1.41-1.66, respectively). Conversely, living in a central district was negatively associated with cervical screening uptake compared to living in suburban districts (aPR: 0.77, 95% CI: 0.74-0.80; p<0.001). Finally, the stratified analysis by residential area showed estimates comparable to the main model, but participants living in the central area had higher aPRs for COVID-19 vaccination status (*Supplementary Table 1 available online*).

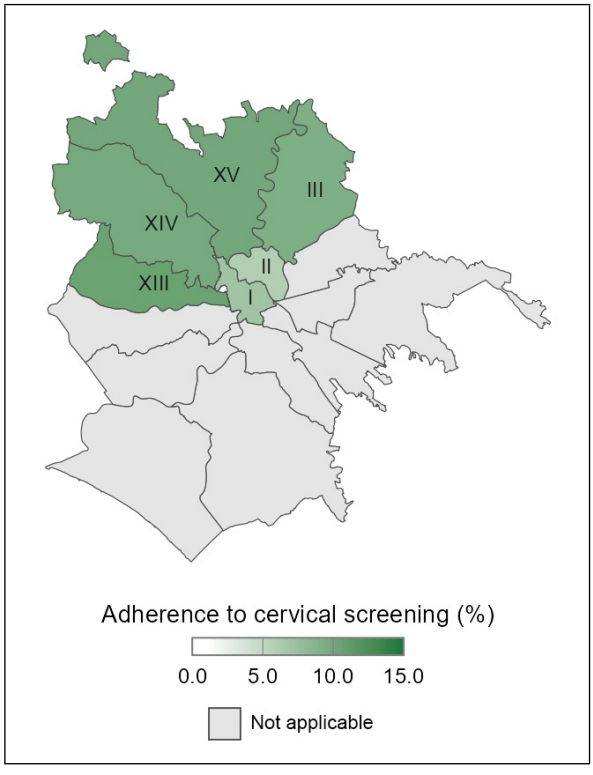


Figure 1
Percentage of study participants with residence in Local Health Authority (LHA) Rome 1 District (N=101,302) adhering to cervical cancer screening.

DISCUSSION

LHA Rome 1, like the rest of Italy, experienced a significant decline in cervical screening coverage during the COVID-19 pandemic. This reduction was unlikely due to service closures, as screenings were suspended only from March to May 2020 and resumed in June [6]. Instead, it was more likely driven by a decreased focus on prevention and heightened fear of accessing healthcare facilities, as documented by data from 2021-2022. However, our study clearly demonstrates a strong association between COVID-19 vaccination uptake and cervical screening participation, supporting the hypothesis that individuals engaging in both activities tend to adopt a broader preventive health approach. This aligns with the concept of a general prevention culture, in which shared factors-such as knowledge, attitudes, risk perception, and trust in health authorities-drive health-related behaviors. This perspective contributes to a comprehensive prevention framework, encapsulated

Table 2
Multivariable log-binomial regression model for adherence to cervical cancer screening among the LHA Rome 1 women invited in the years 2021 and 2022 (N=101,302)

	Adherence to cervical cancer screening	
	aPR (95% CI)	p-value
COVID-19 vaccination		
No dose	Ref.	
One dose	4.62 (3.83-5.52)	<0.001
Primary cycle	4.72 (4.27-5.24)	<0.001
Booster dose	6.34 (5.80-6.95)	<0.001
Age		
≤30 years	Ref.	
31-40 years	1.49 (1.39-1.60)	<0.001
41-50 years	1.53 (1.43-1.65)	<0.001
51-60 years	1.34 (1.25-1.44)	<0.001
>60 years	1.53 (1.41-1.66)	<0.001
Residential area		
Suburbs (Districts III, XIII, XIV and XV)	Ref.	
Central (Districts I and II)	0.77 (0.74-0.80)	<0.001

LHA: Local Health Authority; aPR: adjusted Prevalence Ratio; CI: Confidence Interval. Ref: reference.

in the concept of "one prevention", which integrates both preventive and health-promoting behaviors while fostering individual awareness. Scientific literature indicates that participation in both screening programs [11] it is important that those invited to screening participate. However, uptake rates are suboptimal in many populations and vary between screening programs, indicating a complex combination of patient factors that require elucidation to develop evidence-based strategies to increase participation. In this review, the authors summarize individual-level (sociodemographic and psychosocial and vaccination campaigns is influenced by complex decision-making processes involving multiple, sometimes overlapping, factors [12]. While facilitators and barriers may differ – reflecting variations in motivation, risk perception, and target populations [13] – identifying common determinants is essential for improving adherence to preventive health measures. Despite key differences – such as the fact that vaccinations protect against diseases not yet contracted, requiring the injection of a substance into a healthy body, while screenings enable the early detection of existing conditions with clear individual benefits – shared factors like health literacy and trust in health authorities significantly influence adherence to both practices. Recognizing this overlap underscores the potential of interventions aimed at enhancing participation in both vaccination and screening programs. Additionally, in resource-constrained settings, such as many healthcare systems, adopting an integrated framework that addresses these common determinants can optimize health spending while simultaneously strengthening multiple aspects of prevention.

Beyond COVID-19 vaccinations, our study has also identified other important predictors of adherence to cervical screening, i.e., age and district of residence, that can help define targeted strategies to increase screening coverage. The fact that older age was positively associated with cervical screening uptake could be explained both by greater awareness and knowledge about cancer and screening programs accumulated over a lifetime, and by the increased risk of developing cancer with age, which is generally acknowledged by the population. Indeed, from the age of 50 years, women in Italy are also invited to participate in breast and colorectal cancer screenings, which could further enhance their perception of oncological risk and be reinforced by the influence of family members and friends who have undergone screening tests. This is in the line with a recent systematic review [14] that found that cervical screening adherence was higher among women aged 30-59, while relatively lower among those aged 20-29. Furthermore, the fact that we found a negative association between living in the central districts of Rome and adherence to cervical screening may be because these areas are characterized by higher income levels [15] that have a population that can afford private healthcare services. Within this context, some women may opt for opportunistic screening rather than participating in public screening programs, but the effectiveness and cost-effectiveness of opportunistic screening are less established in the literature than those of organized screening. An organized program ensures quality and appropriateness through continuous monitoring, adherence to guidelines, and regular updates, while also reducing overdiagnosis, overtreatment [16], and health inequalities. However, this lower participation in the organized cervical cancer screening program by women living in central areas may also explained why the association with COVID-19 vaccination was particularly strong, as shown in the stratified analysis. In these districts, the women who chose to adhere to public prevention strategies adopt positive behaviors for both vaccination and screening, hereby reinforcing the general idea that the two practices share common determinants. Therefore, these findings further underscore the importance of designing targeted interventions to foster a health-promoting culture through a holistic approach. In addition, tailoring communication strategies to enhance awareness among younger age groups and advertising the benefits of organized screening over opportunistic approaches in higher-income areas could help bridge any gap in adherence. Furthermore, reinforcing the integration of multiple cancer screening programs within public health initiatives may further encourage participation, leveraging the cumulative impact of preventive behaviors over time.

This study has both strengths and limitations. Its primary strength is that, to the best of our knowledge, it is the first to explore the association between COVID-19 vaccination adherence and participation in cervical cancer screening programs. By highlighting the link between these two preventive behaviors, our findings suggest that addressing shared determinants could improve participation in both. Additionally, our study benefits from the use of anonymized healthcare data from one of Italy's largest LHAs, a large-scale real-world dataset that enabled the analysis of demographic predictors at the local level, offering valuable insights for designing tailored public health campaigns to enhance cancer screening adherence. However, some limitations should be acknowledged. Our analysis covered approximately 82% of females residing in LHA Rome 1, but the missing data are likely evenly distributed across its districts and age categories, minimizing the risk of selection bias. Another limitation is the cross-sectional design, which precludes causal inferences between vaccination and screening adherence. Furthermore, the reliance on routinely collected healthcare data restricted the variables included in the regression model, leaving room for potential residual confounding. A further limitation of our study is the lack of data on socio-cultural and economic characteristics of the women included, which are likely important determinants of adherence to cervical cancer screening programs. The absence of these variables in the dataset restricts our ability to fully understand the factors influencing participation. Nevertheless, the observed association is strong, with a clear gradient between cervical screening adherence and the number of COVID-19 vaccine doses received. While we consider it unlikely that additional variables would fully account for the observed relationship, further research is needed to expand this study, explore the vaccination-screening association in greater depth, and validate our findings.

CONCLUSIONS

In conclusion, our study (i) revealed a strong association between COVID-19 vaccination uptake and cervical cancer screening participation, suggesting that common determinants influence adherence to both preventive practices, and (ii) identified age and area of residence as demographic predictors of cervical cancer screening uptake. These results underscore the need to foster a culture of prevention through integrated strategies and targeted interventions that address shared barriers and enhance overall health literacy, ultimately strengthening public health efforts, while insights on the predictors of screening adherence at local level can inform the design of effective public health campaigns. Further research is needed to explore the underlying determinants of preventive behaviors and to evaluate strategies that can improve adherence.

Conflicts of interest statement

The Authors declare that there are no conflicts of interest.

Received on 21 February 2025.
Accepted on 13 June 2025.

REFERENCES

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-63.
2. Gultekin M, Ramirez PT, Broutet N, Hutubessy R. World Health Organization call for action to eliminate cervical cancer globally. Int J Gynecol Cancer. 2020;30(4):426-7.
3. Yang L, Boily MC, Rönn MM, Obiri-Yeboah D, Morhason-Bello I, Meda N, Lompo O, Mayaud P, Pickles M, Brisson M, Hodgins C, Delany-Moretlwe S, Maheu-Giroux M. Regional and country-level trends in cervical cancer screening coverage in sub-Saharan Africa: A systematic analysis of population-based surveys (2000-2020). PLoS Med. 2023;20(1):e1004143.
4. Eurostat. Preventive cancer screenings – programme data. Lussemburgo: Eurostat; 2024. Available from: https://ec.europa.eu/eurostat/databrowser/view/hlth_ps_prev__custom_17311163/default/table?lang=en.
5. Italia. Decreto del Presidente del Consiglio dei Ministri. Definizione e aggiornamento dei livelli essenziali di assistenza, di cui all'articolo 1, comma 7, del Decreto legislativo 30 dicembre 1992, n. 502. Gazzetta Ufficiale – Serie Generale n. 65, 18 marzo 2017. Available from: https://www.gazzettaufficiale.it/eli/id/2017/03/18/17A02015/sg.
6. Sinopoli A, Baccolini V, Di Rosa E. Killing two birds with one stone: is the COVID-19 vaccination campaign an opportunity to improve adherence to cancer screening programmes? The challenge of a pilot project in a large local health authority in rome. Vaccines (Basel). 2023;11(3):523.
7. Kuitto K, Pickel S, Neumann H, Jahn D, Metelmann HR. Attitudinal and socio-structural determinants of cervical cancer screening and HPV vaccination uptake: a quantitative multivariate analysis. Journal of Public Health. 2010;18(2):179-88.
8. Open Salute Lazio. Dati sullo stato di salute della popolazione residente nella Regione Lazio. Roma: Open Salute Lazio; 2024. Available from: https://www.opensalutelazio.it/salute/stato_salute.php?stato_salute.
9. Italia. Decreto del Ministero della Salute. Approvazione del Piano strategico nazionale dei vaccini per la prevenzione delle infezioni da SARS-CoV-2 costituito dal documento recante "Elementi di preparazione della strategia vaccinale", di cui al Decreto 2 gennaio 2021 nonché dal documento recante "Raccomandazioni ad interim sui gruppi target della vaccinazione anti SARS-CoV-2/COVID-19" del 10 marzo 2021. Gazzetta Ufficiale – Serie Generale n. 72, 24 marzo 2021. Available from: https://www.gazzettaufficiale.it/eli/id/2021/03/24/21A01802/SG.
10. Kramer AA, Zimmerman JE. Assessing the calibration of mortality benchmarks in critical care: The Hosmer-Lemeshow test revisited. Crit Care Med. 2007;35(9):2052-6.
11. Young B, Robb KA. Understanding patient factors to increase uptake of cancer screening: a review. Future Oncol. 2021;17(28):3757-75.
12. Tan SHS, Wang D, Tan WJ, Allameen NA, Fong NP. Facilitators and barriers of Hepatitis B screening and vaccination. Vaccine. 2020;38(34):5447-53.
13. Isonne C, Marzuillo C, Villari P, Baccolini V. The role of vaccine literacy and health literacy in the health prevention decision-making process. Hum Vaccin Immunother. 2024;20(1):2321675.
14. Zhang W, Gao K, Fowkes FJI, Adeloye D, Rudan I, Song P, et al. Associated factors and global adherence of cervical cancer screening in 2019: a systematic analysis and modelling study. Global Health. 2022;18(1):101.
15. Roma Capitale. Annuario statistico 2023. Available from: https://www.comune.roma.it/web/it/dati-e-statistiche-pubblicazioni-annuari.page.
16. World Health Organization. Regional Office for Europe. Screening programmes: a short guide. Increase effectiveness, maximize benefits and minimize harm. World Health Organization. Copenhagen: Regional Office for Europe; 2020. Available from: https://iris.who.int/bitstream/handle/10665/330829/9789289054782-eng.pdf?sequence=1&isAllowed=y.

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 232
DOI: 10.4415/ANN_25_03_10

Book Reviews, Notes and Comments

Edited by
Federica Napolitani Cheyne

I DUBBI DELLA SCIENZA
La ricerca scientifica tra business e malafede
Antonio Cassone,
Peter D'Angelo
Santarcangelo di Romagna (RN): Diarkos Editore; 2025
177 p.
ISBN: 9788836163939
€ 19,00

[The doubts of science. Scientific research between business and deceit]

The doubts of science. Scientific research between business and deceit seeks to examine and critically discuss some of the complex dynamics that are currently reshaping the way scientific research is conducted and disseminated. It offers a well-documented and in-depth reflection on the challenges facing the scientific community in its effort to regain credibility and, consequently, public trust. As indicated in the subtitle *Scientific research between business and deceit*, scientific research is currently going through a particularly difficult time which is reflected both in its practice and in its modes of communication. This period of crisis may be regarded as a form of "pathology" that is spreading within science and the scientific community, undermining its integrity and eroding public confidence.

The work is structured as a dialogue between Antonio Cassone, a distinguished medical microbiologist and former Research Director at the Istituto Superiore di Sanità (National Institute of Health, ISS) in Rome, and investigative journalist Peter D'Angelo. The text is divided into three main sections: *Science and scientific publishing, Scientists' frauds,* and *The cure for restoring credibility*. Each section is followed by a reflective commentary by Cassone, in which he offers personal insights that expand upon the issues discussed.

The first two sections offer a detailed analysis of the current state of scientific publishing and scientific misconduct, tracing the underlying causes that have contributed to the present crisis and identifying the various responsibilities of the different actors in the field. The opening section, *Science and scientific publications*, begins with a broad overview, based on Antonio Cassone's experience, of the evolution of scientific writing and communication over the past fifty years, with particular attention on the impact of the Internet. It addresses the pressures of the "publish or perish" paradigm, the fragility and distortions of the peer-review process, and the problematic overreliance on bibliometric indicators such as the Impact Factor and the H-Index. The second section, *Scientist's frauds*, addresses some of the most pressing threats to the integrity of scientific research and its dissemination. These include the reproducibility crisis, the proliferation of paper mills, the rise of predatory publishing, and the misuse or misinterpretation of preprints by the public or certain sectors of the press.

The final section, *The cure for restoring credibility*, moves from diagnosis to prescription, outlining possible strategies for the reforming of scientific practice and communication to recover lost trust. While the authors refrain from offering simplistic solutions, they emphasize the need for structural changes, cultural shifts within the scientific community, and renewed ethical commitments. They outline several interrelated areas of action, including continuous education in the ethics of scientific publishing, the prioritization of quality over quantity in research outputs and, consequently, a rethinking of how scientific careers are evaluated, as well as the promotion of scientific societies as primary vehicles for dissemination.

Overall, *The doubts of science. Scientific research between business and deceit* offers both a lucid diagnosis of the challenges affecting contemporary science and a call to action for researchers, institutions, and policymakers to foster reforms capable of restoring credibility and integrity to scientific research.

Its blend of investigative journalism and insider expertise makes it a valuable contribution to current debates on research integrity, scholarly communication, and the future of science in society. The significance of the topic, together with the clarity and accessibility of the style, ensures that the work is of considerable interest not only to scholars and researchers but also to citizens interested in this crucial issue.

Annarita Barbaro
Istituto Superiore di Sanità, Rome, Italy
annarita.barbaro@iss.it

Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 233-235
DOI: 10.4415/ANN_25_03_11

Publications from International Organizations on Public Health

Edited by
Annarita Barbaro

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS (FAO)

Di Martino M. **Food safety in personalized nutrition. A focus on food supplements and functional foods.** Rome: Food and Agriculture Organization of the United Nations 2025; 112 p. ISBN 978-92-5-139611-7. In this publication, the Food and Agriculture Organization of the United Nations (FAO), provides a comprehensive overview of potential safety concerns associated with food supplements and functional foods, including adulteration, drug interactions, overdose, and toxicity, supported by case studies from scientific literature and media reports. It also examines regulatory frameworks across various countries and regions, including Argentina, Australia, Brazil, Canada, China, Egypt, Europe, India, Japan, Nigeria, South Africa, the United Arab Emirates, and the United States of America. These frameworks cover key areas in the field of food supplements and functional foods such as classification, labelling, claims, composition, and registration, highlighting the differences in regulatory approaches. The report also explores consumer perceptions of the safety of food supplements and functional foods, analysing the motivations behind their use and the impact of marketing on their adoption.

Food Outlook – Biannual report on global food markets. Rome: Food and Agriculture Organization of the United Nations 2025; 152 p. ISBN 978-92-5-139879-1. Food outlook is a biannual publication (June and November) focusing on developments affecting global food commodity markets. FAO's latest assessments indicate a relatively optimistic outlook for food commodity markets, with production and trade of all commodities, except sugar, anticipated to increase. Global food commodity production remains vulnerable to weather conditions. Additionally, ongoing geopolitical tensions, uncertainties in policy developments, and potential retaliatory actions could negatively affect the trade outlook. In addition to market assessment, each edition contains a set of special features and market indicators. The June 2025 edition offers a feature article on economic impacts and trade implications of high pathogenicity avian influenza. Additional topics, such as changes in the trade flows following the start of the war in Ukraine, fertilizer update, economic drivers of fish fraud, and implications of decarbonization of the international maritime sector for net food-importing developing countries are also discussed.

Sharma R, Barange M, Agostini V, Barros P, Gutierrez NL, Vasconcellos M, Fernandez Reguera D, Tiffay C, and Levontin P, eds. **Review of the state of world marine fishery resources – 2025**. FAO Fisheries and Aquaculture Technical Paper, No. 721. Rome: Food and Agriculture Organization of the United Nations 2025; 515 p. ISBN 978-92-5-139859-3. The aim of this report is to provide FAO Members, national and regional policymakers, academia, civil society, fishers and managers of world fishery resources with a comprehensive, objective and global review of the state of the living fishery resources of the oceans. This document updates the regular reviews of the state of the world's marine fishery resources, based on stock assessments and complementary information up to 2023, and official catch statistics through to 2021. The introductory and methodology chapters provide the wider context in which this updated edition of the Review of the state of world marine fishery resources was prepared, highlighting evolutions in the landscape of fisheries and stock assessment capacities since the previous edition of this report in 2011. The methodology section gives a detailed overview of the updated FAO process for providing the state of stocks index, which involved a highly participatory and transparent process. Importantly, the total number of stocks in the assessments included in this report has significantly increased to 2,570. Discussions on major trends and changes at the global level are explored in a dedicated global overview chapter, while more detailed information on the status of stocks for each of the FAO Major Fishing Areas is set out in dedicated regional chapters. Special sections address the global issue of tunas and tuna-like species, and other high-profile fisheries such as deep-sea fisheries in areas beyond national jurisdiction, and highly migratory sharks. Summary tables are provided for each species grouping used in this assessment, indicating the number of stocks included, their sustainability classification between overfished, maximally sustainably fished, and underfished categories, and the number of stocks classified into tiers based on the availability and quality of information and thus the assessment methods used.

UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION (UNESCO)

Who bears the costs? Addressing inequalities from climate change and climate action. Paris: UNESCO Publishing 2025; 84 p. ISBN 978-92-3-100767-5. This

report explores the disproportional impacts of climate change and the need for designing policies to face climate change that also prioritize inclusivity and fairness. It shows how the impact of nations' green transitions to low carbon economies and sustainable practices varies widely, depending on where people work, their gender, income level, and the place they live in, and highlights the risk of widening socioeconomic inequalities that face our societies. It also reflects on the changes needed for climate policies and responses within and between member countries, to be tailored to all communities' diverse needs and realities. Policymakers, researchers, and others are invited to draw on the message of this report to reflect on how equity and inclusivity can guide the development of climate transition policies, rather than being added as an afterthought.

Climate change in Mediterranean World Heritage cities. Paris: UNESCO Publishing 2025; 72 p. ISBN 978-92-3-100770-5. This report addresses important intersecting concerns around impacts of climate change on cultural heritage, the Mediterranean region as a global climate hotspot, and cities as significant sources of greenhouse gas emissions as well as of climate action, through a study of 114 historic cities and settlements in the Mediterranean region inscribed on the UNESCO World Heritage List. Considering an inclusive approach using diverse knowledge systems to better understand the threats and impacts of climate change, the study uses three different methodologies to analyse and identify threats and subregional variations within the Mediterranean region. The study includes a qualitative overview of observed and reported current climate change-related hazards across inscribed World Heritage Cities and settlements in the Mediterranean region during the Third Cycle of Periodic Reporting (2018–2024) to UNESCO World Heritage Centre; climate model projections of threats to World Heritage Cities based on Earth observation (EO) as well as an ensemble of Earth system models (ESMs) and Regional climate models (RCMs) for projecting future scenarios in the Mediterranean region by the end of the twenty-first century. Finally, spatial mapping is used to analyse geographical patterns in detail across the Mediterranean subregions.

JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS (UNAIDS)

Equity in the HIV response: assessing progress and charting a way forward. Geneva: United Nations Programme on HIV/AIDS 2024; 132 p. As countries transition away from donor assistance and progress towards universal health coverage, there is growing emphasis on the importance of integrating HIV services into national health systems to support sustainability. However, given the equity advantage of the HIV response, there are concerns that many of the equity gains from HIV programmes could be lost in the transition to a more integrated, less disease focused approach unless care is taken to preserve and build on them. To shed light on how best to close existing HIV related equity gaps and to preserve important equity gains in the future, the Technical Working Group on Sustaining the Equity Gains of the Global HIV Response analysed existing programme models and data and undertook reviews of peer reviewed and grey literature. The Technical Working Group drew on these analytical exercises to identify options for the HIV response in moving forward.

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT (OECD)

Introducing the OECD AI capability indicators. Paris: OECD Publishing 2025; 54 p. ISBN 978-92-64-53190-1 (print) ISBN 978-92-64-89309-2 (PDF) ISBN 978-92-64-83602-0 (HTML). This report describes the OECD's new Artificial Intelligence (AI) capability indicators. The indicators have been developed to provide policy makers with an evidence-based framework to understand AI capabilities and compare them to human abilities. Developed over five years, the indicators draw on a large network of AI researchers, psychologists and other experts. The nine indicators cover a range of human abilities that each describes the development of AI towards full human equivalence: language; social interaction; problem solving; creativity; metacognition and critical thinking; knowledge, learning and memory; vision; manipulation; and robotic intelligence. The indicators are presented in scales of five levels, where the most challenging capabilities for AI systems are found towards the top. Each level includes a short description of the sorts of capabilities that AI systems at that level can perform accurately and consistently. The rating of current AI performance on each scale is linked to available evidence.

INTERNATIONAL LABOUR ORGANIZATION (ILO)

Gmyrek P, Berg J, Kamiński K, Konopczyński F, Ładna A, Nafradi B, Rosłaniec K, Troszyński M. **Generative AI and jobs: a refined global index of occupational exposure, ILO Working Paper 140.** Geneva: International Labour Organization 2025; 76 p. ISBN 978-92-2-042184-0 (print) ISBN 978-92-2-042185-7 (web PDF). This ILO Working Paper refines the global measurement of occupational exposure to generative AI by combining task-level data, expert input, and AI model predictions. It offers an improved methodological framework to assess how GenAI may impact jobs across countries and sectors. The 2025 scores are presented in a revised framework of four progressively increasing exposure gradients, with a new set of global estimates of employment shares exposed to GenAI. Clerical occupations continue to have the highest ex-

posure levels. Additionally, some strongly digitized occupations have increased exposure, highlighting the expanding abilities of GenAI regarding specialized tasks in professional and technical roles.

WORLD HEALTH ORGANIZATION (WHO)

Tracking global progress on preparedness for respiratory pandemics. 2023 Report. Geneva: World Health Organization 2025; 30 p. ISBN 978-92-4-011043-4 (electronic version) ISBN 978-92-4-011044-1 (print version). In line with the World Health Organization's (WHO) Framework for tracking global progress on preparedness for respiratory pandemics, this 2023 progress report provides an annual snapshot on the global status of functional capacities needed to prepare for future respiratory pandemics. Thirteen indicators spanning five capacity areas were collated to measure preparedness. Namely, these areas include emergency coordination, collaborative surveillance, community protection, clinical care and access to countermeasures. As this is the first annual progress report, the data was collated retrospectively until September 2024. It is expected that the global community, as well as regional teams, can view this report to identify where indicator progress has been made within each capacity area, and identify activities and actions to further strengthen capacities. This report is not a performance review, but rather a tool to inform planning and implementation.

WHO guidelines for the treatment of patients with cystic echinococcosis. Geneva: World Health Organization 2025; 48 p. ISBN 978-92-4-011047-2 (electronic version) ISBN 978-92-4-011048-9 (print version). The purpose of these guidelines is to provide guidance on the choice of treatment so that patients (adults and children) with cystic echinococcosis (CE) cysts can be offered and receive appropriate and equitable treatment. The aim is to ensure that patients receive the most appropriate and affordable management in the context of infrastructure and expertise sufficient to ensure its safety, and without unnecessary invasive procedures or treatment, to avoid iatrogenic complications by using invasive interventions. These guidelines were developed for clinicians, health facility managers and health practitioners practising at all levels of health services (primary, secondary and tertiary health care) and at all resource levels (low, middle-and high-income countries) that provide care for patients with CE. They were also developed to inform health care policymakers, health system administrators, insurance companies and NTD programme implementors.

WHO report on the global tobacco epidemic, 2025: warning about the dangers of tobacco. Geneva: World Health Organization 2025; 281 p. ISBN 978-92-4-011206-3 (electronic version) ISBN 978-92-4-011207-0 (print version). The tenth WHO report on the global tobacco epidemic tracks the progress made by countries in tobacco control since 2008. The MPOWER (Monitor, Protect, Offer help, Warn, Enforce, Raise taxes) technical package was designed to help countries adopt the demand-reduction measures of the WHO Framework Convention on Tobacco Control. The 2025 report focuses on the W measure: warn about the dangers of tobacco through graphic health warnings and anti-tobacco mass media campaigns and shows that with 6.1 billion people protected by at least one MPOWER measure at best-practice level many countries continue to make progress in the fight against tobacco. Four countries have now achieved the full MPOWER packaged while a further seven are only one measure away. At the same time 40 countries still have no MPOWER measure at best-practice level.

Instructions to Authors

Annali dell'Istituto Superiore di Sanità is a peer reviewed quarterly science journal which publishes research articles in biomedicine, translational research and in many other disciplines of the health sciences. The journal includes the following material: original articles, reviews, commentaries, editorials, brief and technical notes, book reviews. The publication of Monographic Sections on *Annali ISS* has been discontinued. In case you wish to present a limited number of coordinated contributions on specific themes concerning priorities in public health, please contact the Editorial office. If only regional or Italian data are presented in the manuscript, these should be compared with similar data available at European or international level. *Annali* follows the Recommendations for the Conduct, Reporting, Editing, and Publications of Scholarly Work in Medical Journals, issued by the International Committee of Medical Journal Editors (ICMJE) recently updated with a specific section II.A.4. on Artificial Intelligence (AI)–Assisted Technology. www.icmje.org.

MANUSCRIPT SUBMISSION

Manuscripts should be submitted online to https://annali.iss.it/.
The submission should include:
- cover letter where the authors declare that the manuscript has not been published or submitted for publication elsewhere;
- manuscript;
- tables and figures;
- authors' contributions statement (individual contribution to the manuscript);
- conflict of interest statement (a conflict of interest exists when authors or their institutions have financial or personal relationship with other people or organizations that could inappropriately bias conduct and findings of the study);
- permission to reproduce figures, if appropriate.

Receipt of author's paper will be acknowledged by an e-mail containing an identification number which should be used in future correspondence.
If Artificial intelligence (AI)-assisted technologies were used in the production of the submitted work, both the cover letter and the submitted work clearly state this and provide detail on their use.

NOTE FOR ISS AUTHORS

Authors whose affiliation is Istituto Superiore di Sanità can submit their paper only after completing the usual ISS authorization procedure (Infoweb).

REVIEW PROCEDURE

Each paper submitted to *Annali* is subjected to the following procedures:
- it is reviewed by the Editor-in-Chief for general suitability;
- if it is judged suitable, qualified referees are selected and a peer review process takes place;
- based on the recommendations of the referees and replies of the authors, the Editor-in-Chief decides whether the article should be accepted, modified or rejected;
- once the paper has been accepted, authors will receive proofs from the editorial office, which should be corrected and returned (usually within three working days).

MANUSCRIPT PRESENTATION

Please ensure that your manuscript follows these guidelines.
Manuscripts should be written in good English, as concisely as possible to allow a clear understanding of the text. The title should be followed by the complete name of the authors, their affiliations – only one per author and in the original language – town and country. The name of the Working Group should appear at the end of the by-line; its composition should be reported before the References, names and affiliations of each member are required. The name and address, telephone and e-mail of the corresponding author should also be indicated. On the same page a running head of no more than 40 characters (including spaces) should be included.
Original articles should normally be organized into different sections (*i.e.*: Introduction, Materials and methods, Results, Discussion, Conclusions). In the Methods section a specific paragraph on the adopted statistical analysis should necessarily be included.
Each article should be accompanied by:
- an abstract of about 150 words; the abstract should be structured when required (such as in original articles);
- key words up to a maximum number of five (MeSH headings, whenever possible. Refer to: www.nlm.nih.gov/mesh/meshhome.html).

Tables and figures should be kept to a minimum and be presented only if necessary.
Authors should deal responsibly and effectively with security issues that might be raised by their papers (see: Statement on Scientific Publication and Security *Science* 2003;299:1149).
This journal has adopted the SAGER reporting Guidelines for Sex and Gender Equity in Research.
These guidelines apply to original research articles and review papers. Authors should use the terms sex and gender carefully in order to avoid confusing both terms. Where subjects can also be differentiated by gender (shaped by social and cultural circumstances), the research should be conducted similarly at this additional level of distinction. Where the subjects of research comprise organisms capable of differentiation by sex, the research should be designed and conducted in a way that can reveal sex-related differences in the results, even if these were not initially expected.
Please consult the guidelines (https://researchintegrityjournal.biomedcentral.com/articles/10.1186/s41073-016-0007-6).

Authors are also encouraged to use fair, accurate and respectful language, but preferences can change and vary across groups and individuals and can also evolve overtime. The following guidelines may help in use of a correct terminology in the area of HIV: https://www.cdc.gov/stophivtogether/library/stop-hiv-stigma/fact-sheets/cdc-lsht-stigma-factsheet-language-guide.pdf
https://www.hptn.org/resources/HIVLanguageGuide
https://unesdoc.unesco.org/ark:/48223/pf0000144725
The name of the bioresource (and identifier, if available) which provided samples/data useful for the conduct of the study should be reported in extense, either in the Material and methods section or in the Acknowledgements.

LENGTH OF THE TEXT

To provide a text that meets the requirements of our publication:
• the *letter* to the Editor should be about 450 words; it does not need an abstract. Please contact the editorial office in advance if you wish to submit a Letter;
• the *editorial* should be no longer than 1,000 words; editorials are submitted on invitation. Please contact the editorial office in advance if you wish to submit an editorial;
• the *commentary,* 2,000 words; the commentary is an opinion piece or reflection on recent papers previously published on *Annali ISS* or elsewhere; an abstract is required; please contact in advance the editorial office;
• the *brief note*, 3,000 words, including about 15 references, one table and one figure;
• the *article,* 6,000 words, including about 40 references, three tables and two figures;
• the *review* should be no longer than 10,000 words, including no more than 100 references up to a maximum of four tables and three figures.
• *Supplementary materials* should be no longer than two printed pages. If necessary, authors could invite readers to contact them.

FORMATTING GUIDELINES

Text

• Use Times New Roman font, 10 point, single spaced;
• do not use the automated features of your application (endnotes, headers, footers, especially for references);
• avoid using bold characters to emphasise words or sentences within the text;
• indicate clearly titles of chapters and subchapters avoiding numbering.

Tables and figures

They should be understandable also without reference to the text and should be numbered in Arabic numerals in a consecutive and independent way according to their citation within the paper.
Tables should be presented on a separate sheet and preceeded by a title. Each column within the table should have a heading. Abbreviations should be reported in full in the legend.
Figures should be loaded as separate files. The following file formats are acceptable: JPEG, TIFF or EPS. Vectorial images (graphs, flow charts, schemes, and other non bitmap material) should be in Excel, Adobe Illustrator, Microsoft Power Point so as to allow the editorial formatting of the material.
Figures are redrawn into the *Annali* style by our in-house illustrators.
Photographs must have a minimum resolution of 300 dpi.
Captions should be presented on a separate sheet and contain a sufficient explanation of their object. They should be concise but comprehensive.

REFERENCES

All references in the text must be numbered in square brackets, *i.e.,* [1, 2, 3-6], and mentioned at the end of the article in the order in which they are quoted. They should conform to the "Recommendations for the Conduct, Reporting, Editing, and Publications of Scholarly Work in Medical Journals" (www.icmje.org), according to the following examples.
Titles of periodicals should be abbreviated in accordance with the Medline abbreviation of the US National Library of Medicine (www.nlm.nih.gov/bsd/aim.html).
Online journal articles can be cited using, in addition to the complete citation, the DOI number. Do not insert websites among the References but directly in the text in parentheses, where necessary.

Articles in journal

Bozzuto G, Ruggieri P, Molinari A. Molecular aspects of tumor cell migration and invasion. Ann Ist Super Sanità. 2010;46(1):66-80. doi: 10.4415/ANN_10_01_09

Books and chapters in a book

Godlee F, Jefferson T. Peer review in health sciences. London: BMJ Books; 1999.
Van Weely S, Leufkens HGM. Background paper: orphan diseases. In: Kaplan W, Laing R (Eds). Priority medicines for Europe and the world – a public health approach to innovation. Geneva: World Health Organization; 2004.

Proceedings

Fadda A, Giacomozzi C, Macellari V. Comparative measurements to validate a new telemetric pressure insoles system. In: 2. International Symposium on measurement, analysis and modelling of human functions. 1. Mediterranean Conference on measurement. Workshop on evaluation check of traceability. Proceedings. Genova: June 14-16, 2004. p. 425-7.

Technical reports

Della Seta M, Di Benedetto C, Leone L, Pizzarelli S, Siegmund U. ETHICSWEB technical guides. Manual for the creation of standards and guidelines for sharing information about knowledge organization systems on ethics and science. Roma: Istituto Superiore di Sanità; 2011. (Rapporti ISTISAN, 11/32).

Legislation

Italia. Decreto legislativo 29 ottobre, n. 419. Riordinamento del sistema degli enti pubblici nazionali, a norma degli articoli 11 e 14 della legge 15 marzo 1997, n. 59. Gazzetta Ufficiale – Serie Generale n. 268, 15 ottobre 1999.
US Social Security Administration. Evidentiary require-

ments for making findings about medical equivalence. Final rules. Fed Reg. 2006 Mar 1;71(40):10419-33.
The authors should check that each reference cited in the text appears in the reference list and viceversa. References should not include works submitted for publication but not yet accepted or unpublished results, etc. These can be mentioned in the text in parentheses.

CONVENTIONS

All Latin or foreign words should be in italics. The authors should use internationally accepted abbreviations. All abbreviations should be spelled out in full the first time they occur in the text, followed by the shortened term in parentheses; afterwards use the abbreviation only. Avoid abbreviations in the title of the manuscript.
For writing symbols, quantities and units of measurements refer to the International Systems of Units (SI) and the ISO standards.

LICENSES AND AGREEMENTS

Please, contact the Editorial Office for any other information. Annali Editorial Office - Scientific Communication Service
Istituto Superiore di Sanità
Viale Regina Elena, 299 00161 Rome, Italy
Tel.: +39 06 49902945 Fax: +39 06 49902253
E-mail: annali@iss.it
www.iss.it/annali - https://annali.iss.it/