ISSN 0021-2571 (print) · 2384-8553 (online) | Coden: AISSAW 61 (No. 4) | 237-326 (2025)

ANNALI
DELL'ISTITUTO SUPERIORE DI SANITÀ

Volume **61** No. **4**
2025

A SCIENCE
JOURNAL *for*
PUBLIC
HEALTH

www.iss.it

Ann Ist Super Sanità 2025 | Vol. 61, No. 4

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. 4)

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

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

Ann Ist Super Sanità 2025 | Vol. 61, No. 4

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

President of the Istituto Superiore di Sanità
Rocco Bellantone

Responsible Director
Antonio Mistretta
Istituto Superiore di Sanità

Editor-in-chief
Enrico Alleva
Istituto Superiore di Sanità

Assistant Editor
Federica Napolitani Cheyne
Istituto Superiore di Sanità

Scientific Committee
Enrico Alleva, Luca Busani, Paola Fattibene, Alessandro Giuliani, Antonio Mistretta,
Maria Teresa Palamara, Carlo Petrini, Emanuele Scafato, Marina Torre
Istituto Superiore di Sanità

Editorial Committee
Annarita Barbaro, Maria Cristina Barbaro, Alessandra Fuglieni, Maria Salvatorina Graziani,
Federica Napolitani Cheyne, Manuela Zazzara
Istituto Superiore di Sanità

OJS Site Administrator
Daniele Cordella
Istituto Superiore di Sanità

Editorial Advisory Board
Chris Beyrer
Johns Hopkins Bloomberg School of Public Health, Baltimore, USA
Jacqueline N. Crawley
Laboratory of Behavioral Neuroscience, NIMH, NIH, Bethesda, USA
Juana Martín de las Mulas González-Albo
Dpto de Anatomía y Anatomía Patológica Comparada, Facultad de Veterinaria, UCO, Córdoba, Spain
Jean-François Delfraissy
Agence Nationale de Recherches sur le sida et les hépatites virales, Paris, France
Tony Fletcher
London School of Hygiene & Tropical Medicine, London, UK
Sui Huang
Institute for Systems Biology, Seattle, USA
Stefania Maggi
CNR Aging Branch Institute of Neuroscience, Padova, Italy
Francesco M. Marincola
Infectious Disease and Immunogenetics Section, NIH, Bethesda, USA
Ana Marušić
Dept of Research in Biomedicine and Health, University of Split School of Medicine, Croatia
Patrick Smeesters
Université Catholique de Louvain, Louvain-La-Neuve, Belgium
Kurt Straif
ISGlobal, Barcelona and Visiting Professor at Boston College
David Vlahov
School of Nursing, University of California, San Francisco, CA, USA
Bernard Zalc (Boris)
Centre de Recherche de l'Institut du Cerveau et de la Moelle epiniere, UPMC, Paris, France

The cover image shows a cilia of nasal epithelium visualized by 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. 4 2025

Contents

EDITORIAL

ORIGINAL ARTICLES AND REVIEWS

Ann Ist Super Sanità 2025 | Vol. 61, No. 1: 237-238
DOI: 10.4415/ANN_25_04_01

Editorial

At the heart of life: the Italian National Transplant Centre's enduring commitment

Giuseppe Feltrin and Paola Di Ciaccio

Centro Nazionale Trapianti, Istituto Superiore di Sanità, Rome, Italy

Organ and tissue transplantation is a medical miracle, a testament to human solidarity and scientific advancement. At the core of Italy's successful transplant program lies the Centro Nazionale Trapianti (CNT), or National Transplant Centre, established by Law 91/1999 and housed within the Istituto Superiore di Sanità (ISS). The CNT coordinates and supervises all activities related to the donation, allocation and transplantation of organs, tissues, and cells across the national territory, as central authority ensuring the safety, quality, transparency, and traceability of the entire process, upholding an impartial vision that prioritizes the needs of patients suffering from end-stage organ failure.

CNT's general activities are broad, encompassing the technical, scientific, and organizational oversight of the Italian Transplant Network, made up of regional and autonomous province coordinating centres, transplant centres and hospital intensive care units. Among its several tasks, there are coordination and regulation, data management through the Transplant Information System (TIS), communication and training and international relations. The centre is extensively engaged in international activity, focusing on relations, EU-funded projects, cooperation agreements, and participating in international organ exchanges.

A pivotal element in the efficiency of the Italian Transplant Network is the CNToperativo (CNTo), an internal operational structure established at the CNT around 2013: it functions as the 24/7 engine room, providing continuous, systematic oversight and coordination for the most time-critical aspects of the transplant process. Its primary activities include interfacing with all regional and local levels of the Network, maintaining a continuous flow of information to ensure timely decision-making as well as being responsible for the rapid, impartial evaluation of donor and organ suitability for transplantation purposes. It manages the allocation of organs for special national transplant programs, ensuring that even the most complex or rare cases are handled with efficiency and equity across the country. The establishment and subsequent evolution of the CNTo marked a significant turning point, contributing to the systemic growth of donation and transplant numbers in Italy by enhancing the network's organizational effectiveness and speed of response.

Scientifically, the CNT leverages the rich data from the TIS to drive evidence-based medicine. By collecting and analyzing data on donation, organ quality, and transplant outcomes, it supports several scientific studies and monitors program quality. This robust data-driven approach allows for the development and refinement of clinical protocols, such as those related to Donation after Circulatory Determination of Death (DCD), which are crucial for expanding the donor pool. The CNT's ability to evolve its protocols – like the controlled DCD programs – demonstrates its commitment to integrating cutting-edge medical practices safely and systematically into the national framework.

Organizationally, the CNT embodies a model of centralized governance that ensures a uniform application of safety and ethical standards while respecting regional specificities. This three-level coordination structure (national, regional, local) has proven to be effective in fostering a collaborative environment, with all operators working in synergy. The steady growth in both donation and transplant figures over the last two decades (e.g., up to a 54% increase in donations and 33% in transplants between 2004 and 2024) highlights the validity of this organizational model in enhancing transparency, efficacy, and efficiency for the ultimate benefit of the patient.

As a department within the ISS, the leading public technical and scientific body of the Italian National

Address for correspondence: Giuseppe Feltrin, Centro Nazionale Trapianti, Istituto Superiore di Sanità, Via Giano della Bella 34, 00162 Rome, Italy. E-mail: giuseppe.feltrin@iss.it.

Health System, CNT's mandate is intrinsically linked to public health and clinical excellence.

A significant area of collaboration concerns the safe use of organs from donors positive for Hepatitis C Virus (HCV). With the advent of highly effective Direct-Acting Antivirals (DAAs) to cure HCV, the CNT, leveraging the scientific guidance of the ISS, has obtained by the Italian Drug Agency (Agenzia Italiana del Farmaco, AIFA) the authorization to the full reimbursement of these drugs, even for the prompt treatment of HCV infection after an organ or bone marrow transplantation. This allows to utilize HCV-positive organs for both HCV-positive and, in carefully selected cases, HCV-negative recipients. This effective strategy, which involves treating the recipient post-transplant with DAAs, has been instrumental in safely expanding the organ donor pool, demonstrating a dynamic, patient-centric approach to tackling historical contraindications for transplantation.

Another relevant synergy is the application of the Regulation on Substances of Human Origin (SoHO). As the national authority for the donation and transplantation of organs, tissues, and cells, the CNT works closely with the Italian National Blood Centre, the ISS and the Italian Ministry of Health to implement and enforce EU and national safety and quality standards for all human origin substances used in therapy. This ensures compliance with rigorous health and safety requirements for tissues and cells, including their procurement, processing, storage, and distribution through authorized tissue institutes and banks. This collaboration guarantees that the system adheres to the highest European standards, safeguarding recipient health.

Looking ahead, the CNT's focus is on building upon its successful performance and tackling emerging challenges to improve further, namely by:

- *expanding the donor pool*: a major strategic objective is the further development and standardization of DCD programs across all regions, particularly the controlled DCD pathway, by investing in training and the necessary infrastructure, such as mobile Normothermic Regional Perfusion (NRP) teams. Efforts will also continue to improve the identification of potential donors in Intensive Care Units (ICUs) and to support donor families through compassionate, effective communication;
- *promoting innovation and technology*: the CNT will continue to promote and monitor the use of advanced technologies, such as organ preservation and reconditioning devices (e.g., ex vivo perfusion systems), to improve the quality and extend the usability of organs that might otherwise be discarded. The continuous evolution of the TIS will also be paramount to manage increasingly complex data and ensure the system remains robust and adaptive;
- *fostering public engagement and ethics*: reinforcing the culture of donation through targeted public campaigns and educational initiatives remains a core commitment. Furthermore, the CNT must continue to navigate complex ethical and legal considerations – such as the emerging fields of xenotransplantation and the use of bioengineered tissues – ensuring that all advancements are introduced with the utmost respect for human dignity and public trust.

In conclusion, the Centro Nazionale Trapianti is far more than a regulatory body; it is the guiding force of a highly complex and ultimately successful National Transplant Network. Through its centralized operational efficiency (CNToperativo), its scientific rigor, and its crucial partnerships with the ISS, the CNT has secured Italy's position as a leader in Europe for organ donation and transplantation. Its ongoing work is an essential contribution to national public health, offering the invaluable gift of life and health to thousands of patients each year.

Conflict of interest statement

The Authors declare no conflicts of interest regarding this manuscript.

Received on 16 October 2025.
Accepted on 12 November 2025.

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 239-249
DOI: 10.4415/ANN_25_04_02

Psychoeducational group for acute psychiatric care. The Italian experience and suggestions for future needs

Franco Veltro[1], Gianmarco Latte[2], Umberto Serafini[3], Lilia Zappone[4] and Antonella Gigantesco[5]

[1]*Associazione Italiana per la Diffusione degli Interventi Psicoeducativi in Salute Mentale, Campobasso, Italy*
[2]*Dipartimento di Salute Mentale, ASL Na1, Naples, Italy*
[3]*Servizio Psichiatrico Diagnosi e Cura, Ospedale di Arezzo, Arezzo, Italy*
[4]*Centro di Salute Mentale, Campobasso, Italy*
[5]*Centro per le Scienze Comportamentali e Salute Mentale, Istituto Superiore di Sanità, Rome, Italy*

Abstract

Introduction. The implementation of an innovative psychoeducational group intervention in Italian general hospital psychiatric units started in the years 2000-2001 in two Italian regions. The aim of this contribution is to describe the intervention method and the experience of its application, its spread, the results of evaluation studies and its evolution.

Method. The methodology is qualitative/quantitative. The qualitative approach concerns the description of the prevalent clusters of topics in the most used intervention modules. The quantitative approach concerns the analysis of indicators used in the evaluation studies carried out since 2000-2001.

Results. Over time, three topics of the intervention have remained constant: "What happened before the crisis"; "Stress-vulnerability-coping model"; "Psychotropic drugs: shared decisions". Other topics have been introduced based on the patients' preferences: "Psychophysical well-being", "Awareness", "Emotions-thoughts-behaviors connection", "Problem-solving" and "Stigma". The intervention has been applied over time in 15% of Italian psychiatric wards with positive results (main result: decrease in readmissions and restraints).

Discussion. Two main topics are discussed: a) the advantages and obstacles in applying the intervention; b) the need for addressing also the issues of substance dependence and antisocial personality.

Key words
- psychiatric hospital
- psychoeducation
- group intervention

INTRODUCTION

Services for acute psychiatric care are of a great importance for patients and their relatives, and use a significant budget of resources allocated to mental health all over the world. Despite that, for the most traditional service of the system of acute care, the psychiatric ward, according to Johnson *et al.* [1], a little attention has been paid to the explicit definition and discussion of its role and of its function. The same thing happened in Italy during the psychiatric care revolution, whereas we would have expected a greater integration, as well as a clearer definition of the role and of the function of the psychiatric ward allocated in General Hospital in the healthcare community. The conclusion of De Girolamo *et al.* [2] on a nationwide survey of acute inpatient services 20 years after the law 180/78 that changed psychiatric care was really dramatic. In fact, they stated that "*despite the importance, of acute in-patient care, its quantitative and qualitative features remain largely unexplored and many problems still await appropriate solutions and this holds true in Italy as elsewhere*". According to Thornicroft and Tansella [3] admissions to the ward were always judged as a failure of care, rather than a complementary pathway of care; at the same time the ward in itself has not been considered as an integrated clinical service playing a crucial role within a balanced mental health system. The Cognitive-Behavioural Group Intervention (CBGI) that we present here was conceived at the end of the 90s with the awareness of these critical issues and of some of the followings, as reported by Bazzoni *et al.* [4]. These issues have changed little in Italy and in the international context as recently elicited [1]: a) little at-

Address for correspondence: Franco Veltro, Associazione Italiana per la Diffusione Interventi Psicoeducativi in Salute Mentale (AIDPSaM-APS), Via Toscana 85, 86100 Campobasso, Italy. E-mail:francoveltro@gmail.com.

tention has been given to the negative patient experiences as well as the feeling of emptiness and boredom during the day and to the trauma experienced due to hospitalization and to the separation from their environment; b) despair and depression arising from the forced cohabitation and from seeing other unwell patients without understanding their conditions, and stigmatization [5]; c) no interventions designed to reduce conflict and use of restrictive practices; d) no shared decision-making about drugs and plan of care after two days of admission; e) no structured psychosocial approach with the emphasis on the stressors related to the crisis. Moreover, two other aspects were considered lacking, although valuable for inpatients: giving as soon as possible a personalized meaning to the hospitalization as well as understanding what had happened before the crisis. These two aspects emerged forcefully in the various focus groups that two psychologists held with the inpatients at San Filippo Neri Hospital in Rome in 1998 [4]. In fact, for several weeks during the daily meetings, the two topics were the most prevalent and discussed; two other prevalent topics were the need of obtaining more information about psychopharmacotherapy and what to do to avoid relapses. In this respect, the professionals proposed among other domains of interest for interventions the topic of early warning signs that was also quite appreciated by patients. A first draft of the manual contained four topics, each of them daily used during the week, that were labelled as: "What occured before the crisis", "Stress-vulnerability", "Psychotropic drugs" and "Early warning signs". Although the developed group intervention described in three editions of a manual for professionals [5-7] had a psychoeducational matrix focusing on the communication of key-information with strategies belonging to cognitive-behavioural therapy it differs completely from traditional psychoeducation mostly based on the "diagnosis". It differs also from other group approaches generally based on the free discussion. In fact, this intervention has been conceived specifically for the acute psychiatric unit, starting each Monday of the week, with asking to each patient in the group "what had occurred in terms of mental and behavioral problems in the last days before admission" in order to obtain a list of "symptoms" to be written on the board visible to all inpatients. In this way, patients were encouraged to confront each other and to know some aspects of the condition of the others. We would like to underline that these two aspects are considered of great importance by experts [8, 9] as well as the collaborative approach that is receiving more and more attention [10-14]. Finally, it is important to pinpoint that this intervention emphasizes the true nature of psychoeducation, i.e., to extract (etimologically "*e*-ducĕre") the personalized information from the patient that is necessary for the therapeutic action, rather than to input information (to teach, etimologically "insĭgnare", just the opposite of "*e*-ducĕre"). The aim of this paper is to describe in detail the characteristic of the approach used in that group intervention and its evolution based on the preferences of patients and professionals, its spread, the results obtained in several studies, and the advantages and barriers of its implementation.

METHOD

Firstly, we briefly describe the main characteristics of the intervention. Secondly, the topics with the key-questions of some of them, and their evolution are summarised in four parts: the first concerns the years in which the manual had not yet been published, while the other three correspond to the three editions of the manual. Thirdly, the overview of the CBGI spread is summarised in accordance with periods which coincide with the three editions of the manual: 2004-2008; 2009-2014; 2015-2025 [5-7]. Data of the spread are in charge to the teams of Campobasso and Arezzo, accredited for the training of the professionals. In fact, it is possible to implement the CBGI in the wards only by an intensive training of the professionals, invited in turn to give routinely information about the activities/suspension of the intervention and eventually the reasons why the group is interrupted. For this paper we use also data obtained by a previous cross-national survey conducted in 2017 [15]. We would like to specify that data obtained by an *ad hoc* questionnaire regarding specific process or outcome indicators (see the list after in the Results section) filled by the centers for the survey in 2017 showed reproducibility when compared with data in charge to the team of Campobasso and Arezzo [15]. That means this data collected yearly are reliable and useful here as an update.

Main characteristics of the intervention

All admitted patients can participate to the daily meeting, which lasted 1 hour and 45 minutes with a break of 15 minutes. The suggested starting time for group meetings is 9.00 am, from Monday to Friday, every week, in order to dedicate some hours in the afternoon to the exercises assigned at the conclusion of the morning sessions. In fact, every session is structured in the following way: 1) presentation of the unit of work, the session aim, presentation of structure and rules of the group session; 2) introduction of all newly admitted inpatients; 3) summary of the last session and review of homework; 4) topic of the day; 5) summary of the principal points and assignment of homework for the afternoon. These exercises are mainly personal-goal oriented and they are performed by inpatients with the help of the nursing staff in the afternoon. Solutions to the practical exercises of each session are reviewed in the next day session. Sessions follow a didactic treatment guideline presented in the manual for professionals. All rules and strategies are used in a flexible way. The main strategies are: a) encouraging direct communication and dialogue among inpatients rather than professionals giving information and advice to inpatients; b) Socratic questioning [16]; c) helping inpatients make connections between their thoughts, emotions and behaviors; d) normalizing symptoms; e) modelling and role-playing; f) positive reinforcement and constructive feed-back; g) structured problem solving; h) effective communication skills (i.e., expressing unpleasant feelings, active listening, expressing pleasant feelings, making requests). A well-trained professional (called the "conductor") with the assistance of another well-trained professional (the "co-conductor"), conduct the group sessions. The conductor's role is mainly to ask the key-questions written in the manual for each topic and to stimulate a brief confrontation among patients, who are also invited to help some of them not yet "ready" to answer. It is possible to go to the next question only if answers are provided by patients and an agreement among them is reached; the role of co-conductor is to write the answers on the blackboards and to supervise the session.

Topics of the intervention and their evolution mainly based on the needs of patients

From 1999 until 2000 the intervention was applied only in the Ward of San Filippo Neri General Hospital of Rome by the two psychologists that conducted the focus groups in the previous year, with assistance of nurses. The topics were four as listed in the introduction. Generally, the topic of "psychotropic drugs" lasted more than one day. At that time, the topics were well detailed in an unpublished manual. The key-questions for each topic to be asked to each patient were the followings, in the order here illustrated:

- Topic 1. A) "How did you feel and behave before hospitalization?"; B) "What factors may have triggered the crisis?"; C) "What do these factors produce within us?", with the scope to obtain words like discomfort, tension, anger, irritation, depression, but above all the term "stress" or "distress" that is the "magic" word for the next question; D) "How can we define stress?" with the scope to share the following simple definition as an imbalanced condition that occurs between our coping skills and the problematic situations or stressful events that generate discomfort/distress within us;
- Topic 2. A) "What are the signs of stress?"; B) "Does everyone get stressed"; C) "Why do some people have a crisis when faced with the same stressful event, while others do not?" in order to introduce the concept of vulnerability and to the discuss in detail the scheme of diathesis-stress theory; D) "What does this excessive vulnerability depend on?" in order to discuss and to list the main causes such as biological vulnerability, personal characteristics and the use of ineffective strategies or difficulties in dealing with stressful situations;
- Topic 3. A) "What does psychotropic drug mean?"; B) "How do psychotropic drugs work?"; C) after that the co-conductor writes four categories of psychotropic drugs (antipsychotics, anti-anxiety, antidepressants, mood stabilizers) on the blackboard, the conductor asks each patient "What psychotropic drugs are you taking? What are they for? In which category would you put the drugs?". At the end of each answer the co-conductor fills them in the category; D) at this point, each patient is asked to prescribe the therapy himself and other patients are asked to rate the therapy indicated on its appropriateness and correctness about category and dosage. E) "How long should the therapy last?"; F) "What is the risk to suspend the therapy?"; G) "Why are drugs sometimes stopped?" in order to obtain a long list of reasons why the drugs were stopped; E) in accordance with the previous answer is asked "What can be done to counteract the reason for stopping medications?";
- Topic 4. A) "What are the early signs of crisis?"; B) "When you are under stress, do you notice some personal behavioral changes and if so, which ones?" in order to obtain a list of these changes; C) "Do you think it's easy to notice these behavioral changes right away, when we start to feel bad?" in order to obtain an obvious "no" as a reply; D) "Who could help us to recognize these signs?" in order to prompt collaboration with a key-person that could help them; E) "What can we do to cope with these signs?" in order to obtain a list of coping strategies; F) "Why is it important to recognize these signs and to cope with them?" in order to stress the importance to prevent relapses.

From 2001 to 2003 the intervention was applied also in the Ward of Campobasso by psychiatrists (mainly conductors) and nurses (mainly co-conductors). The interest in the approach was so high that many professionals participated to better understand the "health information needs" of inpatients during the several meetings. In the end, on the basis of the requests of inpatients, the following new topics were elaborated: alcohol, hallucinations, anxiety and fear, delusion and psychotic thinking, sadness and joy, anger, secondary advantages, suicide ideation, compulsory treatment. These topics were called "Optional" because addressed at discretion of the healthcare team based on the prevalent needs of hospitalized patients (for instance, if in a day there were more than 5 people admitted for alcohol problems or intensive anger). The original four topics were called "Basic". The first edition of the manual [5] was published in 2003; at the same time the Italian National Institute of Health (Istituto Superiore di Sanità, ISS), Rome, Italy on the basis of the first evaluative study [4] and of some outcome data of the Ward of Campobasso, decided to promote a national training for this approach and to collaborate to relevant future research projects.

From 2004 to 2008 in several centers that applied the intervention, professionals paid particular attention towards new needs of patients and were proposed other topics that were experimentally tested in these centers. One of them was considered as a "Basic topic" called "Personal goals and plan to achieve them". The main key-questions of the fifth basic topic are:

A) "I would like to list the symptoms present at the admission and those still present";

B) "I would like to know when you expect to be discharged on the basis of the symptoms still present";

C) "What pleasant goal do you think is possible to define and achieve in the following three months and what kind of goal is important to prevent a crisis?".

In addition to this, two optional topics were elaborated: "Physical well-being: diet and physical activity" and "Understanding and managing emotions". As a consequence, a new edition of the manual was considered useful and published in 2008 [6].

From 2009 to 2015 new needs emerged from patients and professionals. Patients admitted to different wards often liked to talk about the prejudice related to the mental illness. This topic was considered of great importance by professionals and it was particularly tested in the Ward of the Department of Mental Health of

Ferrara. Other three new topics were proposed; one of them, "Managing aggression", was proposed by professionals of the Institute of Psychiatry – University of L'Aquila to be addressed daily if there were in the ward at least two patients with this kind of problematic behavior. This topic, highly structured, is characterized by 5 psycho-educational sessions of 30-40 minutes to be held one every afternoon. The other two topics, "Awareness" and "Problem solving", were proposed by nurses of Acute Psychiatric Unit Care of the Department of Mental Health of Arezzo, to the patients subsequently hospitalized during a period of one year, who shared them with great interest.

As a consequence, a new and latest edition of the manual, updated both in structure and content, was published in 2015 [7]. The theme of prejudice gave origin to the topic "Stigma" considered as a "Basic topic" while the previous basic topics "Early warning signs" and "Personal goals and plan to achieve them" were considered optional. However, in this last manual there is an explicit recommendation for professionals to use the topic "Personal goals and plan to achieve them" as fundamental if there were 3-4 patients ready to be discharged in a few days. In fact, the name of the topic has been changed in "Discharge: individual goals at discharge". The "Managing aggression" topic is considered as "accessory" because is only treated with some patients in the afternoon and the other two topics, "Awareness" and "Problem solving", were considered "experimental" with the recommendation to further observe their usefulness.

From 2016 to 2025 the two centers responsible for the training of this approach (Campobasso and Arezzo) received many feedbacks and proposals by professionals of several wards applying the intervention to include new topics in the manual. The needs of professionals concerned the addition above all of "comorbidity" with personality disorders, the strategies to cope with antisocial personality disorder and problems with immigrants because of the significant prevalence of this kind of admissions.

Spread of the intervention

From 2004 to 2008, also as a consequence of national training, the intervention was applied in 8 centers in Northern, 8 in Central and 6 in Southern Italy. Three evaluative studies were conducted and published with good results and outcomes [17-19].

From 2009 to 2014 the intervention was interrupted or suspended for a long period of time (>1 year) in 3 wards in Northern, 3 in Central and 4 in the Southern Italy. On the other hand, it was introduced in other 2 wards in the North and 1 in the South of our nation. Other evaluative studies were conducted, discussed at congresses or published [20-24].

From 2015 to 2025 the intervention was interrupted or suspended for a long period of time (>1 year) in 4 wards in Northern, 2 in Central and 1 in Southern Italy. It was introduced in 12 wards in Northern, 3 in Central and 2 in Southern Italy. Several evaluative studies were conducted and published that demonstrate good results and outcomes [15, 25-29].

Finally, the CBGI has been introduced in 42 wards (22 in Northern, 11 in Central, and 9 in Southern Italy). However, it has been interrupted in 17 wards (7 in the North, 5 in the Center and 5 in the South). Thus, we can estimate that the intervention has been applied in 25 wards (15 in the North of Italy, 6 in the Center and 4 in the South).

As for the directors of the Mental Health Departments in which the intervention was implemented, 40% of them had a Cognitive Behavioral Therapy (CBT) and/or psychoeducational background; however, it should be added that 88% shared the Evidence Based Mental Health (EBMH) approach.

RESULTS

In this section, we present the results related to some indicators of the evaluation studies carried out by the several centers that applied the intervention, published in the journals or printed in the congress books where the CBGI has been discussed. We emphasize that in all the studies performed, except three [17, 25, 26] with a controlled non randomized trial, the study design was longitudinal pre-post evaluation with baseline data collected in the year before the introduction of the CBGI intervention; specifically, the authors compared data regarding specific processes or outcome indicators obtained before implementation and 12, 24, or 48 months after the implementation of CBGI. The indicators used in the studies were the following (*Table 1*): proportion of voluntary readmissions [4, 17, 19, 20]; proportion of compulsory readmissions [4, 18-20, 27]; time to relapse [25]; proportion of inpatients escaping from the unit [4]; proportion of restraints [4, 27]; number of violent and angry acts toward other inpatients and/or staff [4, 17, 27]; severity of psychiatric symptomatology [17, 28]; level of insight and awareness of psychiatric conditions [21]; level of specific competences acquired about the Behavioural Cognitive Group Intervention (BCGI) basic topics [28]; inpatient satisfaction [4, 17-19, 25, 26]; ward atmosphere [4, 18-22, 28]; cost and income. The indicators of psychopathology, aggressiveness, level of insight, satisfaction and ward atmosphere were measured by reliable tools, different among the various studies, the psychometric properties of which were reported in each paper by reference. Last but not least is the "Costs and income" assessed in terms of economic value based on the Diagnosis Related Groups (DRG) system, used as indicators of efficiency in Italy [19]. The main statistical measure used was the proportion, calculated as percentage of specific events which occurred (i.e., percentage of voluntary readmissions was calculate as the number of voluntary readmissions to the total number of admissions).

Indicators

The indicators area:

- reduction in percentage of voluntary readmissions was found statistically significant (p<0.01) in 3 out of 4 studies [4, 18, 19], but we pinpoint that the study by Travi *et al.* [20] did not show statistical significance; the minimum, -4.7%, at one year follow-up was observed in Bazzoni *et al*. [4], the maximum -11% in Veltro *et al*. [19] where the indicator was measured also at 4 year follow-up with a reduction of 13%;

- reduction in percentage of compulsory readmissions was found statistically significant ($p<0.01$) in 3 out of 5 studies [4, 18, 19]; the reduction was quite similar: 45% [18] *vs* -47% [4]. However, the reduction was also observed in the other two studies as well as the comparison of the duration in days with the Compulsory treatment that decreased from 58 to 16 in the study by Bellini *et al*. [27];
- reduction in time to relapse [25] was found not statistically significant (hazard ratio 0.59, 95% CI: 0.13-2.75) in cases (exposed to psychoeducation) compared to controls (not exposed);
- reduction in percentage of inpatients escaping from the unit was found statistically significant ($p=0.002$) in the first and unique study that measured it [4] with a reduction from 12 (2.4%) to 1 (0.2%);
- reduction in percentage of restraints was found statistically significant ($p=0.02$) in the study by Bazzoni *et al*. [4] with a reduction from 12 (2.3%) to 2 (0.4%). This percentage decreased also in the other two studies by Veltro *et al*. [18] from 5 (the year before) to 1 in the following first and second year and by Bellini *et al*. [27] from 21 (six months before) to 1 in the following six months. They also conducted a controlled study and observed 6 restraints with a total of 66.7 hours of containment in the CBGI group *vs* 12 with a total of 386.1 hours in the control group;
- reduction in number of violent and angry acts toward other inpatients and/or staff was reported by Bazzoni *et al*. [4] with 211 violent episodes (41.5% - CI 37.2 - 46.0) in the previous year before CBGI implementation, and 121 (24.7% - CI 20.9 - 28.8; $p<0.001$) in the following year. They specified also the number of aggressive acts patient-to-patient (110 before *vs* 73 after) and patient-to-staff (101 *vs* 48). In the study by Travi *et al*. [20], the number of violent acts decreased from 13 to 4, 1, 0 in the last three years of follow-up. Massaro *et al*. [17] observed 22% aggressive acts in the experimental group (BCGI) against 77% in the

Table 1

Indicator, measure collected, and difference between, before and after the implementation of CBGI (D), with the Authors of the cited studies

Indicator	Measure collected	D	Authors
Voluntary readmission	Percentage	-3.03	Travi *et al*. [20]
	Percentage	-4.7	Bazzoni *et al*. [4]
	Percentage	-11	Veltro *et al*. [18]
	Percentage	-13	Veltro *et al*. [19]
Compulsory readmission	Percentage	-45	Veltro *et al*. [18]
	Percentage	-48	Veltro *et al*. [19]
	Percentage	-48	Bazzoni *et al*. [4]
	Absolute value	-42	Bellini *et al*. [27]
Time to relapse	Hazard ratio	0.59	Mattei *et al*. [25]
Escaping from the unit	Percentage	-2.2	Bazzoni *et al*. [4]
Patients with restraints	Percentage	-1.9	Bazzoni *et al*. [4]
	Percentage	-6.1	Veltro *et al*. [18]
	Absolute value	-6	Bellini *et al*. [27]
Violent acts	Percentage	-16.8	Bazzoni *et al*. [4]
	Percentage	-55	Massaro *et al*. [17]
	Absolute value	-13	Travi *et al*. [20]
Psychiatric symptomatology	Average (SD) at BPRS	-10.82 (12.7)	Massaro *et al*. [17]
Satisfaction for the care	Percentage	73%	Bazzoni *et al*. [4]
	Average (SD): rating 1-5	4.6 (0.8)	Veltro *et al*. [18]
	Average (SD): rating 1-5	4.4 (0.8)	Veltro *et al*. [19]
	Average (SD): rating 1-5	3.3 (0.9)	Tarallo *et al*. [26]
Ward atmosphere	Percentage	+38	Bazzoni *et al*. [4]
	Average (SD): rating 1-4	+1 (0.8)	Veltro *et al*. [18]
	Average (SD): rating 1-5	+1.5 (0.5)	Veltro *et al*. [19]
Cost and income	Diagnosis related group (DRG value expressed in euro)	+€ 360 (in four years)	Veltro *et al*. [19]

CBGI: Cognitive-Behavior Group Intervention; SD: standard deviation; BPRS: Brief Psychiatric Rating Scale.

control group; also the average of aggressiveness was statistically significant (p<0.0001);

- decrease in severity of psychiatric symptomatology in the pre-post (admission *vs* discharge) study conducted by Massaro *et al.* [17] was found statistically significant by comparison in the group that received BCGI (p<0.001) but not in the control group (p=0.054). Instead, in the study by Zucca *et al.* [28] there were no differences on the Brief Psychiatric Rating Scale among patients that received the CBGI and patients that did not participate to the group. However, the authors wrote that four months after discharge there were no readmissions for the patients involved in CBGI, while among patients that did not partecipate to the group 13 readmissions (19,7%) with 4 compulsory treatments were observed;
- improved levels of insight and awareness of psychiatric conditions, measured by the Insight scale, was found improved as declared by Adami *et al.* [21] at the "II Conferenza Tematica Nazionale" congress, although they did not report data in the abstract-book;
- improved levels of specific CBGI basic topics competences for all four topics at p<0.005 statistic significance and especially for the psychotropic drugs topic [28];
- high Inpatient satisfaction was found in every study. In Bazzoni *et al.* [4] satisfaction was 73% for the care, 81% for the staff and 91% for group usefulness. In Veltro *et al.* [18] at two-year follow-up the average (code 1 to 5) was 4.6 (p<0.01) for "care received", 4.7 (<0.01) for "availability of professionals when needed by patients", 4.7 (p<0.001) for "helpfulness of professionals", 4.6 (p<0.001) for "information received" and 4.6 (p<0.01) for "activities in the afternoon". These results were quite similar and statistically significant (p<0.001) at 4-year follow-up [17]. In the study by Massaro [17], the difference of satisfaction was found statistically significant between patients that participated to the CBGI and patients that did not participate (p<0.001); the difference was explained by sex (significant for male, but not for female). Mattei *et al.* [25] reported only a qualitative description given by patients at discharge of the CBGI as "useful", that they would "attend it in the future again", and that the "group topics were not difficult", but did not show data. In Tarallo *et al.* [26] the satisfaction for CBGI was found, in all the items of the questionnaire they used, higher and statistically significant (p<0.01) compared to that observed in a sample of control treated by another group intervention;
- improvement in ward atmosphere was found +38% since the first study [4]. In the study by Veltro *et al.* [18] the difference between year baseline and all subsequent 4-year follow-up was statistically significant (F=115.7; df=4; p<0.001). In Travi *et al.* [20] nurses rated over a period of three years the ward atmosphere as good/very good 83% of time. The ward atmosphere was found improved as declared by Adami *et al.* [21] and by Dosa and Cavicchio [22] at the same congress although they did not show data on the abstract-book. Zucca *et al.* [28] reported that 87.5% of patients rated the ward atmosphere "excellent" or "good" after the CBGI implementation;
- "Costs and income". The economic mean value of DRG increased from € 2,450 in 2001, to € 2,514 in 2002, € 2,540 in 2003, € 2,606 in 2004, and to € 2,810 in 2005 [19].

Finally, we have also to pinpoint the participation of about 80% of inpatients to the group as described by Gigantesco *et al.* [15] and reported by the teams of Campobasso and Arezzo.

DISCUSSION

The National Institute for Health and Care Excellence (NICE) guidelines [30, 31] recommend structured psychological therapies during the acute phase of many severe mental health problems and, at the same time, emphasize the need to improve psycho-social culture of care in wards [15, 32, 33]. Nevertheless, the current approach remains dominated by psychiatrists through the traditional ward round model, similar to the surgery unit, and by the use of psychotropic drugs only. This is probably due to many factors. First of all, many studies that investigate the effectiveness of non-pharmacological approaches to managing acute illness are not reported in the scoping or systematic reviews [34]. We regret to have to point out that the studies selected ranged from 16 to 29, with great difference in interventions; very few compared with a very large number of psychiatric wards in the world! This could also be due to, on one hand, dearth of funding for this kind of research; on the contrary, there are many studies about the psychotropic drugs efficacy often supported by pharmaceutical companies. On the other hand, the evaluation of non-pharmacological approaches in psychiatric ward is problematic for many reasons, including both difficulties to carry out a randomized control study (RCT) and to check for many different variables. In fact, in the review of Wood *et al.*, [35] about the individual or group CBT for inpatients the risk of bias for the randomization was assessed for 18 trials out of 23 papers reported. Furthermore, blinding of participants and research staff is the linchpin for this study design, but impossible to ensure within trials of psychological interventions in the ward as participants and therapists know what therapy is being delivered. As a consequence, the same review [35] estimated that "all RCTs had at least one area at high risk of bias, and seventeen RCTs had at least two". This narrow focus of studies could therefore underestimate the interest for non-pharmacological approaches, their spread and also their good impact on the care in the ward. Bearing this in mind, we have to be optimistic looking to the literature on non-pharmacological interventions for psychosis adapted to inpatient settings, which is greater than reported in the review of efficacy. It is slowly increasing in recent years but a great transformation in acute settings has not yet been created [35]. Another problem concerns the nature of non-pharmacological interventions since most of them are structured on the basis of specific diagnoses like bipolar or schizophrenia disorders, and therefore difficult to organize in the first phase of admission. For instance, the study of Chen *et al.*, [36] on the bipolar disorder well underline this aspect: "Participants were referred to the program when their clinical symptoms were alleviated, as defined by Young Mania Rating Scale (YMRS) score of less than 8, and during their discharge period"; too late in our opinion considering that the length of admissions are decreasing all over the world and in the USA it is actually estimated less than 10 days [37]. We should also consider that for the spectrum of schizophrenia the lack of insight about symptoms and judgment at admission is too compromised in 70% of patients and show improvement after days of treatment [38]. This problem emerged more clearly for people at the first episode [39]. In fact, 40% of them declared that in the acute phase, after they have been admitted to a psychiatric hospital, they did not remember much of the conversations about the diagnosis. The phrase of a patient that could be considered as an epigraph in this qualitative research is "I think they have told me before, but I was psychotic at that time. I just don't have a clear memory of it". Finally, it is time to consider that during the crisis period the biomedical narrative is misleading because of the lack of insight; furthermore, it could have a counterproductive effect of reducing the person's locus of control and sense of empowerment with its message that the disease is responsible for their experiences [39]. These considerations are confirmed by an interesting survey made by Phillips [40]. He found a high satisfaction of inpatients for the psychoeducational group characterized by "safety planning, coping with stress, positive self-talk, relapse prevention, spirituality, and creative expression". In some way, these results are similar to those found by Morgan *et al.* [41] that "supports research which suggests that psychological interventions can help people make sense of a crisis and lead to changes at an interpersonal and intrapersonal level". Our approach appears much pertinent with the previous statements since it stimulates the participation asking inpatients "what occurred before the admission?". In this way patients talk about their feelings, their experienced state of mind, their behaviour and their life events. In the second day, dealing with the impact of stress factors, their personal way of reacting to them and their personal vulnerability, seems as a "second episode" of their tale. That means "normalizing the crisis", reinforced by all participants regardless of diagnosis, and also prompting a "meaning of what happened" giving them a sense of reality. We emphasize that "to find a meaning" is encouraged by authors of recovery process [42, 43] since 1993 [44] and it is described as one of the best key-factors in the scoping-review of recovery [45]. The way the topic of psychotropic drug is performed in our CBGI is also attractive for patients because of the collaborative approach based on a pair-to-pair learning, very similar to shared-decision-making approach [45]. Finally, this is the very nature of psychoeducation by asking and actively listening to patients' opinion rather than telling them information, that is psycho-didactics. All these factors probably improve adherence and awareness about the stress-vulnerability model as observed by professionals and reported by Adami *et al.* [21]. The attractiveness of the group is confirmed by the data of participation around 80% reported in the results paragraph. Many evaluative studies showed the effectiveness of our approach about the voluntary and compulsory readmissions as well as of the reduction of aggressive acts and of seclusion. We are aware that other specific effective strategies are available to reduce aggressions, conflicts and seclusion [46] but we believe that it could be easier to apply them, and probably in a more effective way, in a good "ward atmosphere" [47]; however, we need more research [48]. Since these practices concern a team-level intervention to avoid or mitigate potential conflicts resulting from patients-patients and staff-patients interactions, the need to improve engagement of patients and the culture of care on wards has also been emphasized [48, 49, 32]. Again, CBGI demonstrated good results on ward atmosphere in all studies that assessed it [4, 19-22, 28]. In many studies considering satisfaction about CBGI, it was found very high [14] and statistically significant [4, 17-19, 26]. Patient satisfaction has a very long tradition of interest in mental health [50, 51], also for inpatients [52-54] and it has been closely linked to ward atmosphere [47, 48], considered as correlated with "global functioning at discharge, improvement during treatment, and positive interactions with staff" [52]. To date, as we have shown, the CBGI seems to be effective to meet many needs of inpatients, and to contribute to a good quality of care on the basis of pertinent indicators. Considering the data collected by the teams of Campobasso and Arezzo, new needs of users and professionals have to be considered and addressed. Three of them are pressing and require immediate responses. One is the problem of addiction because of its prevalence and "comorbidity" above all with personality disorders. That means a new optional topic should be elaborated and studied. To our knowledge, nurses and technicians of rehabilitation of the team of Psychiatric Ward of University of Brescia are working on it [55]. The key-questions of addiction as elaborated by this team are: A) "When is addiction a problem?"; B) "What are the negative effects caused by a substance?". The answers are categorized in "physical", "mental" and "social"; C) "What does craving mean?"; D) What strategies can be implemented to cope with addiction?". The answers were useful to personalize the care plan and to be used by professionals of community mental health center after the discharge. They found preliminary good results by the process evaluation and thus they are currently considering to carry on a trial. Another need regards people with antisocial behaviour and with measure of legal restriction, who are being more and more frequently admitted to psychiatric wards, especially in Italy after the closure of forensic psychiatric hospital. We propose to integrate effective strategies as Safewards [56] or Six Core Strategies [57] with the Accessory Topic "to manage aggression" of CBGI. Something similar for the patients with antisocial personality disorders or with a high prevalence of violent/aggressive behaviours was made by the team of Department of Mental Health of the fifth area of Rome that manage three Residences for the Execution of Security Measures. They use [29] some topics of the CBGI, optimal strategies to deal with violent behaviour [58] and some topics regarding literacy emotion of another effective intervention called InteGRO [59, 60]. The last need regards immigrants. In this case we believe that the problem is linked to the scarce presence of cultural mediators in the ward; a more structured presence of mediators would probably improve the feeling of participation and integration with other inpatients. The presence of different operators and professionals is one of the current debates [61] since the psychiatric ward is actually dominated by the presence of nurses and psychiatrists. A critical point is the continuous delivering of CBGI that by our qualitative survey and by the survey of Gigantesco *et al.* [15], it is applied in many wards two/three times per week or interrupted sometimes for months/years or permanently.

We think that the most important issue for CBGI and for other structured psychosocial interventions for inpatients concerns the barriers to delivering them extensively as described by Evlat *et al.* [33] and summarized in hospital environments and multidisciplinary staff factors. In our country, based on our large experience and by our surveys three factors appear prevalent: the role of ward's director, the organizational problems and the predominant *medical*/pharmacological approach. We observed that in many Italian psychiatric wards the CBGI was interrupted in conjunction with the turnover of the unit's director on the basis of his personal training, often different from cognitive-behavioural therapy or psychoeducation. As this is the only approach investigated for process, outcome and cost indicators in Italy, that means we are very far from applying Evidence Based Mental Health (EBMH). We suggest then that "formal" guidelines for professional accreditation should be adopted to introduce routinely these interventions linked to the budget system. The second problem frequently outlined by many staffs concerns the difficulties to implement the group because of lack of professionals in the wards. We believe that this problem is strictly linked to the third one, because often the director wants to maintain the traditional ward round model. The CBGI as proposed by the authors is not compatible with the traditional medical model, as it offers a much better opportunity; that is to see the interactions among patients for a long period of time and in this way to collect psychopathological observations in a more effective and efficient way. The third problem is the lack of training for psychiatrists/nurses in psychoeducational interventions, in psychological therapies as well as in approaches of *salutogenesis*. We believe it is time to give more importance to *salutogenesis* also for inpatients because it is promising for recovery [60]. Consequently, we are convinced according to McAllister *et al.* [32] and Weich *et al.* [62] that the care for inpatients can improve by listening to the patients' voice as well as by group interventions based on the transdiagnostic approach [37] like the CBGI.

CONCLUSION

This paper gives a large view about the nature, the spread, the results observed in many studies of the CBGI of Vendittelli *et al.* [7], about the importance of psychosocial interventions for inpatients and of the impact of these interventions on the ward atmosphere and on the users' satisfaction. We are aware that there are no RCT of the CBGI, that most studies have a follow-up with an internal control study design, some with a group of comparison and some are without a control group; these factors limit the interpretation and the generalizability of the results. Nevertheless, there are few studies about the psychosocial interventions as complained by Hawes *et al.* [37]. At the same time, there are many obstacles that limit the spread of CBGI, often interrupted for a short/long period of time or permanently, as well as other psychosocial interventions. Many of these factors are due to the hospital environments, to the organizational problems or to the staff; in our opinion the responsibility of the consultant as well as the lack of the explicit definition of role and the function of psychiatric ward are prevalent. On the other hand, the CBGI has received great interest in Italy and in the international literature as also demonstrated in the recent "call for action" of Hawes *et al.* [37], where two papers [18, 19] about this intervention were cited twice. Undoubtedly, in Italy the CBGI has been widely applied, the request for training is constant as well as for support to activate it, and many studies have been conducted even if not RCT. We can pinpoint that there is abundance of literature on CBGI effectiveness, characterized by several study designs and indicators, by several authors (mostly not involved in the elaboration of the intervention) and in different places of Italy. As we wrote in the discussion paragraph, we have many doubts about the feasibility of RCT to evaluate the effectiveness of ward group approaches. However, the CBGI contrasts the medical model and creates a psychosocial culture in the ward [15], consistent with the same model used in the mental health community centres all over the world. Finally, the CBGI is also "clinically" more accurate because of the transdiagnostic approach, based on a dimensional model and focused on the clinical as well as life variables.

Authors' contributions

FV: conceptualization, data curation, formal analysis, methodology, writing – original draft, writing – review and editing; GL: methodology, supervision, writing – review and editing; US: data curation, writing – review and editing; LZ: supervision, writing – review and editing; GA: methodology, supervision, writing – review and editing.

Funding

The Authors declare that no financial support was received for this paper.

Conflict of interest statement

The Authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received on 14 July 2025.
Accepted on 25 August 2025.

REFERENCES

1. Johnson S, Dalton-Locke C, Baker J, Hanlon C, Salisbury TT, Fossey M, et al. Acute psychiatric care: approaches to increasing the range of services and improving access and quality of care. World Psychiatry. 2022;21(2):220-36. doi: 10.1002/wps.20962
2. De Girolamo G, Barbato A, Bracco R,Gaddini A, Miglio R, Morosini P, et al. Characteristics and activities of acute psychiatric in-patient facilities: national survey in Italy. British J Psychiatry. 2007;191(2):170-7. doi: 10.1192/bjp.bp.105.020636
3. Thornicroft G, Tansella M. Balancing community-based and hospital-based mental health care. World Psychiatry. 2002;1(2):84-90.
4. Bazzoni A, Morosini P, Polidori G, Rosicarelli ML, and Fowler D. Group cognitive behavior therapy in the routine care at a Psychiatric Ward of Diagnosis and Treatment. Epidemiol Psichiatr Soc. 2001;10(1):27-36. doi: 10.1017/S1121189X00008514
5. Vendittelli N, Veltro F, Oricchio I, Bazzoni A, Rosicarelli ML, Morosini P. L'intervento cognitivo-comportamentale nel Servizio Psichiatrico di Diagnosi e Cura. Torino: Centro Scientifico Editore; 2003.
6. Vendittelli N, Veltro F, Oricchio I, Bazzoni A, Rosicarelli ML, Polidori G, et al. L'intervento cognitivo comportamentale di gruppo nel Servizio Psichiatrico di Diagnosi e Cura. II ed. Torino: Centro Scientifico Editore; 2008.
7. Vendittelli N, Veltro F, Oricchio I, Cappuccini M, Roncone R, and Simonato P. L'intervento cognitivo-comportamentale di gruppo nel Servizio Psichiatrico di Diagnosi e Cura. III ed. Milano: Edi-Ermes; 2015.
8. Bowers L, Chaplin R, Quirk A, Ellioot P. A conceptual model of the aims and functions of acute inpatient psychiatry. J Ment Health. 2009;18:316-25.
9. Yalom ID, Leszcz M. The theory and practice of group psychotherapy. 5 ed. New York: Basic Books; 2005.
10. National Council on Disability. From privileges to rights: people labeled with psychiatric disabilities speak for themselves. Washington DC: National Council on Disability; 2000.
11. Wagner EH, Glasgow RE, Davis C, Bonomi AE, Provost L, McCulloch D, et al. Quality improvement in chronic illness care: a collaborative approach. Jt Comm J Qual Improv. 2001;27(2):63-80. doi: 10.1016/s1070-3241(01)27007-2
12. Mueser KT, Corrigan PW, Hilton DW, Tanzman B, Schaub A, Gingerich S, et al. Illness management and recovery: a review of the research. Psychiatric Services. 2002;53:1272-84.
13. Thomas EC. Collaborative approaches in psychiatric rehabilitation: innovations in practice. Psychiatr Rehabil J. 202;47(2):91-3. doi: 10.1037/prj0000624
14. Loos S, Clarke E, Jordan H, Puschner B, Fiorillo A, Luciano M, et al. Recovery and decision-making involvement in people with severe mental illness from six countries: a prospective observational study. BMC Psychiatry. 2017;17(1):38. doi: 10.1186/s12888-017-1207-4
15. Gigantesco A, Pontarelli C, Veltro F; CBGI Italian Study Group. Psycho-educational group therapy in acute psychiatric units: creating a psychosocial culture. An update of spread and effectiveness of a psychosocial intervention in Italian psychiatric wards. Ann Ist Super Sanità. 2018;54(4):272-83. doi: 10.4415/ANN_18_04_03
16. Perris, C. Personality-related disorders of interpersonal behaviour: a developmental-constructivist cognitive psychotherapy approach to treatment based on attachment theory. Clinical Psychol Psychother. 2000:7(2):97-117. doi: 10.1002/(SICI)1099-0879(200005)7:2<97::AID-CPP230>3.0.CO;2-K
17. Massaro CRM, Matrella L, Petito A, Iuso S, De Salvia M, Mazza M, et al. Efficacia di un intervento psicoeducativo di gruppo a orientamento cognitivo-comportamentale applicato a pazienti in fase acuta. Psichiatr Psicoter. 2007;26(1):28-48.
18. Veltro F, Falloon I, Vendittelli N, Oricchio I, Scinto A, Gigantesco A, et al. Effectiveness of cognitive-behavioural group therapy for inpatients. Clin Pract Epidemiol Ment Health. 2006;2:16. doi: 10.1186/1745-0179-2-16
19. Veltro F, Vendittelli N, Oricchio I, Addona F, Avino C, Figliolia G, et al. Effectiveness and efficiency of cognitive-behavioral group therapy for inpatients: 4-year follow-up study. J Psychiatr Pract. 2008;14(5):281-8. doi: 10.1097/01.pra.0000336755.57684.45
20. Travi M, Cappuccini M, Pinzaglia L, Serafini U, and Cesari G. Valutazione nell'SPDC di Arezzo di "L'Intervento Cognitivo-Comportamentale di Gruppo in SPDC". Nuova Rassegna di Studi di Psichiatria, 10. Available from: https://www.nuovarassegnastudipsichiatrici.it/images/pdf/1/NRSP-Vol1-10-Valutazione-nell-SPDC-di-Arezzo-di-Intervento-Cognitivo-Comportamentale-di-Gruppo-in-SPDC.pdf.
21. Adami L, Corradi AT, Pontarelli I, Cavicchio A. Intervento cognitivo-comportamentale di gruppo nel SPUDC dell'Aquila. In: II Conferenza Tematica Nazionale Riprendersi dalle Catastrofi Naturali. Dagli eventi traumatici alla riabilitazione mentale. Abstract book. L'Aquila: 16-18 settembre, 2010. p. 70. Available from: http://www.sirp-abruzzo.it/cms/images/stories/abstract_book_sirp_2010.pdf.
22. Dosa M, Cavicchio A. Gruppi per il miglioramento dell'atmosfera in reparto e la diminuzione di comportamenti aggressivi. In: II Conferenza Tematica Nazionale Riprendersi dalle Catastrofi Naturali. Dagli eventi traumatici alla riabilitazione mentale. Abstract book. L'Aquila: 16-18 settembre, 2010. p. 87. Available from: http://www.sirp-abruzzo.it/cms/images/stories/abstract_book_sirp_2010.pdf.
23. Lepre F, D'Andria V, Faiella N. L'intervento cognitivo-comportamentale di gruppo nel servizio psichiatrico di diagnosi e cura (SPDC) dell'Ospedale Umberto I di Nocera Inferiore (SA). Nuove Prospettive in Psicologia. 2012;47(1):55-61.
24. Caruso R, Grassi L, Biancosino B, Marmai L, Bonatti L, Moscara M, et al. Exploration of experiences in therapeutic groups for patients with severe mental illness: development of the Ferrara group experiences scale (FE- GES). BMC Psychiatry. 2013;13:242. doi: 10.1186/1471-244X-13-242
25. Mattei G, Raisi F, Burattini M, Ferrari S, Galeazzi GM, Mazzi F, et al. Effectiveness of group psychoeducation on psychiatric inpatients. European Psychiatry. 2015;30(Suppl. 1):1656. doi: 10.1016/S0924-9338(15)31278-5
26. Tarallo F, Matarrese A, D'Alessandro M, Griffo S, Marino G, Marazzi M, et al. Cognitive-behavioural group interventions and multifamily psychoanalysis group in a psychiatric ward. Riv Psichiatr. 2020;55(4):222-6. Italian. doi: 10.1708/3417.33998
27. Bellini L, Papini B, Spera M, Vergani V, Mencacci C. L'intervento cognitivo comportamentale di gruppo come strumento per la riduzione dell'aggressività in SPDC. Psichiatria Oggi. 2021;34(2):45-54. Available from: https://www.psichiatriaoggi.it/wp-content/uploads/2021/12/PsichiatriaOggi-annoXXXIV-n2-luglio-dicembre.pdf.

28. Zucca C, Ortolani E, Frattarolo S, Aiello T, Travaglini G, Cro F, et al. Group-based rehabilitative interventions in the Department of Mental Health of Viterbo, Italy. Riv Psichiatr. 2017;52(5):200-7. doi: 10.1708/2801.28347
29. De Luca V, Pompili PM, Paoletti G, Bianchini V, Franchi F, Lombardi M, et al. The reform of Italian forensic psychiatric hospitals and its impact on risk assessment and management. Int J Risk Recovery. 2018;1(3):22-9. doi: 10.15173/ijrr.v1i3.3510
30. National Institute for Health and Care Excellence. Bipolar disorder: assessment and management. London: NICE; 2025. Available from: https://www.nice.org.uk/guidance/cg185/resources/bipolar-disorder-assessment-and-management-pdf-35109814379461.
31. National Institute for Health and Care Excellence. Psychosis and schizophrenia in adults: prevention and management. London: NICE; 2025. Available from: https://www.nice.org.uk/guidance/cg178/resources/psychosis-and-schizophrenia-in-adults-prevention-and-management-pdf-35109758952133.
32. McAllister S, Robert G, Tsianakas, McCrae N. Conceptualising nurse-patient therapeutic engagement on acute mental health wards: an integrative review. Int J Nurs Stud. 2019;93:106-18.
33. Evlat G, Wood L, and Glover N. A systematic review of the implementation of psychological therapies in acute mental health inpatient settings. Clin Psychol Psychother. 2021;28(6):1574-86. doi: 10.1002/14651858.CD002084.pub2
34. Muralidharan S, Fenton M. Containment strategies for people with serious mental illness. Cochrane Database Syst Rev. 2006(3):CD002084. doi: 10.1002/14651858
35. Wood L, Williams C, Billings J, Johnson S. A systematic review and meta-analysis of cognitive behavioural informed psychological interventions for psychiatric inpatients with psychosis. Schizophr Res. 2020;222:133-44. doi: 10.1016/j.schres.2020.03.041
36. Chen R, Xi Y, Wang X, Li Y, He Y, Luo J. Perception of inpatients following remission of a manic episode in bipolar I disorder on a group-based Psychoeducation program: a qualitative study. BMC Psychiatry. 2018;18(1):26. doi: 10.1186/s12888-018-1614-1
37. Hawes MT, Marcello S, and Kleiman EM. We need more research on inpatient group therapy: a call to action. Psychol Med. 2025;55:e150. doi:10.1017/S0033291725000960
38. Schennach R, Meyer S, Seemüller F, Jäger M, Schmauss M, Laux G, et al. Insight in schizophrenia-course and predictors during the acute treatment phase of patients suffering from a schizophrenia spectrum disorder. Eur Psychiatry. 2012;27(8):625-33. doi: 10.1016/j.eurpsy.2012.01.001
39. Huurman ME, Pijnenborg GHM, Sportel BE, van Rijsbergen GD, Hasson-Ohayon I, Boonstra N. Communicating diagnoses to individuals with a first episode psychosis: a qualitative study of individuals perspectives. Front Psychiatry. 2023;14:1098224. doi: 10.3389/fpsyt.2023.1098224
40. Phillips A. Psychoeducational group satisfaction in an acute psychiatric hospital. Social Work With Groups. 2023;46(2):119-28. doi: 10.1080/01609513.2022.2107599
41. Morgan C, Clarkson L, Hiscocks R, Hopkins I, Berry K, Tyler N, et al. What should inpatient psychological therapies be for? Qualitative views of service users on outcomes. Health Expect. 2024;27(1):e13889. doi: 10.1111/hex.13889
42. Slade M, Wallace G. Recovery and mental health. In: Slade M, Oades L, Jarden A (Eds). Wellbeing, recovery and mental health. Cambridge: University Press; 2017. p. 24-34.
43. Clarke SP, Crowe TP, Oades LG, Deane FP. Do goal-setting interventions improve the quality of goals in mental health services? Psychiatr Rehabil J. 2009;32(4):292-9. doi: 10.2975/32.4.2009.292.299
44. Anthony WA. Recovery from mental illness: the guiding vision of the mental health service system in the 1990s. Psychosocial Rehabil J. 1993;16(4):11-23. doi: 10.1037/h0095655
45. Jaiswal A, Carmichael K, Gupta S, Siemens T, Crowley P, Carlsson A, Unsworth G, Landry T, Brown N. Essential elements that contribute to the recovery of persons with severe mental illness: a systematic scoping study. Front Psychiatry. 2020;11:586230. doi: 10.3389/fpsyt.2020.586230
46. Baker J, Berzins K, Canvin K, Benson I, Kellar I, Wright J, et al. Non-pharmacological interventions to reduce restrictive practices in adult mental health inpatient settings: the COMPARE systematic mapping review. Health Serv Deliv Res. 2021;9(5):1-184. doi:10.3310/hsdr09050
47. Hallett, N, Duxbury JA, Björkdahl A, Johnson S. Ward culture and atmosphere. In: Hallett N, Whittington R, Richter D, Eneje E (Eds). Coercion and violence in mental health settings. Cham: Springer; 2024. p. 265-86. Available from: https://doi.org/10.1007/978-3-031-61224-4_12
48. Efkemann SA, Bernard J, Kalagi J, Otte I, Ueberberg B, Assion HJ, et al. Ward atmosphere and patient satisfaction in psychiatric hospitals with different ward settings and door policies. Results from a mixed methods study. Front Psychiatry. 2019;10:576. doi: 10.3389/fpsyt.2019.00576
49. Duxbury JA, Björkdahl A, Johnson S. Ward culture and atmosphere. In: Violence in mental health settings: causes, consequences, management. New York, NY: Springer; 2006. p. 273-91.
50. Sitzia J,vWood N. Patient satisfaction: a review of issues and concepts. Soc Sci Med. 1997;45(12):1829-43. doi: 10.1016/s0277-9536(97)00128-7
51. Williams B. Patient satisfaction: a valid concept? Soc Sci Med. 1994;38(4):509-16. doi: 10.1016/0277-9536(94)90247-X
52. Elgendy H, Shalaby R, Owusu E, Nkire N, Agyapong VIO, Wei Y. A scoping review of adult inpatient satisfaction with mental health services. Healthcare. 2023;11(24):3130. doi: 10.3390/healthcare11243130
53. Boyer L, Baumstarck-Barrau K, Cano N, Zendjidjian X, Belzeaux R, Limousin S, et al. Assessment of psychiatric inpatient satisfaction: a systematic review of self-reported instruments. Eur Psychiatry. 2009;24(8):540-9. doi: 10.1016/j.eurpsy.2009.05.011
54. Gigantesco A, Morosini R, Bazzoni A. Quality of psychiatric care: validation of an instrument for measuring inpatient opinion. Int J Qual Health Care. 2003;15(1):73-8. doi: 10.1093/intqhc/15.1.73
55. Barlati S, Regina V, Deste G, Galluzzo A, Turrina C, Valsecchi P, Vita A. Psychosocial recovery-oriented interventions in schizophrenia. In: Carpiniello B, Vita A, Mencacci C (Eds). Recovery and major mental disorders. Switzerland: Springer Nature; 2022. p. 77-98. doi: 10.1007/978-3-030-98301-7_6
56. Bowers L, James K, Quirk A, Simpson A; SUGAR; Stewart D, Hodsoll J. Reducing conflict and containment rates on acute psychiatric wards: The Safewards cluster randomised controlled trial. Int J Nurs Stud. 2015;52(9):1412-22. doi: 10.1016/j.ijnurstu.2015.05.001. Erratum in: Int J Nurs Stud. 2016;58:102. doi: 10.1016/j.

ijnurstu.2015.12.006

57. Putkonen A, Kuivalainen S, Louheranta O, Repo-Tiihonen E, Ryynänen OP, Kautiainen H, et al. Cluster-randomized controlled trial of reducing seclusion and restraint in secured care of men with schizophrenia. Psychiatr Serv. 2013;64(9):850-5. doi: 10.1176/appi.ps.201200393
58. Roppolo L, Morris D, Khan F, Downs R, Metzger J, Carder T, et al. Improving the management of acutely agitated patients in the emergency department through implementation of Project BETA (best practices in the evaluation and treatment of agitation). J Am Coll Emerg Physicians Open. 2020;1(5):898-907. doi: 10.1002/emp2.12138. Erratum in: J Am Coll Emerg Physicians Open. 2023;4(3):e13002.
59. Veltro F, Vendittelli N, Pontarelli I, Pica A, Nicchiniello I. L'intervento psicoeducativo di gruppo per il raggiungimento di obiettivi (Inte.G.R.O). Roma: Alpes; 2016.
60. Veltro F, Latte G, Pontarelli I, Pontarelli C, Nicchiniello I, and Zappone L. Long term outcome study of a salutogenic psychoeducational recovery oriented intervention (Inte.G.R.O.) in severe mental illness patients. BMC Psychiatry. 2022;22(1):240. doi: 10.1186/s12888-022-03887-2
61. Johnson S, Dalton-Locke C, Baker J, Hanlon C, Salisbury TT, Fossey M, et al. Acute psychiatric care: approaches to increasing the range of services and improving access and quality of care. World Psychiatry. 2022;21(2):220-36. doi: 10.1002/wps.20962
62. Weich S, Fenton SJ, Staniszewska S, Canaway A, Crepaz-Keay D, Larkin M, et al. Using patient experience data to support improvements in inpatient mental health care: the EURIPIDES multimethod study. Southampton (UK): NIHR Journals Library; 2020.

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 250-258
DOI: 10.4415/ANN_25_04_03

Organization and functioning of the Italian Departments of Mental Health in the pandemic and post-pandemic period

Laura Camoni, Fiorino Mirabella, Antonella Gigantesco, Emanuela Medda, Maurizio Ferri, Debora Del Re, Isabella Cascavilla, Cristina D'Ippolito, Nadia Francia, Angelo Picardi, Gemma Calamandrei and the Italian Study Group of Departments of Mental Health*

Centro di Riferimento per le Scienze Comportamentali e Salute Mentale, Istituto Superiore di Sanità, Rome, Italy
**The members of the Italian Study Group of Departments of Mental Health are listed before the References*

Abstract

Introduction. The pandemic significantly affected mental health, leading to a reorganization of services. This study examines changes in Italy's Departments of Mental Health (DMHs), comparing surveys from 2021 (during COVID-19) and 2023 (post-pandemic).
Methods. The two surveys involved 19 Italian DMHs and covered variables related to mental health care (number of centres, available staff, services provided and intervention methods).
Results. Between 2021 and 2023, services show structural stability with a solid territorial network. Organizational changes point to greater flexibility and customization, with a stronger semi-residential hospital offer. Human resources give mixed signals: psychologists and health care social workers are increasing, while social workers and psychiatric rehabilitation technicians are decreasing. Clinically, hospitalizations in General Hospital Psychiatric Units (GHPUs), Emergency Department (ED) visits, and self-harm cases are rising, while psychiatric and psychological visits decline. Remote nursing and psychosocial interventions are increasing. The growth in first psychological consultations and users taken into care suggests a gradual return to in-person access and partial pre-pandemic normality.
Conclusions. The data substantiate the need for continuous attention and adequate support to address post-pandemic mental distress, highlighting the importance of reorganizing services to effectively respond to the new needs of the population.

Key words
- Departments of Mental Health
- health care
- structure and process indicators
- epidemiology

INTRODUCTION

The consequences of the pandemic have affected people's mental health and psychosocial well-being in several ways. These include bereavement, social isolation, fear of infection or infecting others, uncertainty about the economic consequences and loss of livelihood, and anxiety about future developments. The measures implemented to combat the spread of infection have resulted in a marked decline in various protective factors, including social support, engagement in professional and academic studies, opportunities for physical activity, daily routines, and access to healthcare services. The interplay of these factors has resulted in an increase in mental health concerns within the general population, while concurrently exacerbating those already present in individuals diagnosed with a mental disorder [1].

The World Health Organization [2] has indicated that in over ninety percent of cases, services directed at the management of mental disability on a global scale were disrupted during the early months of the pandemic. In response to the crisis, several services attempted to manage the situation by offering remote provisions, including psychological support and virtual psychiatric consults via telephone and video calls. However, it is important to acknowledge the possibility of a deterioration in care conditions, which may be attributable to the organisational stresses experienced by services and

Address for correspondence: Laura Camoni, Centro di Riferimento per le Scienze Comportamentali e la Salute Mentale, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: laura.camoni@iss.it.

the deterioration of mental health in the population. Although mental health services in Italy have appeared to be resilient in maintaining their operations, there is a conspicuous absence of definitive data concerning the scope of their functionality and the accessibility of these services, either in-person or remotely, to individuals in the period after the first waves of the pandemic.

At the end of 2020, the Centre for Behavioural Sciences and Mental Health of the Italian National Institute of Health (Istituto Superiore di Sanità, ISS, Rome), with the support of the Ministry of Health, promoted the project "Consolidation of national sentinel Departments of Mental Health (DMHs) network for monitoring the consequences of the SARS-CoV-2 pandemic on mental health" [3]. Mental health care in Italy is provided by about 139 DMHs that include territorial services for outpatient day care (Community Mental Health Centres, CMHCs); semi-residential facilities (day centres, DCs); non-hospital residential facilities (RFs); General Hospital Psychiatric Units (GHPUs), specialized units of the Department of Mental Health in which diagnostic, therapeutic and care activities carried out in hospital settings. Semi-residential and RFs also involve private contracted facilities and private contracted hospital departments.

The project directly involved the DMHs to conduct a timely and detailed monitoring of the organisational structure of care for people with mental disorders during the pandemic. The survey was then repeated in 2023, with the objective of describing changes over time using some activity indicators.

OBJECTIVE

The objective of the study was to describe the organisation and functioning of mental health services, with respect to a selection of indicators derived from data published by the Mental Health Information System (SISM) of the Ministry of Health, comparing data from the pandemic period (January-June 2021) with data from the post-pandemic period (January-June 2023).

METHODS

The survey involved a monthly assessment of service operations conducted from January to June 2021 and the same period in 2023. The adherence of DMHs was voluntary. Thirty-seven DMHs in 2021 and twenty-three in 2023 agreed to participate in the monitoring. The comparison was made by selecting the nineteen DMHs that had submitted complete data in both 2021 and 2023. The DMHs that participated are listed at the end of the article.

For data collection, an *ad hoc* form was prepared and shared with the DMHs. The information covered: allocation and types of staff present; hospital, residential and semi residential activities; number of users treated in-person and remotely; direct provision of assistances to the person provided by professionals present in the various services; and consultations in emergency rooms. The data collection form was made available on an online platform, built specifically for this survey. The collected data were periodically checked centrally for outliers or inconsistent values. At the end of the survey, the data were further subjected to quality verification by the survey managers at each DMHs and the ISS.

It should be emphasized that this monitoring program does not constitute nor is it intended as a measure of the efficiency or adequacy of a DMH but is only meant to gather information to evaluate the reorganization of DMHs following the pandemic experience.

The rate per 10,000 residents in the catchment area was calculated for each DMH. The "resident population as of December 31, 2020, by Local Health Units (LHUs), age and gender" published on the Ministry of Health website [4] for 2021 and that as of December 31, 2021, for 2023 data were used as the reference population. Given the high variability in the data, the median rate per 10,000 and 100,00 residents was used to summarise the information and to compare the estimates from 2021 and 2023. We also used the percentage difference between the median rate in 2023 and 2021. Changes below ±10% were not considered significant.

RESULTS

Analysis of data on the facilities and beds provided by DMHs (*Figure 1*) shows a median rate of CMHCs of 1.28 per 100,000 residents in 2021 and 1.30 in 2023. The median rate of the GHPUs offering 24-hour psychiatric consult was 0.61 per 100,000 population in 2021 and 0.57 in 2023 with a bed availability in the same services of 6.42 per 100,000 population in 2021 to 6.28 in 2023.

The median rate of GHPUs with available beds in day hospital (DH) was 0.54 per 100,000 population in

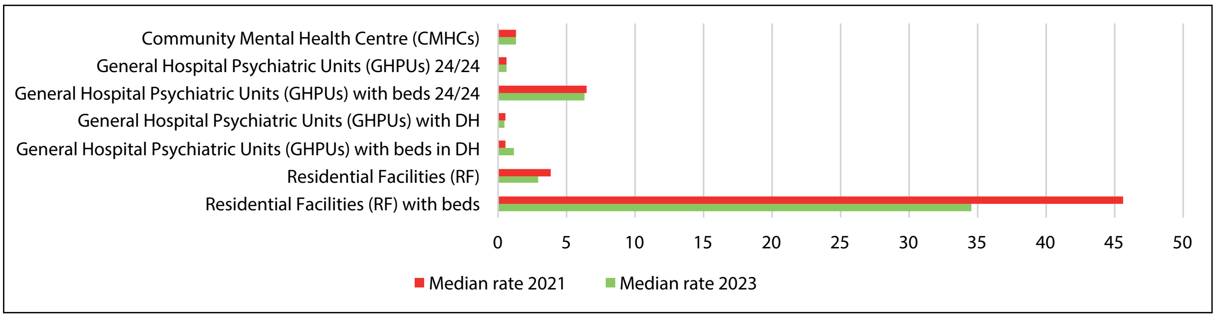


Figure 1
Facilities and beds provided by Departments of Mental Health (DMHs).

2021 to 0.48 in 2023 and the availability of DH beds in GHPUs had a median rate of 0.49 per 100,000 population in 2021 to 1.17 in 2023.

As for RFs the median rate was 3.85 per 100,000 population in 2021 to 2.92 in 2023 and that of available beds at 4.56 per 10,000 population in 2021 to 3.45 in 2023.

The median rate of psychiatrists (*Figure 2*) decreased from a value of 10.15 per 100,000 inhabitants in 2021 to 9.75 in 2023. Psychologists, on the other hand, reported a median rate of 2.98 per 100,000 inhabitants in 2021 to 3.29 in 2023. Nursing staff had a median value of 21.85 per 100,000 inhabitants in 2021 to 21.39 in 2023.

Psychiatric rehabilitation technicians and social workers reported median values of 2.13 per 100,000 inhabitants in 2021 to 1.91 in 2023 and 2.65 per 10,000 inhabitants in 2021 to 2.47 in 2023, respectively.

Health care social workers (HSW) show a median value of 3.32 per 100,000 inhabitants in 2021 and 4.39 in 2023. For administrative and support staff, values of 1.54 per 100,000 inhabitants were observed in 2021 and 1.86 in 2023.

Regarding hospital activity (*Figure 3*), the median rate of admissions occurring in GHPUs increased from 1.0 per 10,000 population in 2021 to 1.20 in 2023, and patients present in GHPUs from 1.40 per 10,000 population in 2021 to 1.55 in 2023.

Compulsory psychiatric treatments (CPT) decreased from a median rate of 0.20 per 10,000 population in 2021 to 0.15 in 2023; compulsory psychiatric evaluation (CPE) vary from 0.02 per 10,000 population in 2021 to 0.03 in 2023.

Patients discharged from RFs, reported a median rate of 0.10 per 10,000 population in 2021 to 0.09 in 2023.

In 2021, the median rate of patients who received at least one health or social provisions either in-person or remotely (provided through remote modalities, e.g., telemedicine, online consultations, etc.) was 67.20 per 10,000 population. In 2023, this value increased to 73.40. The median rate of patients who received health or social provisions exclusively remotely was 0.48 per 10,000 population in 2021 and dropped to 0.03 in 2023 (*Figure 4*).

The median rate of face-to-face provisions provided by DMHs (considering that a patient may receive more than one health and social provisions and considering the total number of psychiatric consults, psychological visits, nursing provisions and psychosocial interventions, excluding first visits) was 193.30 per 10,000 population in 2021 and 203.29 in 2023. Health and social provisions provided remotely decreased from a median of 16.70 per 10,000 population in 2021 to 8.72 in 2023 (*Figure 5*).

Total median rate of remote psychiatric and psychological consult provisions decreased from 5.09 in 2021 to 1.86 in 2023 and from 2.29 in 2021 to 0.76 in 2023, respectively, while remote nursing and psychosocial interventions increased from 2.46 in 2021 to 3.95 in 2023 and from 1.37 in 2021 to 2.57 in 2023, respectively (*Figure 6*). Total median rate in-person psychiatric and psychological consult provisions decreased from 54.18

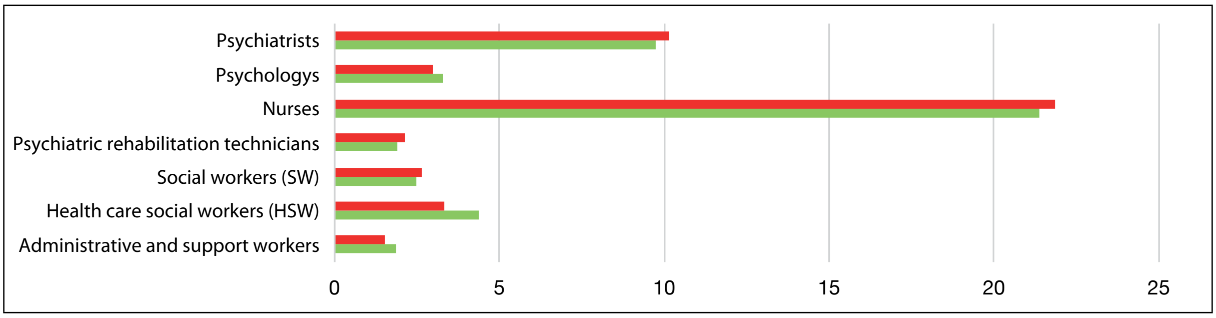


Figure 2
Departments of Mental Health (DMHs) staff.

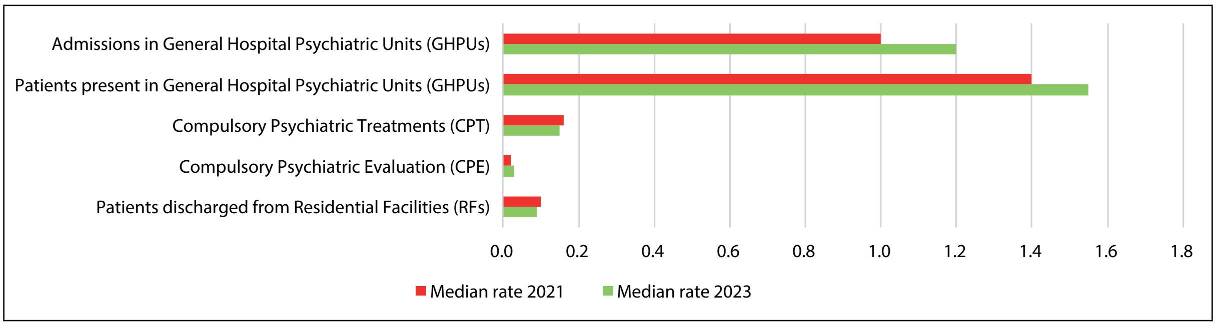


Figure 3
Residential Facilities (RFs) and hospital activities.

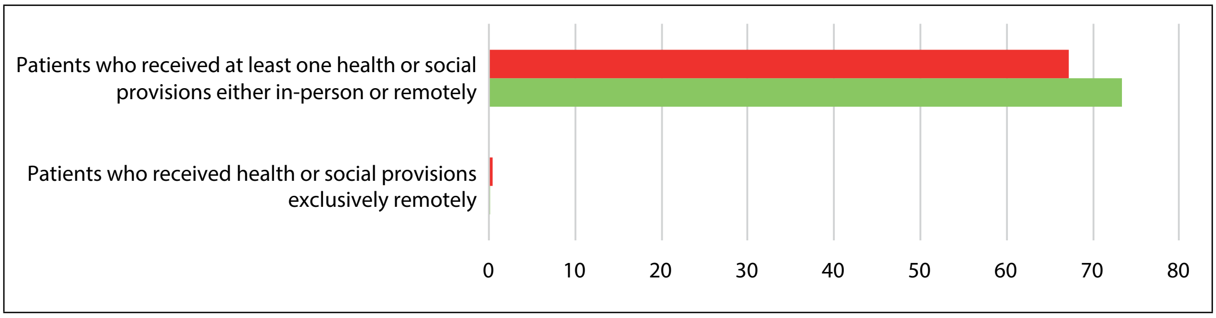


Figure 4
Patients under treatment.

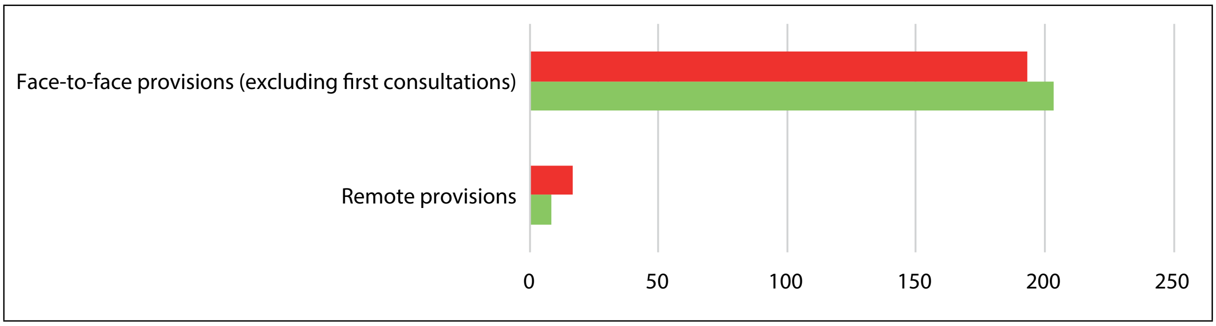


Figure 5
Provisions provided face-to-face or remotely.

in 2021 to 49.90 in 2023 and from 15.35 in 2021 to 8.33 in 2023, respectively. The first psychiatric and psychological consults took place exclusively in presence mode, with no change in the median rates for the two periods (3.90 per 10,000 in 2021 and 4.00 in 2023 for psychiatric consults; 0.60 per 10,000 in 2021 and 0.80 in 2023 for psychological consults). In 2023, the median of psychotherapy sessions was 8.22 per 10,000 population for face-to-face and 0.02 for remote. Data in 2021 was missing. In-person nursing provisions increased from 70.60 per 10,000 to 100.88 in 2023, while remote nursing provisions increased from 2.46 to 3.95 in 2023. In-person psychosocial interventions went from 33.02 per 10,000 to 31.39 in 2023, while

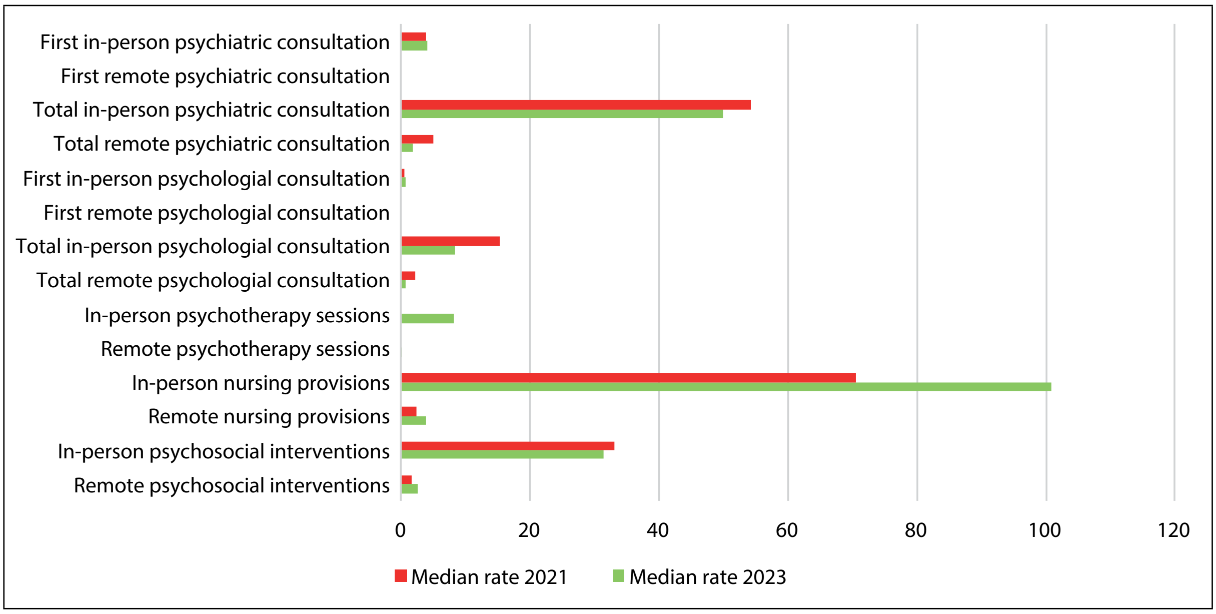


Figure 6
Type of provisions provided face-to-face or remotely.

remote psychosocial interventions went from 1.73 to 2.57 in 2023.

Regarding psychiatric and psychological consultations carried out by DMHs staff at the general hospital Emergency Department (ED) (*Figure* 7), the median rate of consultations was 2.90 per 10,000 population in 2021 and 3.44 in 2023. Self-injurious gestures ascertained at the ED were 0.20 per 10,000 in 2021 and 0.26 in 2023.

A summary of the comparison of key indicators from 2021 and 2023 is shown in *Table 1*.

DISCUSSION

Organization

The stability of the number of CMHCs in the two periods considered seems to confirm the solidity of the territorial network, the cornerstone of the national mental health system in Italy. However, the numerical data alone do not allow a complete evaluation: it will be necessary to delve deeper into the issue of human resources and capacity for care. The number of GHPUs with 24/7 care and the relative availability of beds remain equally stable in the two periods.

Although the number of GHPUs offering DH has slightly decreased (about -11%), the average number of available DH beds has more than doubled with an increase of 138.8% in 2023. This indicates a rise in semi-residential hospital activities, concentrated in a smaller number of facilities, but with greater care capacity. This model can promote greater flexibility in the therapeutic offer and respond more adequately to clinical needs without resorting to prolonged hospitalization.

Human resources

Regarding full-time permanent staff at the DMHs, in 2023, compared to 2021, a fairly stable median value of psychiatrists is observed, a 10.4% increase in psychologists, a slight decrease in social workers (-6.8%) and psychiatric rehabilitation technicians (-10.4%), indicating that some DMHs may have redirected resources towards professional profiles considered more strategic (such as psychologists), penalising other roles. Furthermore, the pandemic might have changed the organization of health service to the detriment of these professional figures. The observed increase of 32.3% in 2023 compared to 2021 in the median value of HSW probably highlights a greater demand of assistance and support to patients following the pandemic, for instrumental activities of daily living, and perhaps a greater sensitivity towards social support for people with mental disorders. The constant presence of nurses highlights their fundamental role in psychiatric health care. In-person and remote nursing provisions (mostly telephone calls aimed at assessing the progress and modulation of ongoing therapy) increased by 42.9% and 60.6% respectively in 2023, which could reflect an enhancement of the role of nursing care, especially in the territorial management of patients, in the administration of therapies and in supporting continuity of care.

Hospital activities

Data on hospital activities show a 20% increase in admissions to GHPUs in 2023 compared to 2021, indicating greater pressure on diagnosis and acute treatment departments, with a potential increase in demand for acute hospital psychiatric care. An increase, albeit smaller (10.7%) from 2021 to 2023, also affected the median rate of patients present in GHPU, suggesting a strengthening of the role of acute hospital services.

In the same period, CPT decreased by 6%, which is consistent with the trend at a national level and can be interpreted as a positive effect of early intervention and timely care by territorial services, reducing the need to resort to coercive measures.

The 50% increased use of CPE (although small in absolute value) could reflect greater attention by services in the early detection of mental distress, activating assessment interventions even in the absence of direct patient consent.

The increase in the median (18.8%) of psychiatric and psychological consultations carried out by psychiatrists and psychologists of the DMH at the ED and of self-harm gestures ascertained at the ED increased by 29.3% in the two-year period could indicate a greater use of the ED for psychological or psychiatric problems and probably an increase in acute situations, crises or states of suffering not previously intercepted in the territory. Furthermore, there is evidence of growing pressure on emergency services, which also find themselves managing aspects related to mental health. Particularly alarming are the data on the growth of self-harm ges-

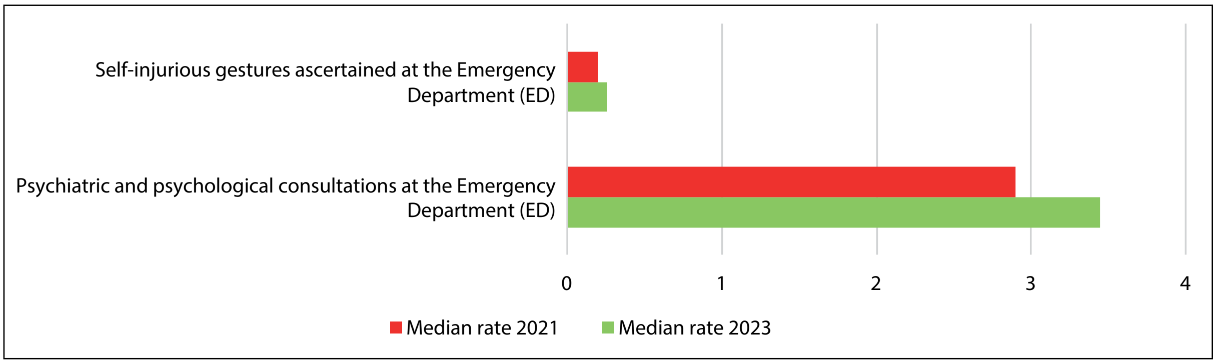


Figure 7
Consultations and ascertained carried out at the Emergency Department (ED).

Table 1
Summary of key indicators

	Median rate 2021	Median rate 2023	Difference 2023-2021*
Facilities and beds provided by Departments of Mental Health (DMHs)			
Residential Facilities (RF) with beds	45.58	34.5	⬇
Residential Facilities (RF)	3.85	2.92	⬇
General Hospital Psychiatric Units (GHPUs) with beds in DH	0.49	1.17	⬆
General Hospital Psychiatric Units (GHPUs) with DH	0.54	0.48	⬇
General Hospital Psychiatric Units (GHPUs) with beds 24/24	6.42	6.28	=
General Hospital Psychiatric Units (GHPUs) 24/24	0.61	0.57	=
Community Mental Health Centre (CMHCs)	1.28	1.3	=
DMHs staff			
Administrative and support workers	1.5	1.9	⬆
Health care social workers (HSW)	3.3	4.4	⬆
Social workers (SW)	2.7	2.5	⬇
Psychiatric rehabilitation technicians	2.1	1.9	⬇
Nurses	21.9	21.4	=
Psychologys	3.0	3.3	⬆
Psychiatrists	10.2	9.8	=
Residential facilities and hospital activities			
Patients discharged from Residential Facilities	0.10	0.09	⬇
Compulsory Psychiatric Evaluation (CPE)	0.02	0.03	⬆
Compulsory Psychiatric Treatments (CPT)	0.16	0.15	⬇
Patients present in GHPUs	1.40	1.55	⬆
Admissions in GHPUs	1.00	1.20	⬆
Patients under treatment			
Patients who received health or social provisions exclusively remotely	0.48	0.03	⬇
Patients who received at least one health/social provisions either in-person or remotely	67.20	73.40	⬆
Provisions provided face-to-face or remotely			
Remote provisions	16.72	8.72	⬇
Face-to-face provisions (excluding first consultations)	193.3	203.49	⬆
Type of provisions provided face-to-face or remotely			
Remote psychosocial interventions	1.73	2.57	⬆
In-person psychosocial interventions	33.02	31.39	⬇
Remote nursing provisions	2.46	3.95	⬆
In-person nursing provisions	70.60	100.88	⬆
Remote psychotherapy sessions		0.02	
In-person psychotherapy sessions		8.22	
Total remote psychologial consultation	2.29	0.76	⬇
Total in-person psychologial consultation	15.35	8.33	⬇
First remote psychologial consultation			
First in-person psychologial consultation	0.60	0.80	⬆
Total remote psychiatric consultation	5.09	1.86	⬇
Total in-person psychiatric consultation	54.18	49.90	⬇
First remote psychiatric consultation			
First in-person psychiatric consultation	3.90	4.00	=
Consultations and ascertained carried out at the Emergency Department (ED)			
Psychiatric and psychological consultations at ED	2.90	3.44	⬆
Self-injurious gestures ascertained at the ED	0.20	0.26	⬆

*Values with differences below 10% were considered equal (=); DMHs: Departments of Mental Health; DH: day hospital; RFs: residential facilities.

tures ascertained at the ED which could reflect a possible difficulty in intercepting such phenomena early.

Provisions provided in-person and remotely

Users with at least one health or social provision in-person or remotely increased by approximately 6 points, equal to a percentage increase in 2023 of 9.2% and could reflect a general slight increase in access to healthcare services probably due to greater availability of services or, not to be excluded, greater demand for services to recover visits/postponements accumulated in previous years. This increase is consistent with the treated prevalence of any mental disorders by psychiatric services trend at a national level. There is a general reduction in total psychiatric and psychological consult provisions with reduction percentage values of 7.9% and 45.7% respectively for in-person visits and 63.5% and 66.8% for remote visits. These data suggest that, in the post-pandemic period, not only has the use of mental health technologies decreased, but there has been a general decline in the provision of psychological and psychiatric consults, with a potentially critical impact on the quality of care.

Between 2021 and 2023, the data show a significant return to face-to-face interventions, with some differences depending on the type of intervention. The comparison between the median of users with at least one remote-only health and social provisions in 2021 and 2023 shows a very significant decrease (by approximately 94%). These data suggest that in 2021 a substantial share of users received provisions exclusively remotely, likely due to the COVID-19 pandemic that had made massive use of telemedicine and other remote provisions necessary. In 2023, however, this modality seems to have drastically decreased and was used in an extremely marginal way. This could reflect a return to the prevalence of in-person provisions with the end of health restrictions, a preference for direct contact or even organizational and technological limitations that did not allow the full integration of remote modalities in the long term.

This is also confirmed by the slight increase in the number of in-person health and social provisions per user (about 5%) which could reflect greater confidence in in-person visits as the pandemic has eased, leading patients to prefer traditional methods for treatment, and decreasing remote provisions.

Unlike psychiatric and psychological consults, psychosocial interventions (informative and psychoeducational interventions aimed at the person and/or the supporting family) show substantial stability in-person and a strong increase remotely (48.6%), signalling a different trajectory in the evolution of services. These interventions are particularly well suited to being delivered remotely, thanks to their more "dialogical" and less clinical nature and have instead found a new opportunity for growth in the digital world probably because they are more easily adaptable and less dependent on direct physical contact.

First in-person psychiatric consults remained stable while first in-person psychological visits increased (33.3% in 2023).

No first remote psychiatric or psychological consultations are being carried out. The increase in first in-person psychological visits and the stability of psychiatric visits indicate a constant attention to the reception and diagnosis phase, which remains strongly anchored to the in-person modality. The absence of first remote consults confirms a clear distinction between access channels: remote is used only for subsequent interventions and not for the start of the clinical path, probably for reasons of clinical accuracy and the need for direct observation.

LIMITATIONS OF THE STUDY

While the study provides an in-depth and detailed overview of changes in mental health services and healthcare resources in a sample of DMHs in Italy, there are several limitations that should be considered.

Firstly, the sample of DMHs involved cannot be considered representative of all Italian DMHs even though almost all Italian Regions were represented. Furthermore, those who agreed to participate may have had better internal organisation, enabling them to participate in research projects alongside their usual activities.

As the study is observational, the data presented can provide useful insights, but they do not allow us to fully understand the underlying causes of certain changes or the clinical and social contexts that could have influenced the observed trends.

Finally, the presented data do not take into consideration the geographical distribution of resources and psychiatric care. The situation in more remote regions or disadvantaged socioeconomic contexts may differ significantly from that in urban areas or richer regions. It is unclear whether this trend is distributed equally across the country.

CONCLUSION

The analysis of the data from the two-year period 2021-2023 offers a complex and evolving picture of mental health in our healthcare system. On the one hand, the structural stability of the territorial network is confirmed. However, important qualitative critical issues and operational processes emerge that require attention and in-depth analysis, regarding human resources, continuity of care and the effective accessibility of services.

The strengthening of the semi-residential offer through the increase in beds in DH, despite the reduction in facilities, highlights an organizational change oriented towards flexibility and personalization of care. At the same time, the contraction of non-hospital psychiatric RFs suggests a trend towards deinstitutionalization and a greater emphasis on territorial care models, although these data are only partially confirmed at national level.

On the staffing front, diversified dynamics are observed: while psychiatrists and nurses remain substantially stable, the number of psychologists and HSWs is increasing – probably in response to greater post-pandemic demand of support in daily activities – while the number of psychiatric rehabilitation technicians and social workers is decreasing, highlighting possible critical issues in the multidisciplinary management of the patient.

The data on clinical activity show contrasting signals: hospitalizations in GHPUs and psychiatric and psychological consultations at the Emergency Department are increasing, together with a worrying increase in self-harm. This draws attention to the increase in mental distress not intercepted promptly and to the growing pressure on emergency services, which are faced with increasingly complex and urgent situations.

At the same time, there has been a significant contraction in psychiatric and psychological consultations, both in-person and remotely, which raises questions about the continuity and adequacy of care. On the contrary, there has been a significant increase in nursing provisions and remote psychosocial interventions, signalling a partial reorganization of the therapeutic offer, which, if well structured, could contribute to a more proactive and integrated management of needs.

Finally, the increase in first psychological consults and users admitted into care, together with the decline in exclusively remote provisions, highlights a return to the centrality of physical presence in the therapeutic relationship and a gradual normalization of access to services after the health emergency.

Overall, the data indicate a system in transformation, which seeks a new balance between in-person and remote care, between hospitalization and territory, between emergency response and continuous care. The challenges that have emerged require a strategic vision and coordinated interventions, capable of strengthening the network of services, enhancing multidisciplinary work and promoting increasingly accessible, personalized and person-centred care.

While providing a detailed picture of the evolution of mental health services between 2021 and 2023, it is necessary to highlight some limitations. The analysis is based on aggregate data from a small and selected number of DMHs, neglecting possible regional and local inequalities that could influence access and quality of services and hide critical or virtuous situations at the local level. Furthermore, the absence of clinical outcome indicators limits the evaluation of the real effectiveness of the interventions. Finally, the lack of consideration of the point of view of users and caregivers reduces the understanding of the impact of changes on care pathways.

Considering what has emerged, it appears essential to promote a more integrated and multidimensional analysis of mental health services, capable of combining quantitative and qualitative data, territorial vision and centrality of the person, to guide strategic choices that are truly effective and sustainable over time.

Funding sources

This study was supported by funds of the National Center for Disease Prevention and Control (Centro Nazionale per la Prevenzione e il Controllo delle Malattie), CCM Programme 2021(CUP: I85F21003210001), Ministry of Health, Italy.

Acknowledgments

The Authors thank Franco Veltro for contributing to the realization of the study with valuable advice and Giuseppe Salamina for the continued support of the study.

Authors' contributions

AP, GM conceived and designed the study; LC, FM and AG wrote the manuscript. LC and FM analysed the data; EM, AP, CG, AG, LC and MF revised and edited the manuscript; MF and LC managed database. DDR, IC and NF supported the study in all stages. All Authors revised the manuscript for important intellectual content and agreed with this article's contents.

Conflict of interest statement

The Authors declare no competing interests.

Received on 11 June 2025.
Accepted on 11 September 2025.

The Italian Study Group of Departments of Mental Health (alphabetic order)

Francesca Aliberti (ASST Monza), Monica Arcellaschi (ASL 4 Chiavarese, Chiavari), Annamaria Armano (ASP Palermo), Miriam Battistel (ASST Rhodense), Antonello Bellomo (ASL Foggia), Sabrina Benedetti (USL Umbria 2 Terni), Anna Maria Beoni (AUSL Valle d'Aosta), Roberto Bezzi (ASL Verbano Cusio Ossola), Andrea Biondi (ASL Foggia), Giuseppe Biondi (ASST Bergamo Ovest), Sonia Biscontini (USL Umbria 2 Terni), Graziella Boi (ASL Cagliari), Paola Calò (ASL Lecce), Marco Capelli (ASL 4 Chiavarese), Alessandro Cecchini (ASL Roma 4), Rosanna Ceglie (ASL 5 Spezzino), Carola Celozzi (ASL Roma 4), Claudia Chiaranda (ASUGI Trieste), Silvia Chiesa (AUSL Piacenza), Massimo Clerici (ASST Monza), Martina Ciminiello (ASL Torino 3 e AOU San Luigi Gonzaga), Fabrizia Colmegna (ASST Monza), Caterina Corbascio (ASL Asti), Giulio Corrivetti (ASL Salerno), Patrizia D'Andrea (ASL Benevento), Andrea Danieli (AULSS8 Berica), Serafino De Giorgi (ASL Lecce), Carmen Di Brita (ASST Monza), Anna Di Lelio (AUSL Latina), Guido Di Sciascio (ASL Bari), Renato Durello (ASST Rhodense), Antonino Figura (ASL 5 Spezzino), Davide Gallicchio (AULSS8 Berica), Nicola Gambardella (ASP Messina), Giancarlo Gibertoni (AUSL Modena), Riccardo Gionfriddo (ASP Siracusa), Michele Giro (ASDAA Merano), Baldo La Sala (ASL Trapani), Gianmarco Latte (ASReM), Valeria La Torre (ASL Bari), Silvana Lerda (ASL Torino 4), Maria Patrizia Lorenzetti (USL Umbria 1 Perugia), Vincenzo Lucarini (AUSL Latina), Rosina Manfredi (ASP Catanzaro), Leonardo Meneghetti (AULSS8 Berica), Cristina Meneguzzi (ASFO Pordenone), Raffaele Minervini (ASST Rhodense), Lorena Miserotti (AUSL Piacenza), Maurizio Montalbano (ASP Palermo), Antonio Montuori (ASL Salerno), Emiliano Monzani (ASST Bergamo Ovest), Luca Morandi (ASST Bergamo Est), Elena Moro (ASFO Pordenone), Gaspare Motta (ASP Messina), Roberto Muratori (AUSL Bologna), Alba Natali (AUSL Imola), Giuseppe Nicolò (ASL Roma 5), Alessandro Norbedo (ASUGI Trieste Gorizia), Laura Novel (ASST Bergamo Est), Elisabetta Olivieri (ASL 5 Spezzino), Sebastiano Pace (ASL Modena), Elisabetta Pascolo Fabrici (ASUGI Trieste), Augusto Pasini (ASL Umbria 2 Terni), Pietro Papili (AUSL Imola), Verena Perwanger (ASDAA Merano), Francesca Picone (ASP Palermo), Carlo Pierotti (USL Umbria 1 Perugia), Ida Potena (ASL Teramo), Roberto Pusceddu (ASL Cagliari), Gianfranco Preiti (AUSL Bologna), Daniela Pucci (ASL Roma 5), Chiara Laura Riccardo (ASL Torino 3 e AOU San Luigi Gonzaga), Rossana Riolo (AULSS8 Berica), Massimo Rosa (ASL Torino 4), Michele Gabriele Rossi (ASP Catanzaro), Maria Concetta Russo (ASL Benevento), Maria Luisa Russo (ASL Napoli 1), Maria Giuseppa Santoro (ASL Bari), Domenico Semisa (ASL Bari), Giorgio Serio (ASP Palermo), Nicola Serroni (ASL Teramo), Paolo Severino (ASL 4 Chiavarese), Elisa Simonini (ASL 5 Spezzino), Fabrizio Starace (ASL Modena), Fulvio Tesolin (ASFO Pordenone), Concetta Tino (ASP Catanzaro), Pierfranco Trincas (ASUGI, Trieste), Mario Tolvo (ASL Napoli 1), Elisa Tomasella (ASFO Pordenone), Pietro Virgilio (ASL Trapani), Gaetano Vivona (ASL Trapani), Franco Veltro (ASReM), Gerald Weber (AUSL Imola), Enrico Zanalda (ASL Torino 3 e AOU San Luigi Gonzaga), Pierluigi Zanchi (ASST Bergamo Est).

REFERENCES

1. Pfefferbaum B, North CS. Mental health and the COVID-19 pandemic. N Engl J Med. 20206;383(6):510-2. doi: 10.1056/NEJMp2008017
2. World Health Organization. The impact of COVID-19 on mental, neurological and substance use services: results of a rapid assessment. Geneva: WHO; 2020.
3. Camoni L, Mirabella F, Medda E, Gigantesco A, Picardi A, Ferri M, Cascavilla I, Del Re D, D'Ippolito C, Veltro F, Scattoni ML, Starace F, Di Cesare M, Magliocchetti N, Calamandrei G e i referenti dei dipartimenti di salute mentale. Indagine sul funzionamento dei Dipartimenti di Salute Mentale durante la pandemia da SARS-CoV-2. Roma: Istituto Superiore di Sanità; 2022. (Rapporti ISTISAN, 22/21).
4. Ministero della Salute. Popolazione residente ASL, età e genere. Roma: Ministero della Salute; 2023. Available from: https://www.salute.gov.it/new/it/banche-dati/popolazione-residente-asl-eta-e-genere/.

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 259-268
DOI: 10.4415/ANN_25_04_04

Integrated care pathways for people with dementia in Italy: assessing key elements for quality of care in a nationwide evaluation

Domitilla Marconi[1], Sara M. Pani[2], Simone Salemme[3], Giacomo Lazzeri[1], Claudia Sardu[2], Patrizia Lorenzini[4], Francesco Della Gatta[4], Elisa Fabrizi[4], Ilaria Bacigalupo[4], Nicola Vanacore[4] and Guido Bellomo[4]

[1]Scuola Post Laurea di Sanità Pubblica, Università degli Studi di Siena, Siena, Italy
[2]Dipartimento di Scienze Mediche e Sanità Pubblica, Università di Cagliari, Monserrato, Italy
[3]Dipartimento di Scienze Biomediche, Metaboliche e Neuroscienze, Università di Modena e Reggio Emilia, Modena, Italy
[4]Centro Nazionale per la Prevenzione delle Malattie e la Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy

Abstract

Background. Person-centred care is central to global and European Union (EU) dementia strategies. This Italian study evaluates compliance of integrated care pathways (ICPs) with the National Guidance for People with Dementia (NGICPD).

Methods. ICPs obtained from national and official sources evaluated using a 43-item NGICPD-based checklist across three domains: framework, elements, and development.

Results. Thirty-nine ICPs were analysed. Fourteen of 21 regions and 30 of 110 Local Health Authorities developed an ICP. Mean scores were 23.5±7.9 for regional and 23.1±5.0 for LHA ICPs, showing low compliance with the NGICPD.

Conclusions. The study assessed national and regional ICPs for dissemination, guideline alignment, and implementation gaps, emphasizing the need for improved monitoring through key quality indicators.

Key words
- quality of care
- care pathways
- dementia
- health services
- primary health care

INTRODUCTION

The number of people aged ≥60 is increasing and expected to reach 2.1 billion by 2050, posing challenges due to non-communicable diseases (NCDs) and growing health needs [1]. Dementia is the seventh leading cause of death globally, responsible for 77% of the disease burden [2] and over 50 million people live with dementia globally [3]. In Italy, more than 1 million people live with dementia, with approximately 3 million family members, with reference to the Italian population in 2023 [4-6]. Around 900,000 people over 60 are diagnosed with mild cognitive impairment (MCI) [7]. Management strategies for this condition range from preventing the onset and delaying the progression of cognitive decline to timely diagnosis, treatment, and post-diagnostic support (https://www.who.int/news-room/fact-sheets/detail/dementia).

The rising burden of chronic illness and multimorbidity highlights the need for integrated, people-centred care. Shifting from disease-based to coordinated systems ensures continuity and comprehensive management. Integrated care pathways (ICPs) are key tools in this approach, supporting holistic care delivery [8-12].

While the World Health Organization (WHO) advocates for integrated dementia care pathways, many national plans lack guidance on developing, implementing, and monitoring person-centred care within health and social systems [3, 13].

Strengthening healthcare systems is key in managing long-term conditions and is a focus of several European initiatives. The EU4Health [14] is one of these initiatives and it aims to strengthen healthcare systems, improve crisis preparedness, and promote equitable access to high-quality care across Europe. The Joint Action Addressing Dementia and Health (JADEHealth) is one of the initiatives associated with the program, and one of its main activities is focused on improving care pathways for people with dementia (PwD) aiming to optimize in-

Address for correspondence: Elisa Fabrizi, 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: elisa.fabrizi@iss.it.

tegrated care models, considering challenges such as resources, accessibility, and sustainability.

According to the international recommendations, at national level, the Italian National Dementia Plan (NDP) underlined the importance of integrated care strategies outlining specific actions for ICPs development [15]. Despite progress in ICP development, research on their implementation and effectiveness remains limited [16, 17]. Most dementia care pathways share a framework focusing on communication, coordination, resource optimization, and person-centred, compassionate care [18]. A National Guidance on Integrated Care Pathway for PwD (NGICPD) developed by a dedicated group within the NDP supports Italian regions and Local Health Authorities (LHAs) in developing ICPs [19-21]. The need for Italian regions to develop their own ICPs is closely linked to the structure of the National Health Service (NHS). In this context, it is important to highlight that the Italian NHS has experienced a gradual decentralisation over the past three decades, with health-related powers being transferred to the regions and autonomous provinces (AP). This decentralisation has resulted in significant variability in health administration and service delivery across the country.

Monitoring and implementation of this guidance were included in the activities of the Italian Fund for Alzheimer's and other dementias conducted by the Dementia Observatory of the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) [22].

In line with our previous research [23], this study aims to assess ICPs' compliance with the NGICPD, identifying key areas for improvement in care and support for PwD, providing a more comprehensive approach to census and evaluation of the ICPs for PwD.

METHODS

Data collection

According to the list of Italian regions, AP, and LHAs active in 2023 [24, 25], we identified the official available ICPs for dementia through: i) institutional websites of regions, APs, and LHAs as listed by the Ministry of Health [24, 25]; ii) email requests sent from the Dementia Observatory's institutional account of the ISS to all official LHAs email addresses provided by the Ministry of Health; iii) a previous survey [26] conducted in 2022 among Centers for Cognitive Disorders and Dementia (CCDDs); iv) direct contact with regional dementia representatives to ensure completeness of the collected documentation. Data collection was conducted between July and December 2023, and documents meeting the following exclusion criteria were excluded: (a) duplicates; (b) drafts; (c) outdated documents with a more recent version available; (d) documents without operational instructions; and (e) documents produced by inactive LHAs in 2023.

Documents belonging to class (c) were excluded to ensure the analysis reflects current practices, as updated versions of the same ICPs were available. Documents lacking operational instructions (d) were excluded because they were primarily descriptive or conceptual, lacking clear implementation details (e.g., procedures, roles, timelines, and tools for care coordination). These elements were considered essential for evaluating compliance with the NGICPD. ICPs from LHAs inactive in 2023 (e) were excluded because they did not reflect current service delivery. These criteria were applied to ensure the inclusion of only currently adopted and operational ICPs. Documents from regions with only one LHA (Molise, AP Bolzano, AP Trento, Valle d'Aosta) were considered regional.

Data analysis

ICPs included in the analysis were evaluated using a bespoke checklist (*Table 1*) developed in 2019 [23] according to the NGICPD and consisting of 3 domains [17] organised into items (total score from 0 to 43; score 0-1 depending on the absence-presence of the item). Domain 1 related to the reference framework, consisting of 15 items (total score from 0 to 15); domain 2, addressing elements related to the integrated management and the adoption of a health information

Table 1
Quality checklist used for the evaluation of the regional and local ICPs for dementia

CHECKLIST
1. Reference framework (15 items)
a. Demographic analysis of the target population
b. Scientific literature or guidelines supporting ICPs
c. Reference legislation (national and/or regional)
d. Identification of the ordering party
e. Presence of a written mandate for the promoting subject
f. Presence of a formal act of appointment of the coordination group
g. Multidisciplinary of the working group
h. Multi-professionalism of the working group
i. Involvement of general practitioners in the working group
j. Involvement of patient representatives and/or relatives in the working group
k. Identification of channels and documents useful for disseminating the ICP
l. Explication of internal dissemination methods (institutions)
m. Explication of the external diffusion methods (population)
n. Presence of date of drafting
o. Presence of revision date and/or update date
2. Elements of the ICP and integrated management (14 items)
a. Active involvement of patients and families
b. Involvement of all the services listed
c. Involvement of all the professionals listed
d. Contact person of the ICP (professional, structure or service) complete with telephone contact
e. Identification of the pivotal role of the general practitioner
f. External communication system (professional-patients/family members)
g. Internal communication system (professional-professional)

Continues

Table 1
Continued

CHECKLIST
h. Development of a HIS
i. Professionals engaged in multiple services within the network (connectors)
j. Counselling activities at the structures and services involved in the network
k. Adoption of guidelines and/or operational protocols useful for formalizing the network
l. ICP facilitators (institutional tables or technical groups)
m. ICP flow diagram
n. ICP matrix representation
3. Construction of the ICP (regional/LHA) (14 items)
a. Explanation of the ICP type
b. Detection of the characteristics of the problem and the specific needs of the local context
c. Recognition of existing methods for managing and taking charge of people with cognitive disorders
d. Definition of the timeline
e. Identification of healthcare goals and expected outcomes
f. Identification of areas of change and reorganization
g. Testing of the reference path (pilot study)
h. Definition and implementation of the ICP
i. Monitoring and evaluation of the ICP
k. Presence of qualitative indicators
l. Presence of structure indicators
m. Presence of process indicators
n. Presence of outcome indicators
o. Presence of economic-administrative indicators
TOT (43 items)

ICP: integrated care pathway; LHA: Local Health Authority; HIS: health information system.

system (HIS), consisting of 14 items (total score from 0 to 14); domain 3, addressing elements related to ICP development and monitoring (regional/LHA) consisting of 14 items (total score from 0 to 14). A total score summing those of the three domains was calculated.

The item "1.c. Presence of the analysis of the local legislation" was applied to the ICPs of the LHAs referring to the regional legislation and the regional ICP, if available.

Our analysis included only ICPs published after the NGICPD (5th July 2017). Two independent reviewers (DM and SMP) assessed ICP compliance with NGICPD; a third researcher (GB) resolving conflicts.

Descriptive analysis was performed by calculating the mean and standard deviation of total and partial score. ICPs were rated on a scale from very low to excellent (1-13: very low; 14-26: low; 27-35: moderate; 36-43: excellent). Scores of regional and LHA ICPs were compared using the Wilcoxon test.

The clarity of the documents was evaluated by measuring the agreement between the assessments performed by the two independent reviewers, defined as interrater reliability. As a measure of reliability, we calculated the intra-class coefficient (ICC) and the 95% confidence interval based on a single rating (k=2), absolute-agreement, and 2-way random-effects model. Moreover, we tested whether the ICC value was different from zero using the F test. A value lower than 0.05 was considered statistically significant. We categorized ICC values as follows: poor ($\text{ICC}<0.5$), moderate ($0.5\leq\text{ICC}<0.75$), good ($0.75\leq\text{ICC}<0.9$), and excellent ($\text{ICC}\geq0.9$) [27].

Statistical analysis was performed using STATA 17.0 (StataCorp, College Station, Texas, USA), and graphs were generated using Microsoft Excel.

We analysed the presence of the following items addressing the availability of a dementia-specific data collection system, the local context analysis, and the monitoring indicators system: 2h. Reference to a HIS, establishing a system for collecting, managing, and sharing clinical and administrative data to support coordinated dementia care; 3b. Detection of the characteristics of the problem and local needs, mapping epidemiology, resources, and service gaps to tailor the ICP; 3c. Recognition of existing methods for managing people with cognitive disorders, integrating current practices and protocols to ensure continuity of care; 3i. Monitoring and evaluation of local ICP, with structured procedures to assess implementation, effectiveness, and areas for improvement; 3k. Presence of qualitative indicators, capturing non-numerical aspects such as patient and caregiver satisfaction and person-centred care; 3l. Presence of structure indicators, describing staffing, facilities, and resources needed for effective pathway delivery; 3m. Presence of process indicators, measuring care delivery operations, adherence to guidelines, and coordination; 3n. Presence of outcome indicators, evaluating effects on patients and caregivers, including functional outcomes and quality of life; 3o. Presence of economic-administrative indicators, assessing costs, resource use, and administrative efficiency for pathway sustainability.

RESULTS

We collected 87 official ICPs, 29 developed by regions or APs and 58 by LHAs. After applying the predefined exclusion criteria, we selected 15 regional and 32 local documents. We excluded 8 ICPs (n=4 regional ICPs; n=4 LHAs ICPs) published before the date of publication of the NGICPD (5th July 2017). We analysed 11 regional ICPs and 28 ICPs of the LHAs. The flowchart (*Figure 1*) shows the identification, screening, and inclusion phases. Among regions and APs, 66.6% (14/21) developed an ICP, whereas among LHAs 27% (30/110) developed an ICP.

ICPs of regions and LHAs were evaluated separately. *Figure 2* shows the score for each domain of the checklist for each included ICP. Overall, no ICP achieved the maximum score. Among the analysed ICPs, 11 ICPs achieved a moderate score (n=4 regional; n=7 LHAs), 26 achieved a low score (n=6 regional; n=20 LHAs) and 2 a very low score (n=1 regional; n=1 LHAs) (*Supplementary Table 1 available online*). Regional ICPs achieved a mean total score (MS) of 23.5 (standard deviation,

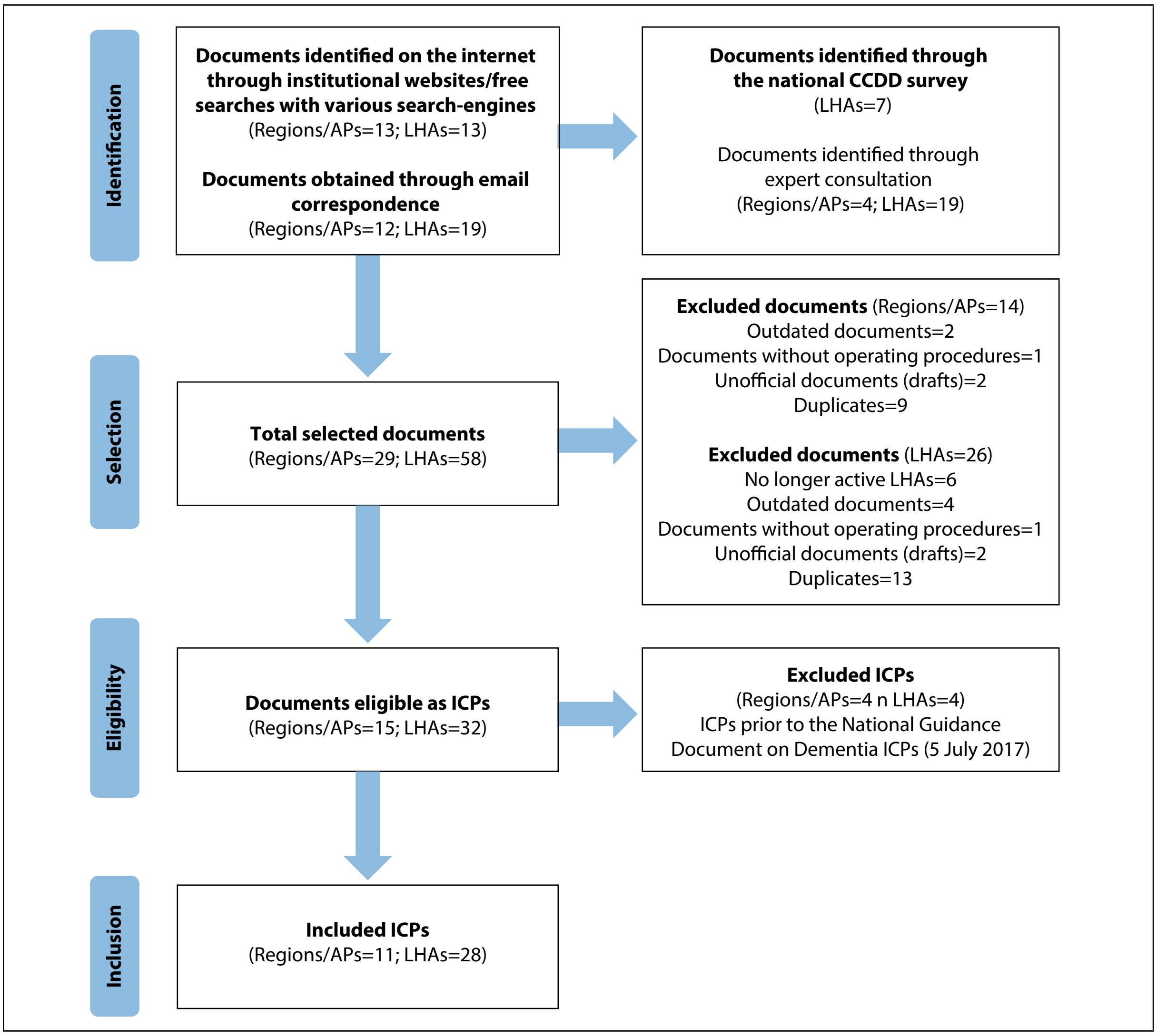


Figure 1
Flowchart of identification, screening, and inclusion phases of ICPs selection.
ICP: integrated care pathway; AP: autonomous province; LHA: Local Health Authority; NGICPD: Italian Guidance on Integrated Care Pathway for People with Dementia; CCDD: Centers for Cognitive Disorders and Dementia.

SD=7.9), with scores ranging from a minimum of 10 (i.e, Umbria) to a maximum of 33 (i.e., Lombardia). ICPs of LHAs obtained a MS of 23.1 (SD= 5.0), with scores ranging from a minimum of 9 (i.e., Brindisi) to a maximum of 31 (i.e., Napoli 2). We observed low compliance with NGICPD and high variability between scores. Domain 3 showed the worst compliance with a MS of 5.8 (SD=2.0) for regional ICPs and a MS of 5.1 (SD=1.3) for ICPs of LHAs. The average scores for domain 1 were 9.1 (SD=4.1) for ICPs of regions and 9.1 (SD=2.8) for LHAs. For domain 2, the average scores were 8.6 (SD=3.4) and 8.9 (SD=2.5). No significant differences were observed between the mean scores of ICPs of LHAs and regions, both globally (p=0.639) and for each domain (domain 1 p=0.950, domain 2 p=0.849, domain 3 p=0.201).

The analysis of the interrater reliability showed an excellent agreement on regional ICPs total scores (ICC of 0.91, 95% CI 0.70-0.98, p<0.001). We observed an excellent agreement on domain 1 scores (ICC 0.95, 95% CI 0.82-0.99, p<0.001), and a good agreement on domain 2 (ICC 0.84, 95% CI 0.52-0.96, p<0.001) and domain 3 (ICC 0.79, 95% CI 0.41-0.94, p=0.001) scores. Similarly, the interrater reliability analysis of ICPs of LHAs evaluation showed moderate agreement on total (ICC 0.73, 95% CI 0.50-0.87, p<0.001) and domain 1 (ICC 0.70, 95% CI 0.42-0.86, p<0.001) scores, good agreement on domain 2 (ICC 0.80, 95% CI 0.49-0.92, p<0.001) scores, and poor agreement on domain 3 (ICC 0.27, 95% CI 0.00-0.57, p=0.071) scores (*Supplementary Figure 1 available online*).

The in-depth analysis (*Table 2*) showed that the development of a HIS was included in 5/11 (45%) of regional and 12/28 (43%) of ICPs of LHAs. The presence of a monitoring system was found in 8/11 (73%) of regional and 25/28 (89%) of ICPs of the LHAs, with the process indicators in 25/28 (89%) and 9/11 (82%) of ICPs of regions or LHAs, respectively, and the outcome indicators

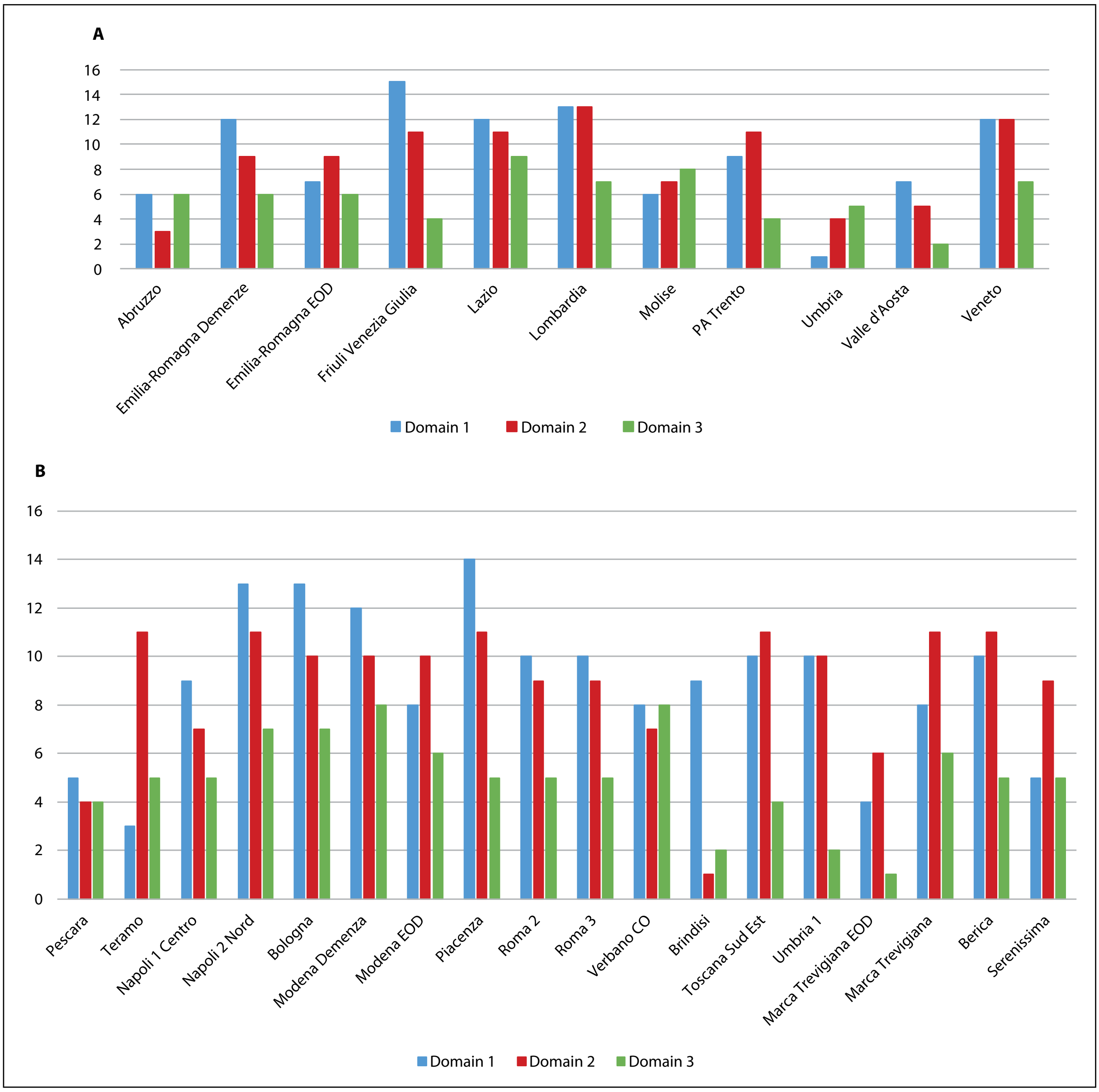


Figure 2

Score of each domain of the checklist for regional ICPs (panel A) and LHAs ICPs (panel B).
ICPs: integrated care pathways; EOD: early onset dementia; LHA: Local Health Authority.

in 19/28 (68%) of the regional and 9/11 (82%) of the ICPs of the LHAs. Instead, only 3/11 (27%) of regional and 2/28 (7%) of ICPs of LHAs included the structure indicators and neither of the ICPs of regions nor LHAs provided economic-administrative indicators.

DISCUSSION

Main findings of this study

This national case study assessed the formal characteristics, quality and compliance of the ICPs for PwD that are currently available in Italy (11 regional and 28 LHAs) with respect to the NGICPD, which summarise the instructions reported in the NDP about integrated care for dementia. This is in line with international recommendations about dementia care at a national level. Through this evaluation, the findings provide insights into the quality of dementia care and integrated management across the country, as reflected in the structure and content of the ICPs. In Italy, the low number of ICPs poses a significant challenge in planning and managing interventions for PwD. In spite of an increase in documents since the last assessment of 2019 (11 new ICPs), more than 30% of the Italian regions still do not have an ICP a figure that rises to more than 70% at the LHAs level. Despite the NDP, published in 2015, underlines the importance of developing ICPs for PwD, the findings of this study highlight gaps in local ICP availability and the need for further definition and implementation efforts. Additionally, access to these documents remains a challenge, as a significant portion is not available online (27% of regional ICPs and 63% of ICPs from LHAs)

Table 2
Overview of ICP compliance with selected checklist items in regions and LHAs

Item	2h	3b	3c	3i	3k	3l	3m	3n	3o
Regional ICP									
Abruzzo	✓	✓	✓	-	✓	-	✓	✓	-
Emilia-Romagna	-	-	-	✓	✓	✓	✓	✓	-
Emilia-Romagna (EOD)	-	✓	✓	✓	-	-	✓	✓	-
Friuli Venezia Giulia	-	-	✓	✓	✓	-	-	✓	-
Lazio	-	✓	✓	✓	-	✓	✓	✓	-
Lombardia	✓	✓	✓	✓	-	-	✓	✓	-
Molise	✓	✓	✓	-	✓	✓	✓	✓	-
AP Trento	✓	-	✓	✓	✓	-	✓	-	-
Umbria	-	✓	-	-	-	-	✓	✓	-
Valle D'Aosta	-	-	-	✓	✓	-	-	-	-
Veneto	✓	-	✓	✓	✓	-	✓	✓	-
ICP of LHAs									
Pescara	-	-	-	✓	-	-	✓	✓	-
Teramo	✓	✓	✓	✓	-	-	✓	✓	-
Napoli 1 Centro	✓	✓	-	✓	-	-	✓	✓	-
Napoli 2 Nord	✓	-	✓	✓	✓	-	✓	✓	-
Roma 2	✓	✓	✓	-	-	-	✓	✓	-
Roma 3	-	-	-	✓	✓	-	✓	✓	-
Verbano-Cusio-Ossola	-	-	✓	✓	-	✓	✓	-	-
Brindisi	-	-	✓	-	-	-	-	-	-
Toscana Sud-Est	-	-	-	✓	-	-	✓	✓	-
Umbria 1	-	-	-	-	✓	-	-	-	-
Bologna	-	-	✓	✓	-	-	✓	✓	-
Modena	-	✓	✓	✓	✓	-	✓	✓	-
Modena (EOD)	-	-	-	✓	✓	-	✓	✓	-
Piacenza	-	-	-	✓	✓	-	✓	✓	-
Parma	✓	-	✓	✓	✓	-	✓	✓	-
Ferrara	✓	-	-	✓	✓	-	✓	✓	-
Reggio Emilia	-	-	✓	✓	✓	-	✓	✓	-
Imola	-	-	-	✓	✓	-	✓	✓	-
Romagna	-	-	-	✓	-	-	✓	✓	-
Dolomiti	✓	-	✓	✓	-	-	✓	✓	-
Marca Trevigiana	✓	-	-	✓	✓	-	✓	-	-
Marca Trevigiana (EOD)	-	-	-	✓	✓	-	-	-	-
Serenissima	-	-	✓	✓	-	-	✓	✓	-
Veneto Orientale	✓	-	-	✓	✓	-	✓	-	-
Polesana	-	-	-	✓	✓	✓	✓	-	-
Euganea	✓	-	-	✓	✓	-	✓	-	-
Pedemontana	✓	-	-	✓	✓	-	✓	-	-
Berica	✓	-	-	✓	-	-	✓	✓	-

Focus on the presence (✓)/absence (-) of specific items of the checklist in the ICP of regions and LHAs. Item: 2h. Development of a HIS; 3b. Detection of the characteristics of the problem and the specific needs of the local context; 3c. Recognition of existing methods for managing and taking charge of people with cognitive disorders; 3i. Monitoring and evaluation of the ICP; 3k. Presence of qualitative indicators; 3l. Presence of structure indicators; 3m. Presence of process indicators; 3n. Presence of outcome indicators; 3o. Presence of economic-administrative indicators.
AP: autonomous province; ICP: integrated care pathway; LHA: Local Health Authority; HIS: health information system; EOD: early onset dementia.

creating substantial barriers to their dissemination and limiting their practical implementation [6].

A major concern is the fragmentation of ICP availability across Italy. According to the results from this study, out of the estimated 2 million PwD/MCI in Italy, only about 30% of them can benefit from an ICP. When analysing data for the 3 main macro-areas, in the North and Center of Italy around 30% of PwD and MCI can benefit from an ICP, while in the South and the islands, only about the 15% leading to significant inequalities in dementia care across different regions [6].

This may significantly impact equity in access to quality dementia services across regions, leading to disparities in availability and care. Literature shows that social, economic, and geographical inequalities often worsen outcomes, including faster disease progression and higher institutionalization risk [28-32].

As for quality of collected ICPs, the in-depth assessment revealed generally low compliance with the NGICPD. Only 12 ICPs (5 regional and 7 from LHAs) demonstrated moderate adherence to the guidelines, and none reached the highest compliance category. A key finding of this assessment is related to the presence of a reference to a HIS in approximately 50% of ICPs. HIS plays a fundamental role in the economic and financial management of healthcare services, enabling standardized data collection for monitoring, evaluating care effectiveness, ensuring appropriateness, and promoting equity. In this sense, integrating a reliable, dementia-specific HIS is essential for enhancing the quality and efficiency of care, as recommended by national guidelines on the use of information systems for dementia [33]. This objective aligns with the National Recovery and Resilience Plan, NRRP (Piano Nazionale di Ripresa e Resilienza, PNRR) and Ministerial Decree 77/2022, both prioritising innovation and digital transformation to enhance governance, data management, decision-making, security, and patient care [34-37].

Lastly, a critical issue identified by the quality assessment is specifically linked to the absence of economic and administrative indicators in all the collected ICPs, and the low presence of structure indicators. The lack of these indicators may have important implications in monitoring use and allocation of resources, also interfering with the organization of the dedicated services. Other critical issues identified in the analysis is related to the process of identification of the specific needs within the local context. Despite understanding the specific needs of the local context is crucial for better plan assistance, only 14% of ICPs of LHAs assessed the health profile of the local context and less than 50% reported data on the existing care strategies for PwD in their ICPs.

What is already known on this topic

The Global Action Plan on Dementia emphasises in the action areas 1 (dementia as a public health priority) and 4 (dementia diagnosis, treatment, care and support) the need to establish effective and coordinated care pathways within the health and social care system, including long-term care, also underlining prioritising person-centred care for PwD [3]. WHO highlights the importance of national guidelines, standards, and protocols as prerequisites for implementing dementia care pathways, stressing the risk that components of the dementia care pathway may be missing, under-recognized, or under-resourced in the absence of protocols [13].

Several European initiatives [14] aim to improve healthcare by enhancing care for chronic diseases, focusing on resilience, equity, access to quality and promotion of ICPs. Despite this, scientific literature about ICPs is still scarce with most of the existing evidence on dementia care pathways focusing more on assessment and post-diagnostic support, with less attention to care management and community-based integrated care [38].

Integrating the services within a pathway could promote a continuum of care from diagnosis to end-of-life care, allowing PwD to continue living at home with better health outcomes, such as quality of life and lower mortality risk [39, 40].

Investigating the effectiveness of ICPs is crucial for improving care for PwD. One study examined a care pathway for agitation and aggression, which included standardized assessments, non-pharmacological interventions, and a medication algorithm [41]. PwD following this pathway had higher early hospital discharge rates, less psychotropic polypharmacy, and a reduced fall risk. Although preliminary, the study highlights the need to evaluate care pathways to assess their impact and effectiveness. Other studies suggest that comprehensive, multidisciplinary care and individualized dementia care plans can reduce hospital and long-term care facility admissions, saving costs and enabling PwD to stay in their communities [42-44].

In this regard, it is essential to emphasize the key role of professionals involved, as the effective delivery of care depends on their expertise, collaboration, and ability to provide coordinated support. The absence of certain professional figures in specific contexts, the lack of adequate training for healthcare workers, and the absence of a truly integrated approach can lead to significant challenges in the definition, development, and implementation of ICPs, undermining their ability to effectively address the complex needs of PwD and with important consequences for the coordinated management of the disease and the continuity of care.

What this study adds

This study contributes to the ongoing discussion on dementia care focusing on the complexities surrounding the definition and implementation of ICPs, emphasizing both the challenges and opportunities they present. Through a structured assessment based on the NGICPD, the study highlights key gaps in ICP development, monitoring, and coverage, as well as regional disparities in access, reflecting the quality of dementia care and integrated management at both regional and local levels. The findings underscore the need for more standardized, accessible, and operationally detailed ICPs to support effective and equitable care for PwD, based on sustainable person-centred models. By evaluating the quality criteria outlined in the NGICPD, the study lays the groundwork for critical discussions about the key obstacles in dementia care and foster innovation, collaboration, and policy advancements to improve outcomes for PwD and their families. One of the key findings of this research is the significant variability in adherence to the NGICPD, revealing major gaps in ICP monitoring, population coverage, and the inclusion of PwD in these care pathways. Additionally, the study highlights regional disparities in access to care, further emphasizing the need for a standardized yet adaptable approach to dementia care at the national level.

To address these issues, the study proposes a structured framework for future initiatives, with a strong focus on conducting systematic censuses and regularly updating ICPs. This would ensure that dementia care remains dynamic, responsive, and aligned with the evolving needs of PwD and their caregivers. Moreover, the study underscores the importance of continuous improvement through evidence-based strategies, tailored interventions to address local challenges, including cultural differences, healthcare infrastructure, and community resources, and enhanced coordination among healthcare professionals, policymakers, and local communities. Ultimately, this initiative seeks to support the establishment of a more responsive, inclusive, and sustainable model of dementia care by fostering the bridging of the existing gaps, favouring the enhancement of the service delivery, and creating the ground for a more equitable healthcare system capable of supporting PwD and their families with the highest standards of care.

Another important insight emerging from the study is the strong connection between guidelines and ICPs since the guidelines play a pivotal role in shaping clinical reasoning throughout the patient's care pathway. In Italy, this becomes particularly relevant in light of the recent publication of the national guideline on the diagnosis and treatment of dementia and MCI, which further emphasizes the need to develop and update ICPs in accordance with its recommendations [45].

Limitations of this study

A limitation of our assessment is the binary checklist format, which captures only the presence or absence of items, missing qualitative differences. Though suitable for our objectives, it may not reflect ICP complexity. A detailed scoring system or qualitative criteria could offer a more comprehensive evaluation.

Funding

The project was carried out with the technical and financial support of the Italian Ministry of Health, through the National Fund for Alzheimer's and other Dementias, which provides targeted resources to support initiatives, research, and activities related to dementia.

Acknowledgments

We thank the Italian Ministry of Health for the support and the Permanent Table of the NDP Study Group, the CCDDs Study Group, regional delegates, and the general directorate of the Italian LHAs for their support.

Authors' contributions

NV and GB conceived the study and supervised the overall work. DM, SMP, PL, IB and GB contributed to the data collection and analysis. DM, SMP, SS, PL, FDG, EF and GB drafted the first draft of the manuscript and created tables and figures. DM, SMP, SS, GL, CS, PL, FDG, EF, IB, NV and GB critically reviewed and edited the manuscript, tables and figures. All Authors have revised the manuscript and approved its final version.

Competing interests

No competing interests or conflicts to declare.

Received on 29 May 2025.
Accepted on 19 September 2025.

REFERENCES

1. World Health Organization. Global health estimates. WHO: Geneva; 2019. Available from: https://www.who.int/data/global-health-estimates.
2. World Health Organization. Global health observatory. WHO: Geneva; 2024. Available from: https://www.who.int/data/gho.
3. World Health Organization. Global action plan on the public health response to dementia 2017-2025. WHO: Geneva; 2017.
4. Bacigalupo I, Mayer F, Lacorte E, et al. A systematic review and meta-analysis on the prevalence of dementia in Europe: estimates from the highest-quality studies adopting the DSM IV diagnostic criteria. Bruni AC, editor. J Alzheimer's Dis. 2018;12;66(4):1471-81.
5. Istituto Nazionale di Statistica. Popolazione e famiglie. Roma: Istat; 2023. Available from: https://www.istat.it/storage/ASI/2023/capitoli/C03.pdf.
6. Istituto Superiore di Sanità, Osservatorio Demenze. Progetto: fondo per l'Alzheimer e le demenze. Le attività dell'Osservatorio Demenze dell'Istituto Superiore di Sanità (anni 2021-2023). Report Nazionale. Roma: ISS; 2023. Available from: https://www.demenze.it/documenti/schede/report_nazionale.pdf.
7. Sachdev PS, Lipnicki DM, Kochan NA, Crawford JD, Thalamuthu A, Andrews G, Brayne C, Matthews FE, Stephan BC, Lipton RB, Katz MJ, Ritchie K, Carrière I, Ancelin ML, Lam LC, Wong CH, Fung AW, Guaita A, Vaccaro R, Davin A, Ganguli M, Dodge H, Hughes T, Anstey KJ, Cherbuin N, Butterworth P, Ng TP, Gao Q, Reppermund S, Brodaty H, Schupf N, Manly J, Stern Y, Lobo A, Lopez-Anton R, Santabárbara J; Cohort Studies of Memory in an International Consortium (COSMIC). The Prevalence of mild cognitive impairment in diverse geographical and ethnocultural regions: the COSMIC collaboration. PLoS One. 2015;5;10(11):e0142388.
8. Monaco A, Palmer K, Marengoni A, Maggi S, Hassan TA, Donde S. Integrated care for the management of ageing-related non-communicable diseases: current gaps and future directions. Aging Clin Exp Res. 2020;32(7):1353-8.

9. Schrijvers G, Hoorn A van, Huiskes N. The care pathway concept: concepts and theories: an introduction. Int J Integr Care. 2012;18;12(6).
10. World Health Organization. Global strategy and action plan on ageing and health. Geneva: WHO; 2017. Available from: https://www.who.int/publications/i/item/9789241513500.
11. World Health Organization. Integrating palliative care and symptom relief into primary health care: a WHO guide for planners, implementers and managers. Geneva: WHO; 2018. Available from: https://www.who.int/publications/i/item/integrating-palliative-care-and-symptom-relief-into-primary-health-care.
12. World Health Organization. Improving the quality of health services: tools and resources. Turning recommendations into practice. Geneva: WHO; 2018. Available from: https://www.who.int/publications/i/item/9789241515085.
13. World Health Organization. Global status report on the public health response to dementia. Geneva: WHO; 2021. Available from: https://www.who.int/publications/i/item/9789240033245.
14. European Commission. EU4Health programme 2021-2027. A vision for a healthier European Union. Brussels: EC; 2021. Available from: https://health.ec.europa.eu/funding/eu4health-programme-2021-2027-vision-healthier-european-union_en.
15. Presidenza del Consiglio dei Ministri – Conferenza unificata. Piano nazionale demenze. Strategie per la promozione ed il miglioramento della qualità e dell'appropriatezza degli interventi assistenziali nel settore delle demenze. Roma: PdCM; 2014. Available from: https://www.trovanorme.salute.gov.it/norme/dettaglioAtto?id=50972.
16. Di Fiandra T, Canevelli M, Di Pucchio A, Vanacore N. The Italian Dementia National Plan. Ann Ist Super Sanità. 2015;51(4):261-4.
17. Ministero della Salute. Tavolo per il monitoraggio del recepimento ed implementazione del piano nazionale demenze. Linee di indirizzo nazionali sui percorsi diagnostico terapeutici assistenziali per le demenze. Roma: Ministero della Salute; 2017. Available from: https://www.salute.gov.it/imgs/C_17_pubblicazioni_3361_allegato.pdf.
18. Ministero della Salute. Tavolo permanente sulle demenze. Roma: Ministero della Salute; 2022. Available from: https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2022&codLeg=88937&parte=1&serie=null.
19. Ancidoni A, Sciancalepore F, Bacigalupo I, et al. The Italian fund for Alzheimer's and other dementias: strategies and objectives to face the dementia challenge. Ann Ist Super Sanità. 2022;58(3):192-6.
20. Sullivan DO, Mannix M, Timmons S. Integrated care pathways and care bundles for dementia in acute care: concept versus evidence. Am J Alzheimers Dis Other Demen. 2017;32(4):189-93. doi: 10.1177/1533317517698791
21. Draper B, Low LF, Brodaty H. Integrated care for adults with dementia and other cognitive disorders. Int Rev Psychiatry. 2018;30(6):272-91. doi: 10.1080/09540261.2018.1564021
22. Riquelme-Galindo J, Lillo-Crespo M. Designing Dementia care pathways to transform non dementia-friendly hospitals: Scoping Review. Int J Environ Res Public Health. 2021;18(17):9296. doi: 10.3390/ijerph18179296
23. Gervasi G, Bellomo G, Mayer F, Zaccaria V, Bacigalupo I, Lacorte E, Canevelli M, Corbo M, Di Fiandra T, Vanacore N. Integrated care pathways on dementia in Italy: a survey testing the compliance with a national guidance. Neurol Sci. 2020;41(4):917-24.
24. Ministero della Salute. Regioni e province autonome. Roma: Ministero della Salute; 2025. Available from: https://www.salute.gov.it/new/it/tema/ssn-principi-e-organizzazione/.
25. Ministero della Salute. Elenco aziende sanitarie locali e strutture di ricovero. Roma: Ministero della Salute; 2024. Available from: https://www.salute.gov.it/portale/documentazione/p6_2_8_1_1.jsp?id=13.
26. Bacigalupo I, Giaquinto F, Salvi E, et al. A new national survey of centers for cognitive disorders and dementias in Italy. Neurol Sci. 2024;45(2):525-38.
27. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016;15(2):155-63.
28. Wu YT, Clare L, Jones IR, Martyr A, Nelis SM, Quinn C, Victor CR, Lamont RA, Rippon I, Matthews FE; Improving the experience of Dementia and Enhancing Active Life (IDEAL) study. Inequalities in living well with dementia. The impact of deprivation on well-being, quality of life and life satisfaction: Results from the improving the experience of dementia and enhancing active life study. Int J Geriatr Psychiatry. 2018;33(12):1736-42.
29. Watson J, Darlington-Pollock F, Green M, Giebel C, Akpan A. The impact of demographic, socio-economic and geographic factors on mortality risk among people living with dementia in England (2002-2016). Int J Environ Res Public Health. 2021;18(24):13405.
30. Watson J, Giebel C, Green M, Darlington-Pollock F, Akpan A. Use of routine and cohort data globally in exploring dementia care pathways and inequalities: A systematic review. Int J Geriatr Psychiatry. 2021;36(2):252-70.
31. Cooper C, Lodwick R, Walters K, Raine R, Manthorpe J, Iliffe S, Petersen I. Inequalities in receipt of mental and physical healthcare in people with dementia in the UK. Age Ageing. 2017;46(3):393-400.
32. Watson J, Green MA, Giebel C, Akpan A. Identifying longitudinal healthcare pathways and subsequent mortality for people living with dementia in England: an observational group-based trajectory analysis. BMC Geriatr. 2024;24(1):150.
33. Ministero della Salute. Tavolo per il monitoraggio del recepimento ed implementazione del piano nazionale demenze. Linee di indirizzo nazionali sull'uso dei sistemi informativi per caratterizzare il fenomeno delle demenze. Roma: Ministero della Salute; 2017. Available from: https://www.salute.gov.it/imgs/C_17_pubblicazioni_3362_allegato.pdf.
34. Presidenza del Consiglio dei Ministri. Piano Nazionale di Ripresa e Resilienza (PNRR). Roma: PdCM; 2021. Available from: https://www.governo.it/sites/governo.it/files/PNRR.pdf.
35. European Commission. Italy's Recovery and Resilience Plan. Brussels: EC; 2023. Available from: https://commission.europa.eu/business-economy-euro/economic-recovery/recovery-and-resilience-facility/country-pages/italys-recovery-and-resilience-plan_en.
36. Adduci A, de Belvis AG, Fattore G, Solipaca A, Ricciardi W, Maresso A, Scarpetti G. Ministerial Decree 77/2022 and the development of new organizational models for primary care. Bruxelles: Health Systems and Policy Monitor (HSPM) – European Observatory on health systems and policies; 2022. Available from: https://eurohealthobservatory.who.int/monitors/health-systems-monitor/updates/hspm/italy-2014/ministerial-decree-77-2022-and-the-development-of-new-organizational-models-for-primary-care.
37. Ministero della Salute. Decreto 23 maggio 2022, n. 77. Regolamento recante la definizione di modelli e standard

per lo sviluppo dell'assistenza territoriale nel Servizio Sanitario Nazionale. Gazzetta Ufficiale – Serie Generale n. 144, 22 giugno 2022. Available from: https://www.gazzettaufficiale.it/eli/id/2022/06/22/22G00085/sg.

38. Saragosa M, MacEachern E, Chiu M, et al. Mapping the evidence on dementia care pathways - A scoping review. BMC Geriatr. 2024;24(1):690. doi: 10.1186/s12877-024-05250-4
39. Olsen C, Pedersen I, Bergland A, et al. Differences in quality of life in home-dwelling persons and nursing home residents with dementia – a cross-sectional study. BMC Geriatr. 2016;16(1):137.
40. Delgado J, Evans PH, Gray DP, Sidaway-Lee K, Allan L, Clare L, Ballard C, Masoli J, Valderas JM, Melzer D. Continuity of GP care for patients with dementia: impact on prescribing and the health of patients. Br J Gen Pract. 2022;72(715):e91-8.
41. Kumar S, Shanbhag A, Burhan AM, Colman S, Gerretsen P, Graff-Guerrero A, Kim D, Ma C, Mulsant BH, Pollock BG, Woo VL, Davies SJC, Rajji TK. Impact of standardizing care for agitation in dementia using an integrated care pathway on an inpatient geriatric psychiatry unit. International psychogeriatrics. 2022;34(10):919-28. doi: 10.1017/S104161022200032
42. Yorganci E, Stewart R, Sampson EL, Sleeman KE. Patterns of unplanned hospital admissions among people with dementia: from diagnosis to the end of life. Age Ageing. 2022;51(5).
43. Knapp M, Chua KC, Broadbent M, et al. Predictors of care home and hospital admissions and their costs for older people with Alzheimer's disease: findings from a large London case register. BMJ Open. 201618;6(11):e013591.
44. Jennings LA, Laffan AM, Schlissel AC, et al. Health care utilization and cost outcomes of a comprehensive dementia care program for medicare beneficiaries. JAMA Intern Med. 2019;179(2):161.
45. Fabrizi E, Ancidoni A, Locuratolo N, et al. The Italian Guideline on diagnosis and treatment of dementia and mild cognitive impairment. Age Ageing. 2024;53(11):afae250. doi: 10.1093/ageing/afae250

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 269-276
DOI: 10.4415/ANN_25_04_05

EpiCHILD assessment tool: identifying exposure to witnessed violence in children and adolescents

Anna Carannante[1], Marco Giustini[1], Emanuele Caredda[2], Vito Montanaro[3], Simona Gaudi[1§] and Maria Grazia Foschino Barbaro[4§]

[1]*Dipartimento Ambiente e Salute, Istituto Superiore di Sanità, Rome, Italy*
[2]*Dipartimento della Prevenzione, Ricerca e delle Emergenze Sanitarie, Ministero della Salute, Rome, Italy*
[3]*Dipartimento Promozione della Salute e del Benessere Animale della Regione Puglia, Bari, Italy*
[4]*Gruppo di lavoro per la governance della rete sociosanitaria per il contrasto della violenza all'infanzia, Regione Puglia, Bari, Italy*
[§]*These Authors equally contributed to the paper*

Abstract

Introduction. Witnessed domestic violence is a widespread yet underrecognized form of childhood trauma, with serious consequences for the emotional, behavioral, and physical development of children and adolescents. In Italy, nearly half of domestic violence incidents occur in the presence of children, yet standardized tools for identifying affected minors remain scarce.

Objectives. This study presents the EpiCHILD assessment tool, designed to support the early identification of psychophysical vulnerabilities in children exposed to domestic violence and to guide targeted prevention and care strategies.

Methods. Developed within the ESMiVA study, EpiCHILD is a multidimensional electronic questionnaire composed of nine sections, incorporating validated instruments for PTSD (ITQ-CA), depression (CDI-2), and psychosocial functioning (SDQ-Ita). Administered by trained professionals in clinical and social service settings, the tool is GDPR-compliant and allows for flexible, child-centered use.

Conclusions. EpiCHILD enables systematic screening and early detection of children at risk due to violence exposure. It standardizes data collection across sectors and lays the groundwork for future research on the biological impact of trauma, including potential epigenetic markers, representing an innovative contribution to precision prevention in child mental health.

Key words
- witnessed domestic violence
- child and adolescent health
- psychological trauma
- early detection
- precision prevention

INTRODUCTION

Intrafamily assisted violence, also known as witnessed violence, is one of the most pervasive yet underrecognized forms of childhood trauma, with profound and lasting implications for a child's development and psychological well-being. Children and adolescents who witness acts of violence, particularly domestic violence within their homes, face an increased risk of a wide range of psychological, behavioral, and developmental problems. These effects may persist into adulthood, impacting not only mental and physical health but also relationships, academic performance, and future parenting practices.

The prevalence of witnessed violence among children is alarmingly high across multiple countries. In the United States, more than 15 million children live in households where domestic violence has occurred at least once [1]. This staggering figure highlights the widespread nature of the issue: millions of children are exposed to violence in what should be their safest environment. Furthermore, studies show that 90% of children in such households are aware of the abuse [2], challenging the misconception that children are unaware of the violence occurring around them.

Globally, research confirms these trends. A meta-analysis by Mitchell *et al.* [3] estimates a prevalence of exposure to domestic and family violence between 11.1% and 23.3% for direct victimization, and between 8.2% and 26.3% for witnessing violence. In Australia, national surveys indicate that approximately 22% of adults report having either been abused or having witnessed parental violence before the age of 15 [4], un-

Address for correspondence: Marco Giustini, Dipartimento Ambiente e Salute, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: marco.giustini@iss.it.

derlining the long-term impact of early exposure across populations.

The Italian context reveals similarly concerning patterns. According to Save the Children, more than 1.4 million women in Italy have reported being victims of domestic violence, and over 427,000 children have been direct or indirect witnesses to such violence against their mothers over a five-year period [5]. Among the more than 6.7 million Italian women who have experienced some form of violence over one in ten feared for their own lives or for their children's [6]. Notably, in nearly half (48.5%) of domestic violence cases, children directly witnessed the abuse, a figure that exceeds 50% in northwestern, northeastern, and southern regions of the country [5].

Figure 1 presents a conceptual framework outlining the multifaceted nature of this public health issue. It illustrates how the often-invisible, yet widespread phenomenon of child-witnessed violence contributes to a complex network of interconnected problems that require coordinated, multidisciplinary strategies for early identification and integrated intervention.

The consequences of witnessing violence are broad and severe. Children exposed to domestic violence are at a 1500% higher risk of also experiencing physical abuse or serious neglect compared to national averages [7]. They are six times more likely to attempt suicide and 50% more likely to engage in substance abuse [8]. These statistics underscore the devastating intergenerational cycle of trauma that unfolds when violence exposure goes unrecognized and unaddressed. These effects can persist in adulthood, leading to psychological, behavioral, and developmental problems.

The concept of poly-victimization further emphasizes the complexity of these experiences. According to Finkelhor *et al.* [9], two-thirds of children exposed to violence have experienced two or more forms of victimization; 30% have experienced five or more, and 10% have endured more than ten.

A recent study by McCarthy *et al.* [10] on the development and validation of a national questionnaire on violence against children in the UK acknowledges witnessing domestic violence as a critical form of child maltreatment. Although the instrument addresses various forms of abuse (including physical, sexual, and emotional abuse, neglect, peer and dating violence, criminal exploitation, and community violence) it involves a dedicated section on witnessing domestic violence. This section contains seven items exploring experiences such as observing violence between cohabiting adults (e.g., parents or partners) and witnessing abuse directed at siblings. This approach reflects growing recognition of the significant psychological and emotional impact that such exposure can have on child development.

Despite the well-documented prevalence and consequences of witnessed domestic violence, standardized assessment tools for identifying affected children remain scarce and fragmented requiring multiple separate assessments to obtain a complete clinical picture. A recent systematic review identified only ten instru-

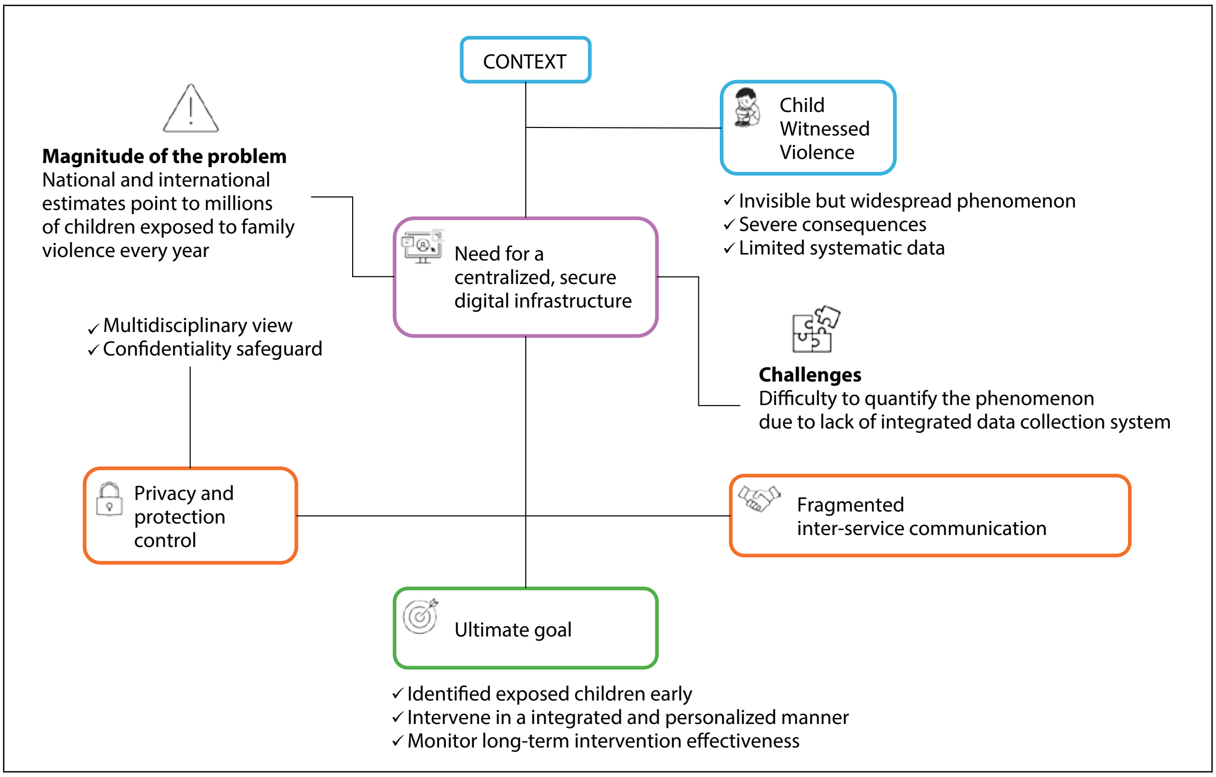


Figure 1

Conceptual framework for addressing child witnessed violence through multidisciplinary early identification and intervention. Original model developed by the Authors within the project "Violence against women: long-term health effects for precision prevention" funded by Ministry of Health (CCM-Centro Nazionale per la Prevenzione e il Controllo delle Malattie-Area Azioni Centrali).

ments specifically focusing on child exposure to domestic violence, most of which were validated exclusively in high-income countries, with only four demonstrating any cross-cultural applicability [11].

Existing measures generally fall into three main categories, each with distinct limitations. Exposure-specific tools, such as the Child Exposure to Domestic Violence Scale (CEDV), provide detailed assessment of exposure events but focus primarily on descriptive rather than clinical outcomes [12]. Broad victimization inventories, such as the Juvenile Victimization Questionnaire-Revised (JVQ-R2), offer comprehensive coverage of multiple forms of victimization but include only limited items on domestic violence specifically [13]. Conflict perception scales, such as the Children's Perception of Interparental Conflict Scale (CPIC), capture children's subjective experiences of interparental conflict but may overlook the broader dynamics and severity of domestic violence scenarios [14].

They also differ substantially in how they conceptualize and operationalize domestic violence exposure, complicating cross-study comparisons and hindering the development of standardized interventions [11].

Furthermore, no currently available instrument has been designed to align with precision medicine approaches that could support future integration with biological markers. As emerging evidence links trauma exposure to potential epigenetic modifications, there is a growing need for tools that can systematically collect multidimensional clinical and sociodemographic data while maintaining compatibility with biological sampling protocols.

Given the profound and multifaceted effects of witnessed violence, early identification of affected children is essential. Developing and implementing validated, specialized assessment tools is vital to equip healthcare professionals, educators, social workers, and other frontline providers with the means to identify and assist these children. Such tools must be sensitive, developmentally appropriate, and culturally informed to ensure timely intervention, disrupt cycles of trauma, and promote resilience and recovery.

The EpiCHILD assessment tool was developed within the framework of the following study: "Administration of a questionnaire to minors exposed to witnessed violence and domestic crimes as a screening tool for the identification of predisposing factors for PTSD and other stress-related disorders: a prospective study (ESMiVA: Health Outcomes in Minors from Witnessed Violence)".

This research is part of a collaborative agreement between the Puglia Region, the Italian National Institute of Health (Istituto Superiore di Sanità), and the Ministry of Health, under the CCM project – Central Actions Area "Violence against women: long-term health effects for precision prevention". This initiative addresses the urgent need for systematic screening and identification of children exposed to witnessed violence in both clinical and community settings. It seeks to bridge the gap between research and practice by providing professionals with evidence-based tools to support vulnerable children and families.

The longitudinal design will allow not only the evaluation of the questionnaire's predictive and incremental validity but also the monitoring the long-term outcomes of violence exposure and assessing the success of potential psychotherapeutic and support interventions that the instrument aims to guide and facilitate. Furthermore, this approach opens doors to exploring transgenerational epigenetic inheritance and the transmission of trauma-related biological changes to future generations.

DEVELOPMENT OF EpiCHILD QUESTIONNAIRE FOR MINORS EXPOSED TO DOMESTIC VIOLENCE

The EpiCHILD interview-based questionnaire was developed to systematically, safely, and comprehensively collect data on minors exposed to witnessed violence and domestic crimes. Its primary objective is to provide an integrated and multidimensional assessment that supports the early detection of psychophysical vulnerabilities, facilitates targeted care, and contributes to the understanding of the biological and psychological impacts of such traumatic experiences.

Moreover, the tool aims to consolidate all relevant information concerning the child's or adolescent's exposure to violence into a single evaluation instrument. This integration enables health and social services to deliver tailored support while identifying early indicators of potential chronic conditions. EpiCHILD aligns with a precision medicine framework and is designed to: *i*) centralize clinical, familial, and behavioral data on the child; *ii*) support professionals in developing individualized therapeutic pathways; *iii*) provide foundational data for future epigenetic studies; and *iv*) standardize the assessment of Post-Traumatic Stress Disorder (PTSD) and depressive symptoms.

METHODS

The questionnaire is structured into nine standalone sections and is designed for use with minors under 18 years of age, including both children and adolescents *(Figure 2)*.

Each section of the EpiCHILD questionnaire is designed to capture a specific dimension of the child's or adolescent's experience, health status, and psychosocial environment *(see Supplementary material available online)*. This modular structure ensures a comprehensive and nuanced assessment of vulnerability factors, while allowing professionals to tailor the administration to the specific context and emotional readiness of the minor. Below is a detailed overview of the questionnaire's structure:

- *Section 1 General data collection:* facility code, child identification code, questionnaire date;
- *Section 2 Sociodemographic data*: gender, age, educational level of child and parents, parental employment, citizenship, household structure, duration of exposure to violence;
- *Section 3 Health and behavioral* conditions: physical and behavioral issues such as asthma, obesity, emotional dysregulation, ADHD, self-harm, etc.;
- *Section 4 Medication intake*: includes listing of any medications taken, especially psychotropics;

- *Section 5 Psychological/psychiatric care*: ongoing therapy, referrals to child psychiatry, or social support interventions;
- *Section 6 Description of violence*: relationship with the perpetrator, perpetrator's gender and age range, type and frequency of violence;
- *Section 7 PTSD assessment (ITQ-CA)*: International Trauma Questionnaire - Child and Adolescent version [15, 16];
- *Section 8 Depression assessment (CDI-2)*: self-report inventory to assess depressive symptoms in children [17, 18];
- *Section 9 Caregiver evaluation (SDQ-Ita)*: Strengths and Difficulties Questionnaire completed by the caregiver [19].

The selection of validated instruments for EpiCHILD was guided by several key criteria: alignment with the International Classification of Diseases, 11th Revision (ICD-11) diagnostic frameworks, established psychometric properties in pediatric populations, cultural adaptation for the Italian context, and complementary assessment approaches combining self-report and caregiver perspectives. All selected instruments demonstrate solid psychometric evidence supporting their use in pediatric populations, with validation studies spanning diverse settings and languages.

The International Trauma Questionnaire – Child and Adolescent version (ITQ-CA) was selected for the standardized assessment of (PTSD) in children and adolescents, recognizing the high prevalence of PTSD in this trauma-exposed population. The questionnaire is specifically designed to capture both PTSD and Complex PTSD (CPTSD) as per ICD-11, making it particularly suitable for complex traumas such as witnessed violence. Multiple studies confirm the ITQ-CA's robust two-factor structure of CPTSD, clearly distinguishing between PTSD symptoms and Disturbances in Self-Organization (DSO) dimensions [15, 16] demonstrating excellent internal consistency across symptom clusters and strong convergent validity and correlating well with related symptoms including depression, anxiety, and dissociation.

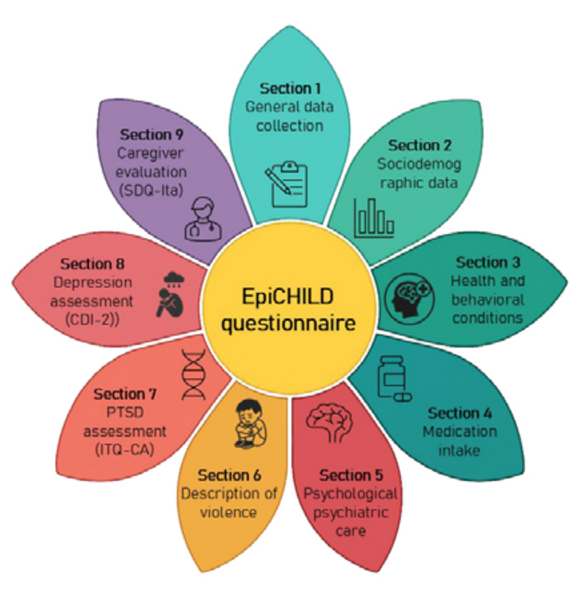


Figure 2
Schematic representation of the EpiCHILD questionnaire structure showing its nine thematic sections for assessing minors exposed to domestic violence and witnessed violence.

The ITQ-CA has been validated across diverse trauma-exposed populations and cultural contexts, including foster children, clinical outpatient samples, and abuse-exposed youth. Notable validation includes a study of 135 foster children in Austria, where confirmatory factor analyses supported the ICD-11 model structure [16]. The instrument showed strong psychometric properties across various language versions, including German, Danish, Chinese, and Farsi, supporting its cross-cultural adaptability. A complementary caregiver version (ITQ-CG) has also shown strong validity and good agreement with child self-reports. In the Italian context, the adult version of the ITQ has already been validated in late adolescents affected by the 2009 L'Aquila earthquake in Central Italy, supporting the six first-order correlated-factors model and providing national prevalence estimates for PTSD and CPTSD [17].

The Children's Depression Inventory 2 (CDI-2) was included for the objective and standardized assessment of depressive symptoms. Depression is a significant and well-documented comorbidity in children and adolescents exposed to violence, with long-term impacts on their well-being [18, 19]. The CDI-2 offers age-appropriate language and content, making it suitable for the wide age range targeted by EpiCHILD. The CDI-2 was standardized on a normative sample of over 1,100 children and adolescents aged 7-17 years [18]. It demonstrates good internal consistency (Cronbach's α typically ranging from 0.80 to 0.90) and adequate test-retest reliability over 2-4 weeks ($r \approx 0.80$) [18], This tool demonstrates sensitivity to developmental and cultural variations, and its use in national pediatric settings is further supported by the availability of standardized Italian norms.

The Strengths and Difficulties Questionnaire – Italian version (SDQ-Ita) was selected to capture caregiver perspectives on psychosocial functioning. The SDQ-Ita has been validated on 1,917 Italian school-aged children [20]. The original five-factor structure was confirmed through factor analyses demonstrating good internal consistency for the total difficulties score ($\alpha \approx 0.73$) and acceptable reliability for individual subscales ($\alpha \approx$ 0.62-0.76), as well as appropriate test-retest reliability. Age- and sex-specific Italian norms are available, and cross-informant agreement between parents and teachers has been established. Completed by the caregiver, it provides an external and complementary perspective to the self-report, crucial for a holistic picture of the child's and adolescent's well-being and is widely validated. Although the SDQ is translated into Italian, it is primarily utilized in our context for a broader assessment of psychosocial functioning rather than as a formally validated PTSD-specific instrument for the Italian population. This multi-informant approach (child self-report for internal experiences, caregiver report for observable behaviors) strengthens the comprehensiveness and validity of the assessment while acknowledging developmental considerations in symptom recognition and reporting.

These psychometric properties support the inclusion of ITQ-CA, CDI-2, and SDQ-Ita as reliable and valid components of the EpiCHILD assessment tool.

The administration of the entire EpiCHILD interview can take place in healthcare settings or during social service consultations. Its flexible design ensures it can be used when the child is emotionally stable and willing to engage. For very young children (0-5 years), assessment must necessarily be based on caregiver reports, given the impossibility of obtaining reliable direct information from the children themselves. For school-aged children (6-12 years) and adolescents (13-18 years), the transition requires a shift in the diagnostic paradigm to account for increased self-report capabilities. On average, completion of the full questionnaire takes 20-30 minutes, though this may vary depending on the child's condition and responsiveness. Crucially, the modular structure allows for partial completion, accommodating the child's pace and comfort.

All data are collected electronically and stored in secure digital environments, in strict compliance with the EU General Data Protection Regulation (GDPR). Access is restricted to authorized personnel only, ensuring the confidentiality and ethical management of sensitive information

The implementation of EpiCHILD offers several advantages. It promotes systematic identification of clinical and behavioral indicators associated with exposure to domestic violence. By incorporating internationally validated instruments (ITQ-CA, CDI-2, SDQ), it ensures the reliable assessment of PTSD, depressive symptoms, and psychosocial functioning.

Furthermore, the tool facilitates early activation of protection and care pathways for at-risk children and lays the foundation for future research on the biological impacts of trauma, including potential epigenetic effects. Its closed-ended questions reduce cognitive and emotional strain on the child, enhance clarity and consistency of responses, and streamline statistical analysis of the collected data.

DISCUSSION

According to the World Health Organization, one in three women globally has experienced intimate partner violence (IPV). Among children living in households where IPV occurs, 85% directly witness violent episodes, and up to 50% are subjected to direct abuse, predominantly by fathers or other male family members [21]. In Europe, survey data reveal that 19% of Italian women have experienced physical or sexual violence by a partner, and 38% have reported repeated psychological abuse [22]. Alarmingly, 65% of these women stated that their children had witnessed at least one violent episode [6].

A growing body of evidence highlights that witnessing domestic violence can have serious, long-term effects on children's emotional, behavioral, and developmental well-being, effects comparable to those of direct abuse [23, 24].

Such exposures are associated with negative health outcomes, including neurobiological, immune, metabolic, and cardiometabolic issues, and can lead to high levels of inflammation [25-27]. Studies have shown that exposure to psychosocial stress, particularly early in life, can alter brain development and promote chronic inflammation, an important mechanism that increases susceptibility to a wide range of negative physical and mental health conditions, including chronic diseases such as asthma, diabetes, and cardiovascular disease [28].

Despite the increasing implementation of laws aimed at combating domestic violence, there remains a critical gap in research regarding the actual impact of these legislative measures on children's health and recovery. Recent studies argue that future research should explore whether these laws achieve their intended goals (deterrence, protection, rehabilitation) and whether they result in tangible benefits or unintended consequences for children and families [29]. This gap underscores the need for evidence-based evaluations of legal and policy approaches to domestic violence.

The health consequences of witnessing violence often mirror those of direct victimization. In the absence of visible physical injuries, these children and adolescents may be overlooked by healthcare providers and social services, leading to a further layer of psychological trauma. Centralizing clinical data through standardized electronic tools like EpiCHILD is essential for longitudinal tracking and for understanding the cumulative effects of witnessed violence.

Assessing, contextualizing, and monitoring the short-, medium-, and long-term effects of exposure to violence is vital. Such efforts enable the acquisition of contextual information that can be linked in the future to molecular profiles. The health and well-being of children are investments in society's future; thus, identifying both risk and resilience factors is critical. It is now well established that trauma can affect genome functioning through epigenetic mechanisms, including DNA methylation, histone acetylation, and non-coding RNAs. In parallel research involving adult women exposed to violence (and in some cases their mothers) such epigenetic modifications are being studied as potential biomarkers for long-term health outcomes.

Extending this approach to minors could illuminate the biological underpinnings of trauma and provide new avenues for precision prevention. Investigating epigenetic profiles in children may help develop tailored protocols to prevent the early onset of non-communicable, chronic, and disabling conditions.

One particularly urgent issue is the plight of children orphaned by femicide, who often lose both parents in the aftermath, one to death, the other to incarceration. These children face profound psychological and emotional shock, which can have enduring consequences for their mental and physical health. There is an urgent need to establish national and regional protocols for long-term psychosocial and healthcare support to mitigate trauma and foster resilience. The development of a dedicated electronic assessment tool such as EpiCHILD is a significant step toward standardized data collection and comprehensive monitoring of violence-related impacts on children.

Gender-specific dynamics must also be considered. In the context of witnessed domestic violence, boys are more frequently exposed to physical aggression, while girls are more often subjected to sexual victimization [30]. These differences can shape how trauma is processed and manifested. Studies suggest that gender influences identification patterns and behavioral modeling: males who witness maternal abuse are ten times more likely to become perpetrators themselves, while females raised in abusive households are six times more likely to experience sexual violence later in life [9].

Understanding the gendered manifestations of intrafamilial violence is essential for effective assessment and intervention. While men are more often the aggressors, both men and women can be victims or enablers of violence. Gender-sensitive approaches must account for power imbalances, challenge harmful stereotypes, and provide inclusive, trauma-informed care. Intra-familial assisted violence comprises a spectrum of abusive behaviors, including coercion, neglect, and complicity, and necessitates the implementation of comprehensive, culturally responsive interventions. The EpiCHILD tool integrates these perspectives providing a foundational platform for long-term, data-driven interventions. By supporting early diagnosis and enabling future research into trauma's biological and psychological impacts, it serves both public health and child protection goals, helping to break the intergenerational cycle of violence and contribute to understanding psychophysical vulnerabilities.

While EpiCHILD integrates well-established validated instruments, its use as a unified battery requires comprehensive empirical validation. Future studies should examine its predictive validity by assessing its ability to forecast clinical outcomes, treatment response, and long-term developmental trajectories in children exposed to domestic violence. Research is also needed to evaluate its incremental validity, determining whether the integrated multidimensional assessment adds clinically meaningful information beyond existing approaches. Longitudinal studies will be crucial to assess its sensitivity to change, refine age-specific administration protocols, and define evidence-based cutoff scores to guide clinical decision-making.

CONCLUSIONS AND OUTLOOK

As outlined in this study, the EpiCHILD electronic questionnaire serves not only as a tool for early detection but also as a gateway to understanding the long-term biological and psychological consequences of witnessed violence in childhood. Emerging research suggests that domestic violence may leave lasting molecular traces, or "epigenetic scars", that alter gene expression through mechanisms such as DNA methylation, histone modification, and non-coding RNA regulation. Preliminary findings from our EpiWE pilot study revealed increased DNA methylation in PTSD-related genes among women who experienced violence [31]. When integrated with psychological assessments, these epigenetic markers may become powerful tools for developing targeted therapies within a precision medicine framework, potentially mitigating the long-term impact of trauma by addressing its biological roots [32]. Extending this line of research to children is essential. Investigating whether similar epigenetic modifications occur in the offspring of women exposed to violence could help unravel the complex molecular architecture of PTSD and other trauma-related disorders in childhood and adolescence. The prevalence of PTSD among children and adolescents is estimated at 16.6%, making this a significant area for research and clinical intervention [33].

The identification of epigenetic markers in minors could enable the design of novel therapeutic targets and preventive interventions. Moreover, it opens the door to exploring transgenerational epigenetic inheritance, the transmission of trauma-related biological changes to future generations. This field redefines our understanding of heredity, psychological vulnerability, and the intergenerational impact of violence.

Long-term monitoring and support for affected children are crucial. By collecting longitudinal data on pediatric cohorts, we can gain insights into the enduring effects of violence and develop more effective, personalized prevention strategies. Such efforts contribute not only to improved individual outcomes but also to the reduction of broader societal and economic pressures on healthcare systems.

The EpiCHILD tool is an important step toward this vision. It exemplifies how child-centered, science-driven approaches can strengthen public health systems, inform clinical practice, and empower caregivers and professionals alike. Through early identification, interdisciplinary collaboration, and integration with emerging research in epigenetics, we can move toward a model of precision prevention, protecting the health and futures of the most vulnerable children and adolescents of our society.

Ethics Committee

The EpiCHILD assessment tool was approved by the Local Ethics Committee of the Puglia Region, Italy (Protocol Number: 734 of 29/07/2025 – Substantive amendment No. 1 – Prot. 2235/CEL-Studio ESMiVA).

Acknowledgments

The Authors thank the Italian Ministry of Health for the technical and financial support: CCM – Central Action Project "Violence against women: long-term health effects for precision prevention."

The Authors are especially grateful to Giuseppina Mandarino, whose expert linguistic revision significantly improved the clarity, fluency, and overall quality of the manuscript, and Cecilia Fazio for contributing to the revision of the text.

Some portions of the manuscript were also revised with the support of artificial intelligence (AI) tools to enhance language structure and consistency. All content, including any AI-assisted revisions, was critically reviewed and explicitly approved by the Authors, who verify its accuracy, scientific validity, and integrity.

Authors' contributions

AC, MG, SG and MGFB conceived and designed the study and wrote the manuscript. EC and VM revised and edited the manuscript. All Authors revised the manuscript for important intellectual content and agreed with this article's contents.

Funding

This work is supported by Centro nazionale per la prevenzione ed il Controllo delle Malattie (CCM) Azione Centrale “Violenza sulle donne: effetti a lungo termine sulla salute per una prevenzione di precisione” – EA38 (2024-2026).

Conflict of interest statement

The Authors declare no competing interests.

Received on 16 July 2025.
Accepted on 23 September 2025.

REFERENCES

1. McDonald R, Jouriles EN, Ramisetty-Mikler S, Caetano R, Green CE. Estimating the number of American children living in partner-violent families. J Fam Psychol. 2006;20(1):137-42. doi: 10.1037/0893-3200.20.1.137
2. Holt S, Buckley H, Whelan S. The impact of exposure to domestic violence on children and young people: a review of the literature. Child Abuse Negl. 2008;32(8):797-810. doi: 10.1016/j.chiabu.2008.02.004
3. Mitchell KJ, Jones LM, Turner HA, Shattuck A, Wolak J. The role of technology in peer harassment: does it amplify harm for youth? Psychol Violence. 2018;8(5):568-76. doi: 10.1037/vio0000199
4. Australian Bureau of Statistics. Personal safety, Australia [Internet]. Canberra: ABS; 2021-22. Available from: https://www.abs.gov.au/statistics/people/crime-and-justice/personal-safety-australia/latest-release.
5. Inverno A, Muratore MG, Corazziari I. Abbattiamo il muro del silenzio: bambini che assistono alla violenza domestica. Roma: Save the Children Italia Onlus; 2018. Available from: https://s3.savethechildren.it/public/files/uploads/pubblicazioni/abbattiamo-il-muro-del-silenzio-il-dossier_1.pdf.
6. Istituto Nazionale di Statistica. La violenza contro le donne dentro e fuori la famiglia. Anno 2014. Roma: ISTAT; 2015. Available from: https://www.istat.it/it/files/2015/06/Violenze_contro_le_donne.pdf.
7. United Nations Agency for Children. Behind closed doors: the impact of domestic violence on children. New York: UNICEF; 2006. Available from: https://www.ojp.gov/ncjrs/virtual-library/abstracts/behind-closed-doors-impact-domestic-violence-children.
8. Silvern L, Karyl J, Waelde L, Hodges WF, Starek J, Heidt E, Min K. Retrospective reports of parental partner abuse: relationships to depression, trauma symptoms and self-esteem among college students. J Fam Violence. 1995;10(2):177-202. doi: 10.1007/BF02110599
9. Finkelhor D, Turner H, Ormrod R, Hamby SL. Violence, abuse, and crime exposure in a national sample of children and youth. Pediatrics. 2009;124(5):1411-23. doi: 10.1542/peds.2009-0467
10. McCarthy A, Rudolph JI, Fry D, Monks CP, Pacella R, Meinck F. Measuring violence against children in a national prevalence survey in the UK: Questionnaire development and content validity. Child Abuse Negl. 2025;167:107578. doi: 10.1016/j.chiabu.2025.107578
11. Harris RJ, Channon AA, Morgan SA. Childhood exposure to domestic violence: can global estimates on the scale of exposure be obtained using existing measures? Front Public Health. 2024;12:1181837. doi: 10.3389/fpubh.2024.1181837
12. Edleson JL, Shin N, Johnson Armendariz KK. Measuring children's exposure to domestic violence: The development and testing of the Child Exposure to Domestic Violence (CEDV) Scale. Child Youth Serv Rev. 2008;30(5):502-21. doi: https://doi.org/10.1016/j.childyouth.2007.11.006
13. Finkelhor D, Hamby SL, Ormrod R, Turner H. The Juvenile Victimization Questionnaire: reliability, validity, and national norms. Child Abuse Negl. 2005;29(4):383-412. doi: https://doi.org/10.1016/j.chiabu.2004.11.001
14. Moura O, Santos R, Rocha M, Matos P. Children's Perception of Interparental Conflict Scale (CPIC): factor structure and invariance across adolescents and emerging adults. Int J Test. 2010;10(4):364-82. doi: https://doi.org/10.1080/15305058.2010.487964
15. Cloitre M, Shevlin M, Brewin CR, Bisson JI, Roberts NP, Maercker A, Karatzias T, Hyland P. The International Trauma Questionnaire: development of a self-report measure of ICD-11 PTSD and complex PTSD. Acta Psychiatr Scand. 2018;138(6):536-46. doi: 10.1111/acps.12956
16. Haselgruber A, Sölva K, Lueger-Schuster B. Symptom structure of ICD-11 Complex Posttraumatic Stress Disorder (CPTSD) in trauma-exposed foster children: examining the International Trauma Questionnaire – Child and Adolescent Version (ITQ-CA). Eur J Psychotraumatol. 2020;11(1):1818974. doi: 10.1080/20008198.2020.1818974
17. Rossi R, Socci V, Pacitti F, Carmassi C, Rossi A, Di Lorenzo G, Hyland P. The Italian version of the International Trauma Questionnaire: Symptom and network structure of PTSD and complex PTSD in a sample of late adolescents exposed to a natural disaster. Front Psychiatry. 2022;13:859877. doi:10.3389/fpsyt.2022.859877
18. Kovacs M. Children's Depression Inventory 2 (CDI 2): technical manual. North Tonawanda: Multi Health Systems; 2011.
19. Cole DA, Martin NC. The longitudinal structure of the children's depression inventory: testing a latent trait-state model. Psychol Assess. 200;17(2):144-55. doi: 10.1037/1040-3590.17.2.144
20. Tobia V, Marzocchi GM. The strengths and difficulties questionnaire-parents for Italian school-aged children: Psychometric Properties and Norms. Child Psychiatry Hum Dev. 2018;49(1):1-8. doi: 10.1007/s10578-017-0723-2
21. World Health Organization. Global status report on violence prevention 2014. Geneva: WHO; 2014. Available from: https://www.who.int/publications/i/item/9789241564793.
22. European Union Agency for Fundamental Rights. Violence against women: an EU-wide survey. Main results. Luxembourg: Publications Office of the European Union; 2015. Available from: https://fra.europa.eu/en/publication/2014/violence-against-women-eu-wide-survey-main-results-report.

23. Kitzmann KM, Gaylord NK, Holt AR, Kenny ED. Child witnesses to domestic violence: a meta-analytic review. J Consult Clin Psychol. 2003;71(2):339-52. doi: 10.1037/0022-006x.71.2.339
24. Evans SE, Davies C, Di Lillo D. Exposure to domestic violence: A meta-analysis of child and adolescent outcomes. Aggress Violent Behav. 2008;13(2):131-40. doi: 10.1016/j.avb.2008.02.005
25. Shonkoff JP, Garner AS; Committee on Psychosocial Aspects of Child and Family Health; Committee on Early Childhood, Adoption, and Dependent Care; Section on Developmental and Behavioral Pediatrics. The lifelong effects of early childhood adversity and toxic stress. Pediatrics. 2012;129(1):e232-46. doi: 10.1542/peds.2011-2663
26. Danese A, McEwen BS. Adverse childhood experiences, allostasis, allostatic load, and age-related disease. Physiol Behav. 2012;106(1):29-39. doi: 10.1016/j.physbeh.2011.08.019
27. Slopen N, Kubzansky LD, McLaughlin KA, Koenen KC. Childhood adversity and inflammatory processes in youth: A prospective study. Psychoneuroendocrinology. 2013;38(2):188-200. doi: 10.1016/j.psyneuen.2012.05.013
28. Deighton S, Neville A, Pusch D, Dobson K. Biomarkers of adverse childhood experiences: A scoping review. Psychiatry Res. 2018;269:719-32. doi: 10.1016/j.psychres.2018.08.097
29. Reott EC, Hulkower R, Lancaster C, Frey MT, Smith RC, Thomas C, Godoshian V. State laws on intimate partner violence witnessed by children in the United States. J Public Health Policy. 2025;46(2):284-94. doi: 10.1057/s41271-025-00550-4
30. Ehrensaft, MK., Cohen P, Brown J, Smailes E, Chen H, Johnson JG. Intergenerational transmission of partner violence: A 20-year prospective study. Journal of Consulting and Clinical Psychology. 2003;71(4):741-53.
31. Finkelhor D, Turner H, Ormrod R, Hamby SL. Violence, abuse, and crime exposure in a national sample of children and youth. Pediatrics. 2009:124(5):1411-23.
32. Piccinini A, Bailo P, Barbara G, Miozzo M, Tabano S, Colapietro P, Farè C, Sirchia SM, Battaglioli E, Bertuccio P, Bertuccio P, Manenti G, Micci L, la Vecchia C, Kustermann A, Gaudi S. Violence against women and stress-related disorders: seeking for associated epigenetic signatures, a pilot study. Healthcare. 2023;11:173.
33. Costello EJ, Erkanli A, Fairbank JA, Angold A. The prevalence of potentially traumatic events in childhood and adolescence. J Trauma Stress. 2002;15(2):99-112. doi: 10.1023/A:1014851823163

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 277-284
DOI: 10.4415/ANN_25_04_06

Comparing results from a traditional multivariable model and seven propensity score-based models for estimating COVID-19 vaccine effectiveness

Daniele Petrone[1], Chiara Sacco[1], Alberto Mateo-Urdiales[1], Emmanouil Alexandros Fotakis[1], Marco Alfò[2], Patrizio Pezzotti[1] and Massimo Fabiani[1]

[1]*Dipartimento di Malattie Infettive, Istituto Superiore di Sanità, Rome, Italy*
[2]*Dipartimento di Statistica, Sapienza Università di Roma, Rome, Italy*

Abstract

Background. Accurate estimation of vaccine effectiveness (VE) in real-world settings is essential for guiding immunization strategies, especially in older populations. However, observational studies are prone to bias due to confounding factors, and the choice of statistical method can significantly influence VE estimates.
Materials and methods. We compared the performance of a multivariable Cox proportional hazards model with seven propensity score (PS)-based models to estimate the relative vaccine effectiveness (rVE) of the bivalent Original/Omicron BA.4-5 mRNA vaccine as a second or third booster, compared to a first mRNA booster received ≥120 days earlier. Data from 11,879,461 individuals aged ≥60 in Italy (April-June 2023) were analyzed.
Results. All models produced consistent rVE estimates, with values ranging from 16.4% to 22.1%. Over time, booster effectiveness declined, with the reference model showing a drop in rVE from 45.6% (15-60 days) to 14.3% (181-265 days). PS-based methods improved covariate balance but did not outperform the Cox model in terms of precision or interpretability.
Conclusions. In large, relatively balanced datasets, traditional multivariable models remain a robust and reliable choice for estimating VE. While PS-based methods offer theoretical advantages, their practical benefit may be limited when confounding is well controlled.

Key words
- COVID-19
- effectiveness
- propensity score
- matching

BACKGROUND

Vaccination against COVID-19 was considered the key strategy in limiting the spread of the highly mutable SARS-CoV-2 virus. In this context, observational studies remain crucial to assess and monitor the effectiveness of approved vaccines. However, observational vaccine effectiveness (VE) studies, although crucial for understanding the real-world impact of vaccines, are prone to bias (e.g., due to confounding) [1, 2]. Compared to randomized trials, where all participants have an equal probability to receive the vaccine, in observational studies the choice to get vaccinated or not is not evenly distributed across the population. Indicatively, confounding factors like age, pre-existing health conditions, comorbidities, and socio-economic background influence the individual decision to get vaccinated and the probability of a COVID-19 associated event, thus introducing potential bias in the VE estimates [3]. The risk of bias due to differences between vaccinated and unvaccinated populations could be amplified by the seasonal booster campaigns implemented in Italy and other European countries, targeting the elderly population and those with risk factors.

Several statistical methods have been proposed in the literature to consider the presence of potential confounding factors, aiming to balance the difference between those who received the intervention and those who did not. These methods include covariates adjustment, stratification, matching, regression models that use instrumental variables, and methods based on

Address for correspondence: Daniele Petrone, Dipartimento di Malattie Infettive, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: daniele.petrone@iss.it.

propensity score (PS), representing the probability of receiving a specific treatment, given a set of observed covariates [4].

The performance of these methods in limiting bias could significantly impact the accuracy of VE estimates, particularly in the context of seasonal COVID-19 vaccine programmes. Nonetheless, there is a lack of studies comparing VE estimates considering potential confounding, especially in the context of large, real-world datasets.

Based on published data recorded in Italy [5], we aimed to compare estimates of relative VE (rVE) using different PS-based methods – i.e., inclusion of the PS as an adjustment variable, inverse probability weight (IPW), stabilized IPW, truncated stabilized inverse probability weights (SIPW) and matching – [6-12] with a reference approach based on a Cox proportional hazards regression analysis.

MATERIALS AND METHODS

Study design

We conducted a retrospective cohort study based on the individual data previously used by our study group to estimate the rVE of a booster dose of the bivalent (Original/Omicron BA.4-5) mRNA vaccine in preventing severe COVID-19 among people ≥60 years during a period with prevalent circulation of the Omicron XBB subvariant (3 April-4 June 2023) [5].

Specifically, we analyzed time to infection leading to severe COVID-19 consequences (i.e., hospitalization or death within 28 days of the swab date for a test that was SARS-CoV-2-positive) comparing individuals who had received only the first booster dose of an mRNA vaccine at least 120 days earlier and those who had received a second or third booster dose of the bivalent Original/Omicron BA.4-5 mRNA vaccine during the study period.

After splitting individual data into multiple records to account for the time-varying vaccination status, we estimated rVE both overall and by time since booster administration (i.e., 15-60 days, 61-120 days, 121-180 days and 181-265 days).

More details about the data sources, the selection of the study population, and the outcome classification have been published elsewhere [5].

Statistical analysis

Reference model

The reference model (M0) used in the original analysis was a multivariable Cox proportional hazards model M0 include the following demographic and clinical variables as covariates to adjust for: sex, age group (5-year age group from 60-64 to 90-94, then grouping individuals ≥95), country of birth (Italian-born or foreign-born), geographical area where the vaccination took place (NUTS 21 regions/autonomous provinces of Italy), and high-risk group (none or individuals residing in long-term care facilities and/or with health risk conditions; see *Supplementary Table S1 available online*). Additional covariates included the days since 1st booster dose (≤180, 181-365, >365), days since prior infection (≤180, 181-365, >365, no prior infection) and type of 1st booster vaccine (mRNA monovalent, mRNA bivalent Original/Omicron BA.1, mRNA bivalent Original/Omicron BA.4-5).

Alternative models

In order to take into account potential imbalance between the analyzed groups in the observed covariates we estimated adjusted VE against severe COVID-19 using seven alternative PS-based Cox regression models (M1-M7), as reported in *Table 1*. The alternative models are still Cox proportional hazards, but instead of using covariates for adjustment (as in the reference

Table 1
Models description and covariates included in the study

Model name	Differences with respect to baseline Cox proportional hazard model	Covariates included
M0	-	Exposure level, sex, age group, country of birth, geographical area, high-risk group, days since 1st booster vaccine, days since prior infection, type of 1st booster vaccine
M1	Including (only) the PS	Exposure level, PS
M2	Including (also) the PS	Exposure level, sex, age group, country of birth, geographical area, high-risk group, days since 1st booster vaccine, days since prior infection, type of 1st booster vaccine, PS
M3	Weighting observations with IPW	Exposure level
M4	Weighting observations with SIPW	Exposure level
M5	Weighting observations with STIPW 1%	Exposure level
M6	Weighting observations with STIPW 5%	Exposure level
M7	Matching observations	Exposure level

Exposure level: time since administration of a second or third booster dose of the bivalent Original/Omicron BA.4-5 mRNA vaccine: 15-60 days, 61-120 days, 121-180 days and 181-265 days; sex: male, female; age group: 5-year age group from 60-64 to 90-94, then grouping individuals ≥90; country of birth: Italian-born or foreign-born; Geographical area: geographical area where the vaccination took place (NUTS 2, which are the 19 regions and two autonomous provinces of Italy); high-risk group: none or residents in long-term care facilities and individuals with health risk conditions (*Supplementary Table S1 available online*); days since 1st booster vaccine: ≤180 days, 181-365 days, >365 days; days since prior infection: ≤180 days, 181-365 days, >365 days, no prior infection; type of 1st booster vaccine: mRNA monovalent, mRNA bivalent Original/Omicron BA.1, mRNA bivalent Original/Omicron BA.4-5.
PS: propensity score; IPW: inverse probability weight; SIPW: stabilized inverse probability weights; STIPW: stabilized truncated inverse probability weights.

model), covariates are used for the calculation of PS, weighting and matching.

To calculate the PS we used a logistic regression model based on individual data, estimating the probability of receiving a second or third booster dose of the bivalent Original/Omicron BA.4-5 mRNA vaccine as a function of the covariates used in model M0. The first alternative model (M1) was based on adjusting for the propensity score (PS), used as the only covariate in addition to the exposure variable (vaccination status). The second model (M2) was adjusted including the covariates considered in model M0 plus the PS. In models M3-M6, observations were weighted and only the exposure variable was included. Specifically, in model M3, observations were weighted using the inverse probability weighting approach (IPW) with individual weights defined as 1/PS if the subject received the treatment and 1/(1-PS) otherwise. To account for the different size of the treated/untreated groups and to reduce the variance of the estimated hazard ratios (HRs), we calculated the stabilized inverse probability weights (SIPW) by dividing the IPW by the total sum of the IPWs of the subjects in the same treatment group; and used these weights in model M4. To further reduce the variance due to extreme values of the PS and to study the sensitivity of the model to these values, we calculated the stabilized truncated inverse probability weights (STIPW) including only cases with PS between the 1st and the 99th percentile (M5) or between the 5th and 95th percentile (M6) when calculating SIPW. Finally, we matched 1:1 without replacement the observations according to the PS, before splitting the data, using the nearest neighbour matching with a calliper of 0.05, and then run a univariate Cox regression analysis on split data from the matched sample (M7).

All models based on IPW (M3-M6) were run using a robust variance estimator [6]. To verify the covariates balance after IPW, SIPW, STIPW and PS-matching (M3-M7) we used the Standardized Mean Difference (SMD), assuming a satisfactory balance where SMD values were less than 0.1.

For all models, the HRs and 95% confidence intervals (CI) were used to calculate the adjusted rVE against severe COVID-19 using the formula ((1-HR)x100). In addition, we calculated the BIC and AIC for all models to compare their performance. All the analyses were carried out with RStudio 2023.12.1+402 under R 4.3.2 [13].

RESULTS

We analysed data on 11,879,461 subjects included in the original study [2], of which 1,970,598 (16.6%) received at least the second booster dose. Among all subjects, there were 4,405 (0.04%) severe events, most of which occurred before receiving a second or third booster dose (n=3,565; 0.036%). After receiving a second or third booster doses, the highest event rate was observed in the time interval 121-180 days post administration (n=467; 0.025%) (*Table 2*).

All the coefficient estimates obtained with the logistic regression model used to calculate the PS were statistically significant, although there was not much heterogeneity between the two treatment groups (*Figure 1*). The estimated area under the curve (AUC) obtained with the model is 0.72.

After matching (3,941,196 subjects, 33.2% of the total, including all vaccinated individuals, were matched successfully), all the potential confounding variables appeared balanced according to the SMD values (SMD<0.1). The same was observed after weighting data through IPW, SIPW and the STIPW (truncation at level 1% removed 239,155 subjects, 2.01% of the total; truncation at level 5% removed 1,217,007 individuals, 10.24% of the total) (*Figure 2* and *Supplementary Figure S1 available online*).

Model comparisons

The overall analysis shows homogeneous results between all models, with the point estimate going from a minimum of 16.4% with model M7 to 22.1% with model M5. The 95% CI width also does not change much increasing slightly when the observations in the models M3-M6 are weighted (from 12.7 in the models M0-M2 to 15.4 in model M7). Both BIC and AIC, using the "lower is better" rule, indicate as better performing the models based on SIPW, with little difference between

Table 2
Number and percentage of severe events by exposure level

Time since booster	Number of individuals[a]	Number of events	Percentage (%)
First booster ≥120 days	9,912,672	3,565	0.036
Second or third booster			
15-60 days	90,807	11	0.012
61-120 days	715,375	135	0.019
121-180 days	1,843,177	467	0.025
181-265 days	1,259,968	227	0.018
Total	**13,821,999**	**4,405**	**0.032**

[a] The sum of the number of individuals in each time interval is greater than the total number of individuals included in the analysis because of the possible change in vaccination status during the observation period leading an individual to be counted more than once.
First booster vaccine: Comirnaty monovalent Original strain mRNA vaccine (BNT162b2 mRNA, BioNTech-Pfizer); Spikevax monovalent Original strain mRNA vaccine (mRNA-1273, Moderna); Comirnaty bivalent Original/Omicron BA.1 mRNA vaccine (BNT162b2 mRNA, BioNTech-Pfizer); Spikevax bivalent Original/Omicron BA.1 mRNA vaccine (mRNA-1273.214, Moderna) or Comirnaty bivalent Original/Omicron BA.4-5 mRNA vaccine (BNT162b2 mRNA, BioNTech-Pfizer). Second or third booster vaccine: Comirnaty bivalent Original/Omicron BA.4-5 mRNA vaccine (BNT162b2 mRNA, BioNTech-Pfizer).

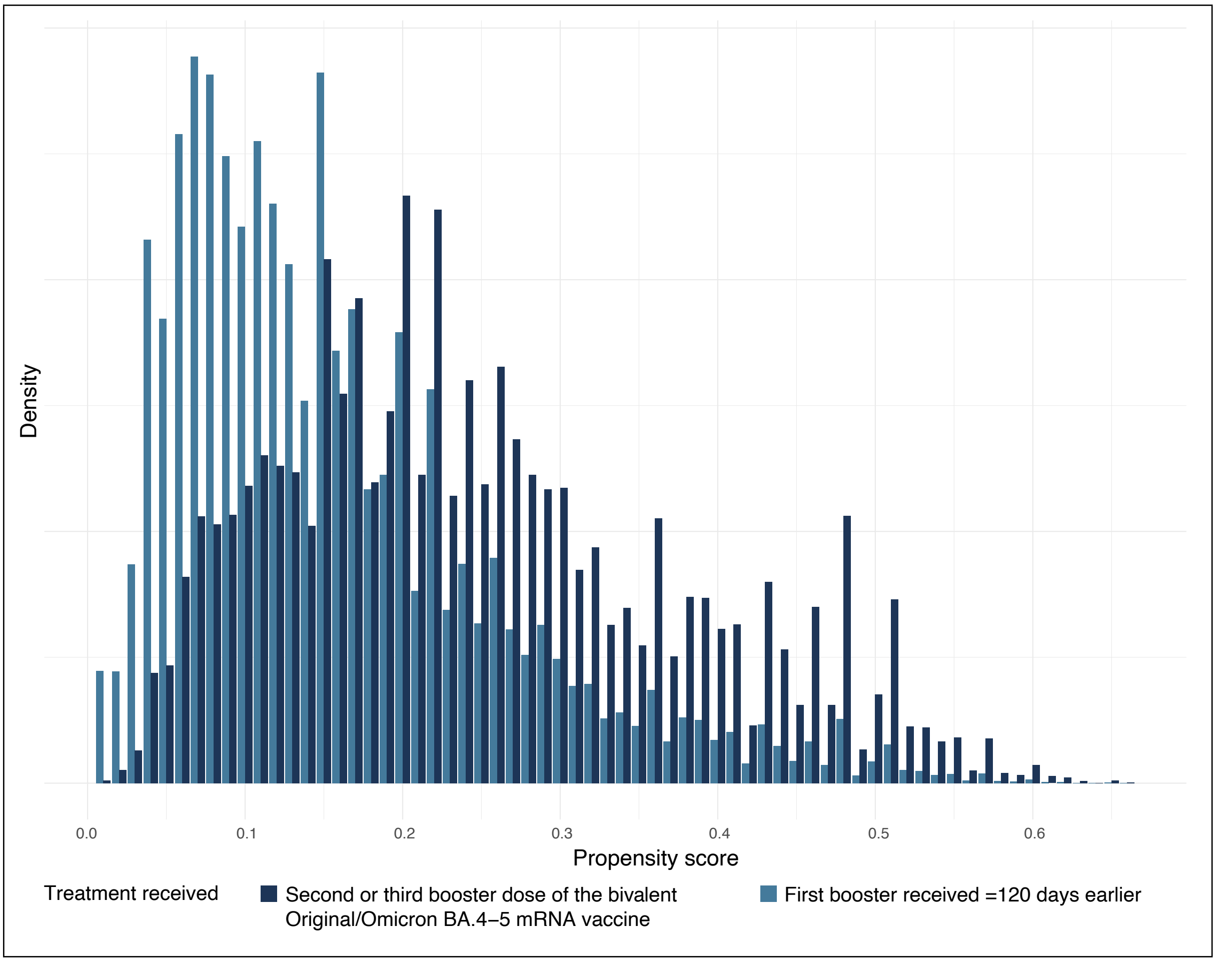


Figure 1
Density distribution of the propensity score for individuals aged ≥60 years who received either a second or third booster dose of the bivalent Original/Omicron BA.4-5 mRNA vaccine, Italy, 3 April-4 June 2023 (n=11,879,461).

using truncation or not (*Table 3* and *Supplementary Figure S2 available online*).

The results from the reference model (M0) show that, compared with a first booster of an mRNA vaccine received at least 120 days earlier, the rVE against severe COVID-19 for a second or a third booster dose of bivalent Original/Omicron BA.4-5 mRNA vaccine in the time interval 15-60 days post-administration was 45.6% (95% CI: 1.6-69.9). Relative VE progressively decrease to 14.3% (95% CI: 1.6-25.3) in the interval 181-265 days post-administration (*Table 3* and *Figure 3*). The same decreasing trend is shown by all the models, except models M5 and M6 where we used the STIPW. In these cases, the rVE obtained in the first time-interval post-administration is lower than that obtained in the second one. The rVE estimates with 95% CIs obtained with models M1, M2 and M7 are similar to those obtained with model M0, although models M1 and M7 showed slightly lower estimates than M0 in the first time-interval post-administration (42.3% and 39.6%, respectively, both with a 95% lower bound of opposite sign than M0). In addition, model M1 shows slightly higher estimates in the other time-intervals. Model M2 shows estimates very close to those from model M0 (45.6% *vs* 45.8% in the 15-60 days interval, 24.7% *vs* 25.1% in the 61-120 days interval, 17.0% *vs* 17.3% in the 121-180 days interval, and 14.3% *vs* 14.5 in the 181-265 days interval). There are no differences between the rVE estimated with model M3 with respect to those estimated using model M4. The rVE estimates and 95% CIs obtained with the IPW-based models M3-M6 are generally similar to those derived from the reference model M0, except in the first period post-administration (15-60 days). This applies especially to model M6, which estimates a rVE more than 6 times lower and with a much higher variability than that derived from M0 (7.1%, 95% CI: -91.2-54.9). In the other time-intervals post-administration the differences appear much reduced, with slightly higher rVE estimates and slightly larger 95% CIs for models M3-M6 compared to M0. Looking at the AIC and BIC values, conclusions are similar to those made previously for the overall analysis (*Table 3*).

DISCUSSION

Our study showed homogeneous VE estimates among all the models. In particular, two groups appear, whereby the rVE values estimated by models including

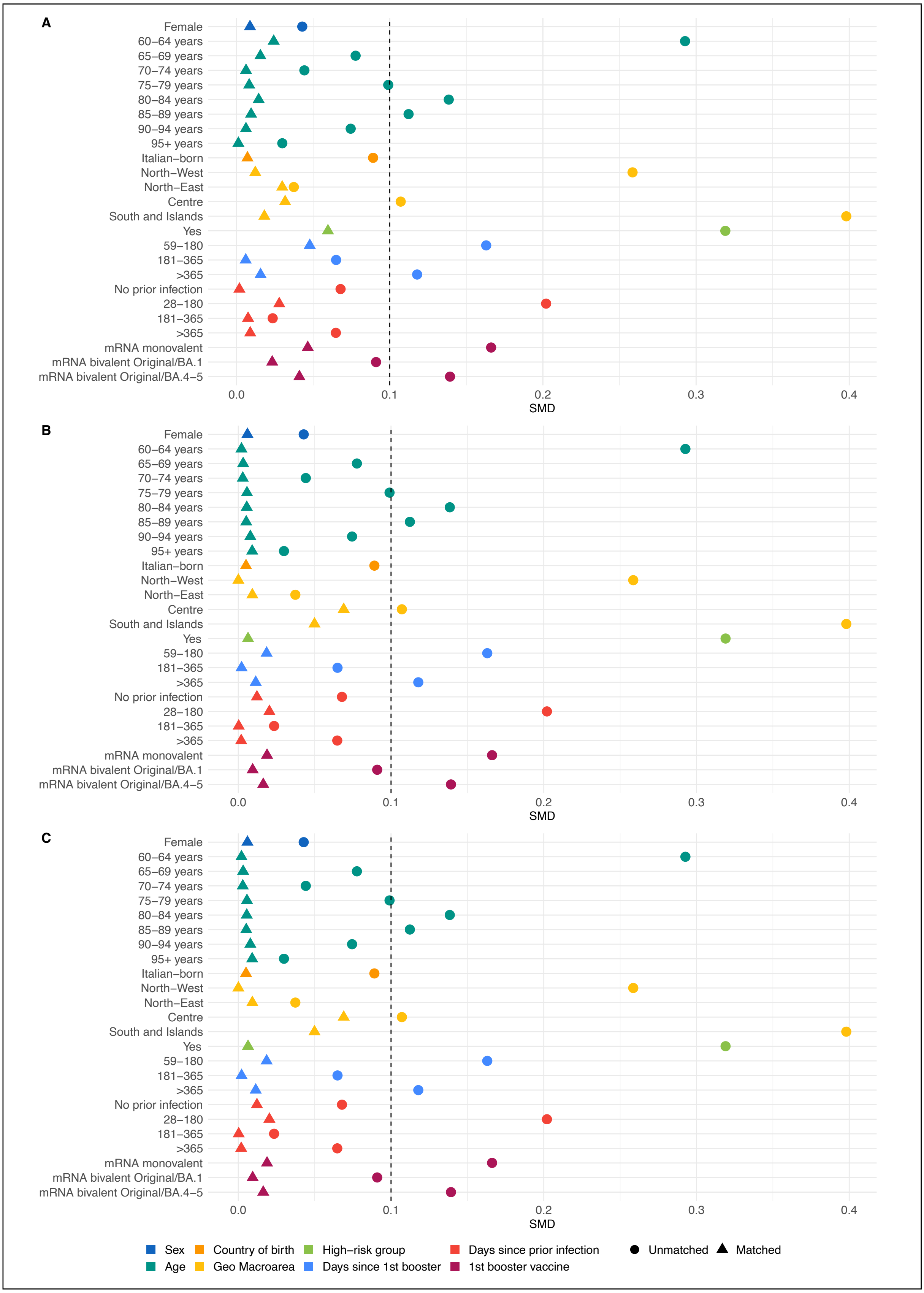


Figure 2

Standardized mean differences for covariates used in the models before and after observation matching (A), and weighting with IPW (B) and weighting with SIPW (C).

In the analysis we considered the Regions or Autonomous Provinces (NUTS 2) but for graphical reasons we represented the macroarea (NUTS 1). In both cases the covariates are balanced. IPW: inverse probability weight; SIPW: stabilized inverse probability weights.

Table 3
Point Estimation, 95% confidence interval and interval width of the estimated rVE against severe COVID-19 of a second or third booster of the bivalent Original/Omicron BA.4-5 mRNA vaccine relative to a first booster of an mRNA vaccine received at least 120 days earlier, Italy, 3 April-4 June 2023

Time since 2nd or 3rd booster		M0	M1	M2	M3	M4	M5	M6	M7
15-60 days	Point Es.	45.6	42.3	45.8	34.5	34.5	18.6	7.1	39.6
	95% CI	1.6-69.9	-4.5-68.1	2.0-70.1	-32.2-67.5	-32.2-67.5	-64.0-59.6	-91.2-54.9	-9.5-66.7
	In. Width	68.3	72.6	68.1	99.7	99.7	>100	>100	76.2
61-120 days	Point Es.	24.7	25.8	25.1	30.7	30.7	31.6	27.9	23.8
	95% CI	10.5-36.7	11.7-37.7	10.8-37.0	16.0-42.9	16.0-42.9	16.5-44.0	10.8-41.7	8.7-36.5
	In. Width	26.2	26.0	26.2	26.9	26.9	27.5	30.9	27.8
121-180 days	Point Es.	17.0	18.3	17.3	21.2	21.2	22.0	21.4	15.5
	95% CI	8.4-24.8	9.7-26.0	8.7-25.1	11.9-29.5	11.9-29.5	12.6-30.4	10.9-30.7	5.7-24.3
	In. Width	16.4	16.3	16.4	17.6	17.6	17.8	19.8	18.6
181-265 days	Point Es.	14.3	17.0	14.5	15.5	15.5	16.4	17.9	11.3
	95% CI	1.6-25.3	4.7-27.7	1.9-25.5	0.0-28.5	0.0-28.5	0.7-29.6	1.2-31.8	-2.8-23.4
	In. Width	23.7	23.0	23.6	28.5	28.5	28.9	30.6	26.2
Overall	Point Es.	18.2	19.7	18.5	21.6	21.6	22.1	21.3	16.4
	95% CI	11.6-23.3	13.1-25.8	11.9-24.6	14.5-28.2	14.5-28.2	14.8-28.7	13.3-28.6	8.3-23.7
	In. Width	12.7	12.7	12.7	13.7	13.7	13.9	15.3	15.4
AIC (overall)		138,461.7	142,356.6	138,461.5	278,371.3	2.0	2.0	2.0	47,330.3
BIC (overall)		138,704.6	142,369.3	138,710.7	278,377.7	8.4	8.4	8.2	47,335.9

Point Es.: Point Estimation; 95% CI: 95% confidence interval; In. Width: Interval Width; AIC: Akaike's information criterion; BIC: Bayesian information criterion; M0: multivariable model; M1: PS model; M2: PS and M0 covariates; M3: IPW, M4: SIPW; M5: STIPW 1%-99%; M6: STIPW 5%-95%; M7: matching model; rVE: relative vaccine effectiveness; PS: propensity score; IPW: inverse probability weight; SIPW: stabilized inverse probability weights; STIPW: stabilized truncated inverse probability weights.

PS as a covariate (M1 and M2) and by the model run after PS-matching (M7) are very close to the rVE values estimated by the reference multivariable model (M0). On the other hand, PS models based on IPW (M3), SIPW (M4) and STIPW (M5 and M6) yield estimates that are further away from the reference multivariable model (M0), especially in the early time-interval after vaccination for STIPW models (M5 and M6).

According to several studies [9-11], SIPW (M4) can increase the variance estimate compared to that obtained with IPW (M3). Our results show the same estimated values, probably due to the homogeneity (i.e., absence of excessive skewness) of the PS values between the treated and untreated groups. A factor that influenced the difference of the estimates obtained with models M5 and M6 compared to the other models is related to having removed records with extreme PS values from the sample (truncation at level 1% removed 239,155 individuals, 2.01% of the total; truncation at level 5% removed 1,217,007 individuals, 10.24% of the total). Truncation is used to improve estimation accuracy by truncating extreme values of the PS [12], many of them falling in the first exposure level (15-60 days after vaccine uptake), when the lowest percentage of severe events (study outcome) was observed.

Based on our results, we found no clear advantage in applying PS-based methods instead of multivariable analysis. Previous studies have shown that these methodologies can produce similar results under certain conditions [14, 15], especially when the starting dataset is relatively balanced and the sample size is large [8, 16], as in our case. Moreover, it is important to note that, even using PS methods, a residual bias due to unmeasured confounders might remain, as with all analytic methods based on observational data [17, 18].

Although PS-based methods are sensitive to misspecifications of the model used to calculate it (e.g., omission of interaction effects, or misspecification of functional form of the included covariates [19]), they may still prove advantageous when many covariates are considered as potential confounders in the analysis, in which case reference models might result unstable. Furthermore in addition to the PS-based methods presented in this article, there are other PS-based methods in the literature, aiming to optimise survival data [20] and time-dependent exposure analyses [21-23]. The purpose of this study, however, was to present and compare the most widely used methods in the literature.

CONCLUSIONS

Our study, based on a large study population and a relatively low number of potential confounders, does not show advantages in using PS-based models compared to using a traditional multivariable model.

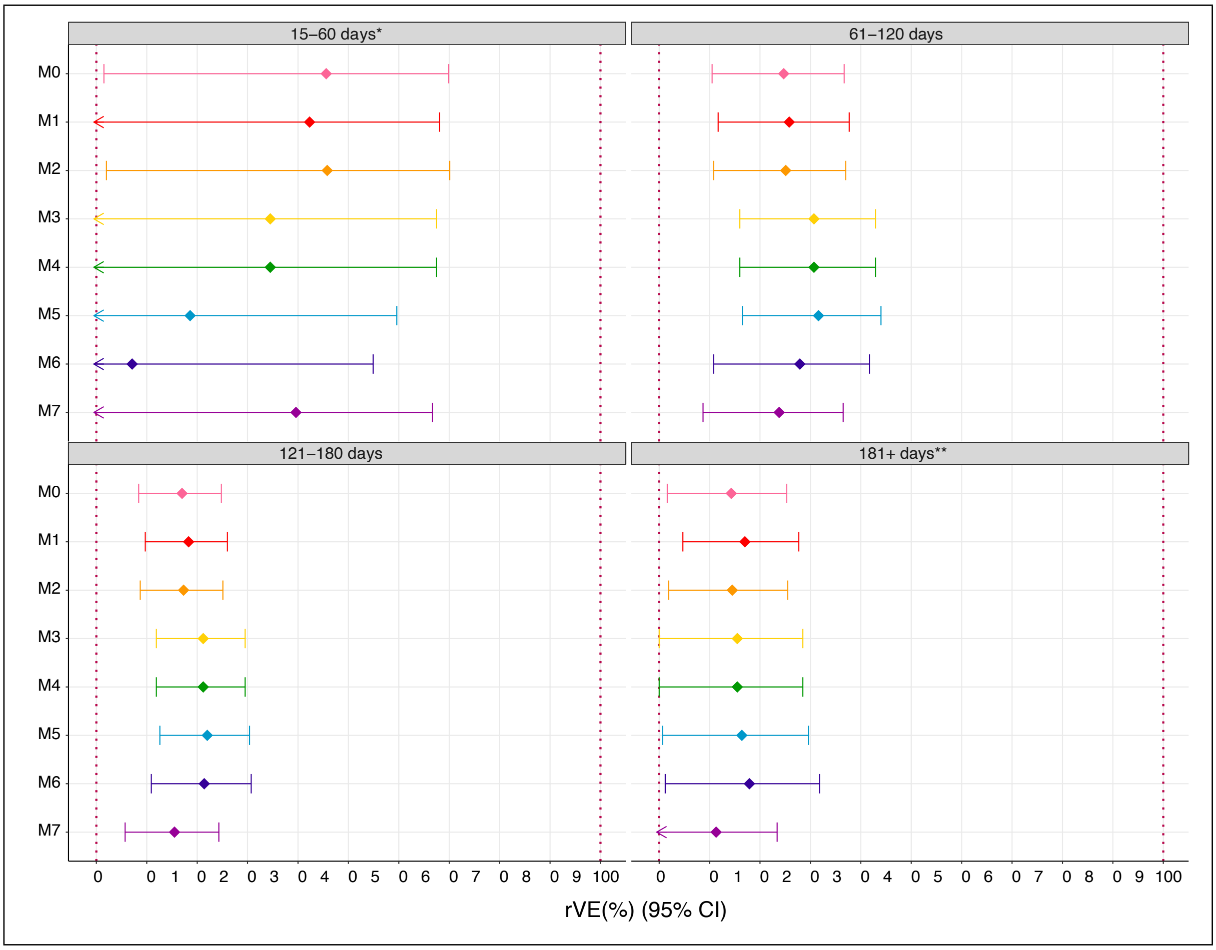


Figure 3

Point estimation and 95% confidence interval of rVE against severe COVID-19 of a second or third booster of the bivalent Original/Omicron BA.4-5 mRNA vaccine relative to a first booster of an mRNA vaccine received at least 120 days earlier with truncated lower bounds for visual clarity, Italy, 3 April-4 June 2023.

*For graphical reasons, the negative lower bounds were set at -0.5. Below are the true values: M1: -4.5%; M3 -32.2%; M4 -32.3%; M5: -64.0%; M6: -91.2%; M7: -9.5%.
**For graphical reasons, the negative lower bounds were set at -0.5. Below are the true values: M7: -2.8%.

Acknowledgments

Preliminary results of this study were presented as an abstract at the PNRR meeting held in Pavia, Lombardy, Italy, 11-12 September 2024. Daniele Petrone has a temporary PNRR contract since 19 July 2023.

Authors' contributions

PP, MF and DP designed the paper; DP, CS, AMU and MF ensured quality of COVID-19 surveillance; DP, supported by MF, AMU, CS and EAF, carried out the analysis; DP, MF, MA, AMU, EAF, CS and PP wrote the manuscript which was reviewed and approved by all Authors.

Conflict of interest statement

The Authors declare that they have no competing interests.

Funding source

This research was supported by EU funding within the NextGeneration EU-MUR PNRR Extended Partnership Initiative on Emerging Infectious Diseases (Project n. PE00000007 INF-ACT).

Received on 10 March 2025.
Accepted on 9 October 2025.

REFERENCES

1. Kahn R, Schrag SJ, Verani JR, et al. Identifying and alleviating bias due to differential depletion of susceptible people in postmarketing evaluations of COVID-19 vaccines. Am J Epidemiol. 2022;191(5):800-11. doi: 10.1093/aje/kwac015
2. Barda N. The ups and downs of observational vaccine research. Lancet Infect Dis. 2023;23(7):767-8. doi: 10.1016/S1473-3099(23)00119-6
3. Primieri C, Bietta C, Giacchetta I, et al. Determinants of COVID-19 vaccination acceptance or hesitancy in

Italy: an overview of the current evidence. Ann Ist Super Sanità. 2023;59(1):10-25. doi: 10.4415/ANN_23_01_03

4. Austin PC. An Introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res. 2011;46(3):399-424. doi: 10.1080/00273171.2011.568786
5. Fabiani M, Mateo-Urdiales A, Sacco C, et al. Relative effectiveness of bivalent original/omicron BA.4-5 mRNA vaccine in preventing severe COVID-19 in persons 60 years and above during SARS-CoV-2 Omicron XBB.1.5 and other XBB sublineages circulation, Italy, April to June 2023. Eurosurveill. 2023;28(32):2300397. doi: 10.2807/1560-7917.ES.2023.28.32.2300397
6. Austin PC. Variance estimation when using inverse probability of treatment weighting (IPTW) with survival analysis. Stat Med. 2016;35(30):5642-55. doi: 10.1002/sim.7084
7. World Health Organization. Evaluation of COVID-19 vaccine effectiveness: interim guidance, 17 March 2021. Geneva: WHO; 2021. Available from: https://iris.who.int/bitstream/handle/10665/340301/WHO-2019-nCoV-vaccine-effectiveness-measurement-2021.1-eng.pdf?sequence=1.
8. Ioannidis JPA. Factors influencing estimated effectiveness of COVID-19 vaccines in non-randomised studies. BMJ Evid Based Med. 2022;27(6):324-9. doi: 10.1136/bmjebm-2021-111901
9. Pezzi A, Cavo M, Biggeri A, et al. Inverse probability weighting to estimate causal effect of a singular phase in a multiphase randomized clinical trial for multiple myeloma. BMC Med Res Methodol. 2016;16(1):150. doi: 10.1186/s12874-016-0253-9
10. Westreich D, Cole SR, Schisterman EF, et al. A simulation study of finite-sample properties of marginal structural Cox proportional hazards models. Stat Med. 2012;31(19):2098-109. doi: 10.1002/sim.5317
11. Xu S, Ross C, Raebel MA, et al. Use of stabilized inverse propensity scores as weights to directly estimate relative risk and its confidence intervals. Value Health. 2010;13(2):273-7. doi: 10.1111/j.1524-4733.2009.00671.x
12. Crump RK, Hotz VJ, Imbens GW, et al. Dealing with limited overlap in estimation of average treatment effects. Biometrika. 2009;96(1):187-99. doi: 10.1093/biomet/asn055
13. R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2023. Available from: https://www.r-project.org/.
14. Biondi-Zoccai G, Romagnoli E, Agostoni P, et al. Are propensity scores really superior to standard multivariable analysis? Contemp Clin Trials. 2011;32(5):731-40. doi: 10.1016/j.cct.2011.05.006
15. Shah BR, Laupacis A, Hux JE, et al. Propensity score methods gave similar results to traditional regression modeling in observational studies: a systematic review. J Clin Epidemiol. 2005;58(6):550-9. doi: 10.1016/j.jclinepi.2004.10.016
16. Cepeda MS, Boston R, Farrar JT, et al. Comparison of logistic regression versus propensity score when the number of events is low and there are multiple confounders. Am J Epidemiol. 2003;158(3):280-7. doi: 10.1093/aje/kwg115
17. Xu S, Huang R, Sy LS, et al. A safety study evaluating non-COVID-19 mortality risk following COVID-19 vaccination. Vaccine. 2023;41(3):844-54. doi: 10.1016/j.vaccine.2022.12.036
18. Amoah J, Stuart EA, Cosgrove SE, et al. Comparing propensity score methods versus traditional regression analysis for the evaluation of observational data: a case study evaluating the treatment of gram-negative bloodstream infections. Clin Infect Dis. 2020;71(9):e497-e505. doi: 10.1093/cid/ciaa169
19. Chesnaye NC, Stel VS, Tripepi G, et al. An introduction to inverse probability of treatment weighting in observational research. Clin Kidney J. 2021;15(1):14-20. doi: 10.1093/ckj/sfab158
20. Chen W-C, Lu N, Wang C, et al. Propensity score-integrated approach to survival analysis: leveraging external evidence in single-arm studies. J Biophar Stat. 2022;32(3):400-13. doi: 10.1080/10543406.2022.2080701
21. Thomas LE, Yang S, Wojdyla D, et al. Matching with time-dependent treatments: a review and look forward. Stat Med. 2020;39(17):2350-70. doi: 10.1002/sim.8533
22. Zhang Z, Li X, Wu X, et al. Propensity score analysis for time-dependent exposure. Ann Transl Med. 2020;8(5):246. doi: 10.21037/atm.2020.01.33
23. Wijn SRW, Rovers MM, Hannink G. Confounding adjustment methods in longitudinal observational data with a time-varying treatment: a mapping review. BMJ Open. 2022;12(3):e058977. doi: 10.1136/bmjopen-2021-058977

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 285-292
DOI: 10.4415/ANN_25_04_07

Lymphedema and psychosocial well-being: a mixed-methods exploration of resources and challenges in the Italian context

Stefania Fantinelli[1], Teresa Galanti[2], Michela Cortini[2], Pierluigi Zolesio[3] and Chiara Buldrini[4]

[1]*Dipartimento di Scienze Teoriche e Applicate, Università degli Studi eCampus, Rome, Italy*
[2]*Dipartimento di Psicologia, Università degli Studi "G. d'Annunzio" Chieti-Pescara, Chieti, Italy*
[3]*Physical Medicine and Rehabilitation Specialist, formerly Università degli Studi di Cagliari, Cagliari, Italy*
[4]*Dipartimento di Scienze Biomediche, Chirurgiche e Odontoiatriche, Università degli Studi di Milano, Milan, Italy*

Abstract

Introduction. Individuals affected by lymphedema, both primary and secondary, experience a significant reduction in quality of life and functional capacity. However, the impact of lymphedema on occupational life, specifically on return-to-work processes, remains largely unexplored.
Objectives. This study explores the psychosocial, occupational, and health-related challenges experienced by individuals with lymphedema, with a focus on work reintegration.
Methods. A mixed-method approach was adopted through the development of an online survey, which included both standardized psychometric scales and open-ended questions.
Results. The mediation analysis confirmed that return to work self-efficacy serves as a key mechanism through which optimism contributes to job satisfaction. Qualitative findings highlight the need for multilevel and systemic interventions. From an individual perspective, targeted self-efficacy training programs for workers with lymphedema appear crucial.
Conclusions. Considering a community and an organizational perspective, it is essential to implement training initiatives for healthcare professionals aimed at improving their knowledge and awareness of lymphedema.

Key words
- lymphedema
- return-to-work
- self-efficacy
- optimism
- job satisfaction

INTRODUCTION

Primary lymphedema is a chronic condition that can present from birth, especially in syndromic and/or hereditary forms, or it can progressively develop over the course of life. In both cases, individuals must shape their identity while living with lymphedema, surely facing significant social, occupational, and psychological challenges over time.

A slightly different situation is related to individuals with secondary lymphedema: impressive advancements in cancer treatment have significantly improved survival rates. However, a modest proportion of these survivors develop secondary lymphedema, with an estimated prevalence ranging from 10% to 30%, which may further increase depending on the type of oncological treatment received (surgery, radiotherapy, chemotherapy, or combinations thereof).

This twofold experience, surviving cancer and facing a lifelong physical burden as a lasting consequence of the cure, is a source of severe psychological distress, reduced quality of life, and challenges in personal, social, and occupational domains. The relief of cancer survival can be transformed into a daily struggle with physical limitation, altered self-perception and as a condition that is often misunderstood, underestimated, and insufficiently supported in both clinical and occupational settings.

What is particularly concerning and represents a serious and urgent issue from a multidisciplinary perspective, is the unexpected gap between the remarkable, and widely praised advances in cancer treatment and the limited attention given to lymphedema, from diagnosis to treatment, as well as in both community and individual management. Indeed, it was in 2012 when a

Address for correspondence: Teresa Galanti, Dipartimento di Psicologia, Università degli Studi "G. d'Annunzio" Chieti-Pescara, Via dei Vestini 31, 66100 Chieti, Italy. E-mail: teresa.galanti@unich.it.

qualitative exploration raised critical themes commonly reported by patients with secondary lymphedema, such as social marginalization, lack of support from healthcare professionals, impact on psychological well-being [1], which are still profoundly relevant today.

Despite the several studies on lymphedema across the years, the significant gap in psychosocial dimensions persists, even more concerning the professional lives of patients with lymphedema. Therefore, the aim of this mixed-method study is twofold:

- to explore the lived experience of individuals affected by lymphedema and the impact of this condition on their quality of life;
- to investigate whether individual and dispositional variables interact to support a successful return to work after lymphedema diagnosis.

The following sections of the manuscript present the theoretical framework related to psychological impact of lymphedema, dispositional optimism, job satisfaction and return-to-work self-efficacy.

LITERATURE REVIEW

According to our literature review, the first study examining lymphedema from a psychological perspective was conducted by Williams *et al*. [2]. Authors collected data from a very small sample of 15 individuals with different types of lymphoedema, exploring their experiences and perceptions. As a result, the theme of *uncertainty* emerged as a key major concern, as patients had very little information about lymphedema and it was a very disorienting factor.

Others critical psychological domains relevant to patients with lymphedema have emerged across several studies, mainly in United States (US), the most frequently reported difficulties were: body image disturbance, a negative perception of self, negative emotions such as fear, sadness, and loneliness, psychological distress, social isolation [1, 3-5].

The existing literature on the psychosocial impact of lymphedema is relatively extensive but remains largely focused on narrowly defined populations, particularly breast cancer survivors. One of the earliest and rare studies to explore perceptions and experiences in the work environment was conducted by Fu [6], their results highlighted a lack of support in the workplace and difficulties in performing specific physical tasks, featuring the occupational challenges faced by individuals with lymphedema [6].

Several subsequent studies investigated the psychosocial consequences of lymphedema, primarily in the context of breast cancer survivors [7-9]; a constant pattern emerged: patients with lymphedema reported significantly poorer general well-being compared to cancer survivors without lymphedema. These findings confirm a distinct psychological level associated with the lymphedema condition, more demanding of the experience of cancer alone.

A hypothetical complementary perspective is offered by Ridner *et al*. [1], who emphasized the critical role of nursing professionals in patient education and interdisciplinary training. Their study, which also focused on breast cancer survivors with lymphedema in the US, highlighted the importance of providing both patients and healthcare providers with knowledge about the physical and psychosocial challenges associated with lymphedema.

With regard to social consequences, such as work reintegration or employability concerns, research has demonstrated that lymphedema can cause negative measurable consequences in terms of reduced productivity [10], changing work roles [11], or career abandonment [10, 12]. The majority of studies considered women with post breast cancer lymphedema, thereby framing work-related challenges primarily in relation to physical limitations deriving from the impaired arm function.

Moreover, literature shows as workplace relationships with both colleagues and supervisors are affected by the lymphedema condition, making the return to work even more demanding because of the risk of stigmatization, a general lack of knowledge of the lymphedema among colleagues and supervisors, and the reduced perceived social support [13].

However, some studies also documented evidence of supportive interpersonal relationships at work, which can be a key resource enhancing a successful return to work. Perceived social support in the workplace has been also associated with improved quality of life among workers with lymphedema [14]; these research findings indicate that occupational health professionals can play an important role in raising awareness about lymphedema, and in facilitating a more inclusive and supporting return to work process [14, 15].

In the broader context of return to work after chronic illnesses or cancer diagnoses, there is an extensive literature on breast cancer survivors and only a portion of studies includes specifically individuals affected by lymphedema. What emerges as a recurrent and common theme across different conditions is the multidimensionality of the return-to-work experience. It is a process influenced by clinical dimensions, psychosocial factors, occupational and social environments and relationships [16, 17]. The return to work is also a rich symbolic phase, it cannot be reduced to a mere functional need of individuals who desire to overcome the physical consequences of the chronic condition, such as pain, fatigue, or swelling due to lymphedema. Returning to work represents a crucial stage in regaining a sense of personal control, identity and quality of life [18]. With a specific attention to return to work after diagnosis of lymphedema, the available evidence from the literature suggests a series of interrelated both positive and negative factors, which can be categorized into two main categories: individual or dispositional variables and contextual or environmental variables.

The latter ones, the contextual factors, include workplace relationships, policies, and dynamics that can either facilitate or threaten a successful return to work; these factors include positive dimensions such as perceived support from employers and co-workers, the flexibility of tasks and workstation as well. Conversely, those work contexts that lack adaptability or open communication, may enhance exclusion and feeling of psychological distress [19].

Moreover, the contextual elements are able to deeply impact a successful reintegration process, which should be meant as a profound social and psychological change and challenge, not a merely functional or logistical issue.

With regard to individual variables, there are demanding and objective physical constraints derived by the lymphedema condition, such as swelling, reduced mobility, or pain [17]. In addition, some psychological dimensions have been identified as potential barriers to an effective reintegration, and they are anxiety, reduced self-esteem, or depression [17, 18]. The positive side of psychological factors is represented by coping strategies, proactive attitude, self-efficacy, or resilience; for instance, individuals with higher levels of resilience and self-efficacy, reported a more effective return to work [18]. Moreover, evidence shows how coping strategies can be developed and learnt through experience, in particular when facing a challenging task as it is a new functional and physical status [13].

There are some specific psychological resources, which have received greater attention in the realm of specific theoretical models such as the social cognitive theory [20] that emphasizes the central role of self-efficacy in shaping personal goals and behaviours. Specifically, return to work self-efficacy refers to individuals' confidence in their ability to perform work related tasks in spite of physical or psychological limitations, or changes derived from a chronic illness. According to Bandura, self-efficacy is a powerful psychological mechanism able to produce an impact on wellbeing and general satisfaction with life; it is a significant predictor of motivation and successful occupational reintegration [21, 22].

Several studies have often suggested a relation between positive health outcomes and a personal characteristic, such as dispositional optimism. Research findings have linked optimism to some clinical and objective data, for example optimistic women resulted more likely to show a slower progression of carotid artery disease [23]; optimistic people with multiple sclerosis seem to have an easier pursuing life goal [24]; optimism has been associated also with a reduction of pain perception [25]. Thus, optimism has been shown in the literature to have a significant positive impact on psychological and physical well-being, but very few studies have investigated its role on return-to-work outcomes [26]. It seems to us particularly interesting to explore the potential interaction between these two key dispositional variables: return to work self-efficacy and optimism. They have a profound difference as the former can be trained and strengthened over time, as a dynamic factor. In contrast, optimism is considered as a stable personality trait, although in some conditions it may increase or decrease, depending on life events [27]. Some questions drove the hypotheses formulation: could a high level of optimism facilitate a more efficient and satisfactory return to work process? What can be the interplay between optimism and self-efficacy in the return to work after lymphedema diagnosis?

Based on these premises and framed by the theoretical approach defined by the social cognitive theory [28], this study proposes the following hypotheses (H).

H1. Dispositional optimism was positively associated with job satisfaction. Although this relationship has been supported in previous studies, we aimed to further test it in the specific context of return to work after lymphedema. Furthermore, dispositional optimism is thought to enhance individuals' belief in their ability to manage challenging situations, which aligns with the construct of return-to-work self-efficacy. Since optimistic individuals tend to approach setbacks with greater motivation and persistence, we hypothesized that dispositional optimism would be positively associated with return-to-work self-efficacy (H2).

Self-efficacy, in turn, is a well-established predictor of job attitudes. Employees who feel capable of performing their duties are more likely to experience positive emotions at work and report higher satisfaction. In line with previous literature on work reintegration and self-efficacy, e.g., [28, 29], H3 postulated a positive association between return-to-work self-efficacy and job satisfaction.

Finally, drawing from social cognitive theory, we expected that return-to-work self-efficacy would mediate the relationship between dispositional optimism and job satisfaction. This mediated model (H4) suggests that optimism indirectly enhances job satisfaction by fostering greater self-efficacy in managing work after lymphedema, highlighting a pathway through which personal traits influence work-related outcomes in the context of chronic illness recovery.

In addition, as the occupational life of individuals with lymphedema is still underexplored, this study also aimed to give voice to the personal and subjective dimensions of living with this chronic condition. To this end, a set of exploratory, open-ended questions was included with the specific aim of identifying key areas or themes that may inform the design and implementation of targeted future interventions.

METHODS

The study adopted a triangulated research design to ensure both the heuristic effectiveness of qualitative data and the reliability of quantitative techniques. In light of the methodological appropriateness paradigm [30], it was particularly important to investigate the research topic by a multidimensional approach as the phenomenon under investigation is complex and still partly unexplored.

Within this framework, an online *ad hoc* questionnaire was structured, including a brief section with open-ended questions and a survey with psychometric scales. The survey included the measures described below, followed by a series of open-ended questions to identify key areas or themes related to lymphedema experience.

Dispositional optimism was assessed using the 6-item scale developed by Chiesi *et al.* [31], an example of an item is: "In moments of uncertainty, I usually expect the best". Job satisfaction was assessed using the 3-item scale developed by Hackman *et al.* [32]; an example item is: "In general, I like working here". Return-to-work self-efficacy was assessed with the 11-item scale of Gjengedal *et al.* [33], an example item is: "I will be able to carry out my tasks at work." For each of these scales, a 5 or 7-point Likert scale (1="strongly disagree", 5 or 7="strongly agree") was used.

Data were analyzed applying the principles of grounded theory methodology [34], specific attention was also given to metaphors, symbolic representations, and individuals' narratives, thus contributing to a data-driven theoretical interpretation.

All research procedures complied with international ethical standards, despite the inclusion of human participants the ethical approval was not necessary for this study, because of the absence of specialized procedures or treatments that might inflict stress or harm on the participants. The research adheres to the principles outlined in the Declaration of Helsinki (World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects, 2024). Additionally, participants were informed about the handling of personal data, and we ensured anonymity in accordance with European Union (EU) Regulation. All participants were informed about the nature and purpose of the research and voluntarily participated after giving informed consent, in accordance with the principles of the General Data Protection Regulation (EU Regulation 2016/679). Participants were also explicitly informed that the data would be anonymized and used solely for research purposes in their aggregated way.

RESULTS

Participants and procedures

The cross-sectional study presented here was conducted from September 2024 to April 2025. The data collection took place online through a questionnaire with closed and open questions, administered via the Qualtrics platform, which took about 15 minutes to complete. The study sample comprises 131 individuals, 9 of whom were excluded due to incomplete data, resulting in a final sample of 122 participants. Of these, 11 were men and 111 women, with ages ranging from 21 to 87 years (mean=53.90, standard deviation, SD=2.47). Participants came from various parts of Italy: 39% from the North, 17.1% from the Centre, and 43.8% from the South, reflecting a fairly heterogeneous geographical distribution. Regarding educational attainment, 49.2% had completed secondary school, 6.6% held a three-year bachelor's degree, 36.1% held a two-year master's degree, and 8.2% had a postgraduate master's qualification or a doctoral degree. Regarding marital status, 62.3% of participants reported being married or in a domestic partnership, 24.6% were single, 4.1% were widowed, and 9% were separated or divorced.

Concerning the clinical characteristics, 51 participants reported being affected by primary lymphedema and 71 by secondary lymphedema. In 44 cases, the condition affected the upper limbs, and in 78 cases, the lower limbs. The onset occurred less than one year prior in 6.6% of cases, less than five years prior in 24.6%, between five and ten years prior in 30.3%, and more than ten years prior in the remaining 38.5%.

Most participants (64.8%) reported returning to work within six months of diagnosis, while 7.4% were unable to do so due to the condition. Another 15.6% were no longer employed at the time of diagnosis. Overall, 77 participants were employed, 10 unemployed, 4 on leave or sabbatical, and 31 retired. The majority (77%) reported current or past employment involving direct contact with clients or the public, while only 40% had held leadership or coordination roles. Descriptive statistics, correlations, and Cronbach's alphas are reported in *Table 1*. All variables correlate in the expected direction.

The qualitative section was created according to the explorative aim of the study; some questions are reported as follows:

- Which is your personal experience living with lymphedema (in terms of clinical, social, occupational dimensions)?
- Can you tell us what are the major challenges that you are facing because of lymphedema?

Qualitative evidences

The triangulation approach was ensured through both data collection and data analysis of qualitative information [35], in order to raise trustworthiness of data, to fully capture and maximise the participants' impressions and perceptions, and to enhance the understanding of the phenomenon. This procedure is consistent with the Standard for Reporting Qualitative Research (SRQR) [36] and it follows the guidelines established by the Critical Appraisal Skills Programme [37] for qualitative research.

The explorative and bottom-up analysis was performed independently by two separate researchers, with subsequent accordance calculated, conforming to the Cohen Kappa (0.87). The research team adopted an iterative and reflexive process to analyse and interpret the textual material, this process implied full openness to participants' contributions. Through the identification of recurring themes or patterns expressed by individuals, a categorical tree was developed to systematically organize and interpret the qualitative findings.

Table 1
Descriptive statistics for gender, Cronbach's alphas, and correlations among the variables

	2	3	Mean female	Mean male	SD female	SD male	Cronbach alfa
Satisfaction	0.534**	0.339**	5.00	5.71	1.31	0.98	0.91
RTW self-efficacy		0.336**	4.32	4.98	0.67	0.69	0.81
Dispositional optimism			3.67	4.64	1.02	0.54	0.80

SD: standard deviation; RTW: return to work self-efficacy; **the correlation is significant at the 0.01 level (two-tailed).

Four main themes emerged, each of which was related to others through both meaning and life implications:

1. personal and social identity: most participants (36 occurrences) reported feelings of discomfort, shame, and isolation. For instance, one participant stated: "I feel constantly observed and uncomfortable when I am around others"; others explicitly mentioned perceptions of shame or embarrassment. These narratives tell that lymphedema is not only a medical condition, but the physical manifestation is a threat to the expression of identity and self-confidence, and it directly impacts patients' ability to maintain their professional roles. The cycle starts with physical symptoms and aesthetic changes, affecting self-image, which in turn undermine occupational identification;
2. occupational or professional challenges: several participants (28 occurrences) refer to work and the professional sphere. In particular, 9 participants talk about work-related difficulties due to physical symptoms (pain, swelling, fatigue, posture). Some examples are: "At the end of the working day I no longer have the strength to do anything", "It is no easy to manage this condition: you must steal time from everyday life, family and work", "Certain jobs are detrimental for lymphedema". 9 participants refer to work limitations and adjustments after lymphedema diagnosis, including economic costs, such as: "I requested part-time work to allow more time for care" or "I was reassigned to lower-level tasks that are more compatible with the disease". 8 participants declare a lack of protections and recognition of disability (e.g., "Those with secondary lymphedema are not considered unfit for work by the national social security system"; "It is unfair that it is not officially recognized as a disabling condition"). Finally, only 2 participants underline resilient work experiences ("I am lucky to work from home, which allows me to manage this condition" and "I have been able to maintain a decent quality of life thanks to workplace adjustments"). These experiences reveal how the workplace can amplify social exclusion and reduce autonomy, and highlight the compelling need for organizational policies more sensitive to chronic conditions like lymphedema;
3. psychological well-being: 42 participants refer to the concept of overall well-being, articulating the discourse in different ways, reflecting the complex and multifaceted nature of living with lymphedema. The most frequently represented aspects were psychological well-being and self-acceptance (14 occurrences). Participants described the emotional difficulty of accepting the illness and its visible consequences, often referring to psychotherapy or personal reflection as crucial steps toward adaptation. Statements such as: "I don't accept myself physically", "I had to start psychotherapy", and "I'm beginning to find some balance" highlight the ongoing process of rebuilding one's identity and emotional stability. References to quality of life and daily functioning (10 occurrences) reflect the profound impact of lymphedema on daily living. Respondents write that the disease "changes one's life completely" and "transforms everyday routines", making simple actions more complicated. Mentions of physical well-being, health, and symptom management (9 occurrences) revealed how much effort is invested in maintaining bodily functionality. Participants stressed the importance of exercise, compression garments, and adherence to medical advice "I try to keep my leg active", "I'm forced to use compression aids", or "I manage it autonomously following physiotherapists' guidance". A smaller number of participants address relational well-being and social support (6 occurrences), emphasizing how understanding from relatives or contact with other patients could sustain motivation and psychological balance. For instance, "The people around me understand my difficulties" or "Talking with other patients helped me overcome my limits";
4. lack of knowledge about lymphedema: one of the most meaningful metaphoric statements was: "we are totally groping in the dark". Several participants (30 occurrences) reported that they experienced a profound knowledge gap since post oncological interventions, where healthcare professionals often do not inform patients about the potential onset of lymphedema. Moreover, participants revealed a sense of frustration and disorientation for the diagnosis: "Doctors need to be trained to avoid delayed diagnoses and prevent mistakes".

In addition to the identified specific categories, an interesting theme emerged from some participants: someone expressed gratitude toward the researchers for the collecting data initiative. This expression of gratitude is perfectly coherent with the feeling of being lost or confused among the healthcare sector and it also coexists with the declared limited knowledge about lymphedema.

Thus, qualitative data call for a more holistic and patient-centered approach, where invisible consequences of the disease need to be addressed in order to protect personal identity, psychosocial well-being and occupational or social roles. The specific interest toward occupational context and the return-to-work personal resources, was investigated through the quantitative section of the study, as illustrated in the following paragraphs.

Quantitative results

We tested the hypotheses of this study by running the mediation model in PROCESS for SPSS [38]. *Figure 1* shows that dispositional optimism was positive but not significantly related to job satisfaction (B=0.22; p=0.08), thus disconfirming H1. In contrast, dispositional optimism was positively and significantly associated with return-to-work self-efficacy (B=0.25; p=0.002), confirming H2. The relationship between return-to-work self-efficacy and job satisfaction was positive and significant (B=0.78; p=0.000), confirming H3. The mediation hypothesis (H4), according to which dispositional optimism relates through job satisfaction with return-to-work self-efficacy, was confirmed (B=0.20; p=0.07).

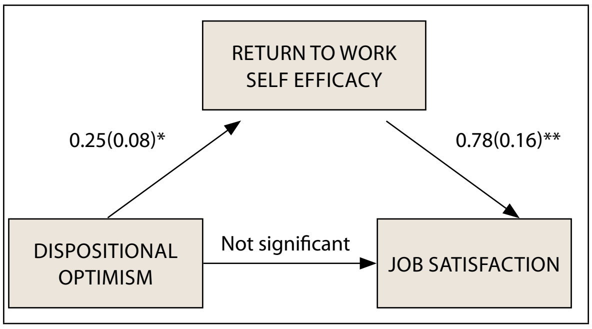


Figure 1
Conceptual model of the hypothesized mediation.
(*): $p<0.05$; (**): $p<0.01$.

DISCUSSION

The findings of this study offer important insights into the psychological factors that may facilitate return to work among individuals living with lymphedema. Contrary to our expectations, dispositional optimism was not significantly directly associated with job satisfaction, suggesting that optimism alone may not directly translate into more positive evaluations of one's work experience following a chronic condition. This result contrasts with previous research linking optimism to workplace wellbeing [26] and may reflect the specific challenges and constraints faced by individuals coping with a chronic and visible condition like lymphedema, which can moderate the impact of general positive expectations.

However, optimism did show a significant and positive relationship with return-to-work self-efficacy, supporting the idea that optimistic individuals are more likely to believe in their capacity to manage the transition back to work after illness. This aligns with the self-regulatory role of optimism in coping with adversity [39] and highlights its value as a resource for promoting confidence in work-related functioning despite physical limitations.

As predicted, return to work self-efficacy was strongly and significantly related to job satisfaction, reinforcing existing evidence on the central role of self-efficacy beliefs in shaping work attitudes and motivation, particularly in rehabilitation contexts. Importantly, the mediation analysis confirmed that return to work self-efficacy serves as a key mechanism through which optimism contributes to job satisfaction. This indirect effect suggests that optimism enhances satisfaction at work not by directly altering perceptions of the job itself, but by increasing individuals' belief in their ability to effectively re-engage with work demands. Taken together, these results underscore the importance of fostering psychological resources – especially self-efficacy beliefs – during the return-to-work process for individuals with lymphedema. Interventions aimed at enhancing optimism and, more critically, return to work self-efficacy, may be particularly effective in improving work reintegration outcomes and subjective well-being at work in this population.

Moreover, it is reasonable to question whether there may be a difference in the level of awareness and perception of the condition between individuals who enter the workforce already living with primary lymphedema, and those who, having developed secondary lymphedema later in life, face the challenge of returning to work after the diagnosis.

In a more in-depth way, the qualitative evidence collected through patient interviews reveals the profound and multifaceted impact of living with lymphedema, both primary and secondary, on individuals' daily lives, psychosocial well-being, and occupational experiences, partly already confirmed in past literature [40]. Participants highlight recurring themes of physical limitations, and the persistent psychological strain associated with the condition. A significant number of individuals emphasized feelings of frustration and isolation, often exacerbated by the lack of awareness and understanding of lymphedema among healthcare professionals and the community in general. Another serious and critical barrier is represented by inadequate access to specialized care, high costs of care, and the scarcity of trained healthcare professionals. At the same time, some patients expressed resilience, reporting that consistent self-management, lifestyle adaptations, and lucky encounters with competent healthcare providers contributed to maintaining an acceptable quality of life. However, the psychological and emotional burden, difficulties in body image acceptance, high challenging return to work, and limited social recognition of the disease remain significant demanding tasks. From an organizational perspective, employers should adopt inclusive workplace practices and tailored support mechanisms, aligned with diversity and disability management principles [41].

STUDY LIMITATIONS

Despite offering valuable insights into the psychological and occupational experiences of individuals living with lymphedema, this study is not without limitations. First, the cross-sectional design does not allow for causal inferences: while mediation relationships were tested, the direction of the associations remains theoretical and should be confirmed through longitudinal research. Second, the sample size may limit the generalizability of the quantitative findings, particularly in capturing the heterogeneity of experiences between individuals with primary and secondary lymphedema. Future studies should aim to include larger and more diverse samples to strengthen external validity. Moreover, the reliance on self-report measures may have introduced bias due to social desirability or subjective interpretation of results, the depth and nuance of participants' experiences may be constrained by the format and length of questions.

Importantly, systemic issues such as healthcare accessibility, financial burden, and lack of professional training in lymphedema care – highlighted in the qualitative findings – suggest that individual-level interventions alone may not be sufficient to address return to work challenges.

FUTURE RESEARCH DIRECTIONS

Starting from the present findings, future research should adopt longitudinal designs to better capture the dynamic nature of psychological adjustment and return-to-work trajectories among individuals with lymphedema. Tracking changes in optimism, self-efficacy, and job satisfaction over time would allow for a more precise understanding of how these variables interact and influence each other throughout the rehabilitation and reintegration process. In addition, further studies should explore potential moderating variables, such as type of employment, workplace accommodations, severity of lymphedema, or access to healthcare services, that may affect the return-to-work experience. Lastly, intervention-based studies are needed to test the effectiveness of programs designed to enhance return to work self-efficacy and psychological resilience in this population.

CONCLUSIONS

According to our literature review, this study represents the first and, to date, the only research in Italy addressing a specific and targeted sample of individuals affected by both primary and secondary lymphedema. Even more significant, from our point of view, is the focus on effective reintegration, which remains largely unexplored, except for studies on samples of individuals with lymphedema related to specific types of cancer.

Our findings highlight the potential relevance of promoting interventions aimed at enhancing individuals perceived self-efficacy in relation to returning to work. Other key findings include the relevance of psychological dimensions in shaping the lived experience of people with lymphedema; moreover, participants strongly emphasize the widespread lack of awareness and clinical expertise regarding lymphedema within the healthcare system.

These findings underscore the urgent need for a systemic and coordinated approach at multiple levels, highlighting the lymphedema as a complex, disabling condition requiring integrated, and person-centered care. In particular, return-to-work processes for people living with lymphedema should not only focus on individual psychological resources, but also be embedded in broader organizational efforts to implement effective diversity management strategies. Creating supportive work environments that are responsive to the needs of employees with chronic and visible conditions can contribute to both personal well-being and organizational health.

Acknowledgments

The Authors would like to express their sincere gratitude to the Association against Lymphedema Resilia ETS (Associazione contro il Linfedema Resilia Ente del Terzo Settore) for their invaluable collaboration, for facilitating participant recruitment, and for having proposed the development of this research.

Authors' contributions

SF conceptualized and designed the study; TG and SF analysed the data; SF and TG wrote the first draft; CB and PZ critically reviewed the manuscript. All Authors have revised the manuscript and approved its final version.

Conflict of interest statement

None of the Authors declare competing financial interests.

Received on 4 July 2025.
Accepted on 9 October 2025.

REFERENCES

1. Ridner SH, Bonner CM, Deng J, Sinclair VG. Voices from the shadows: living with lymphedema. Cancer Nurs. 2012;35(1):E18-E26. doi: 10.1097/ncc.0b013e31821404c0
2. Williams A, Moffatt C, Franks P. A phenomenological study of the lived experiences of people with lymphoedema. Int J Palliat Nurs. 2004;10:279-86. doi: 10.12968/ijpn.2004.10.6.13270
3. Fu MR, Rosedale M. Breast cancer survivors' experiences of lymphedema-related symptoms. J Pain Symptom Manage. 2009;38:849-59. doi: 10.1016/j.jpainsymman.2009.04.030
4. Maxeiner S, Downer A. Comparing the psychosocial issues experienced by individuals with primary vs secondary lymphedema. Rehab Oncology. 2009;27(2):9-15.
5. Bulley C. Making a case for funding for lymphoedema services. J Lymphoedema. 2007;2:22-9.
6. Fu MR. Women at work with breast cancer related lymphoedema. J Lymphoedema. 2008;3:20-7.
7. Ridner S. Quality of life and a symptom cluster associated with breast cancer treatment related lymphedema. Support Care Cancer. 2005;13:904-11. doi: 10.1007/s00520-0050810-y
8. Lam R, Wallace A, Burbidge B, Franks P, Moffatt C. Experiences of patients with lymphoedema. J Lymphoedema. 2006;1:16-21.
9. Paskett ED, Naughton MJ, McCoy TP, Case LD, Abbott JM. The epidemiology of arm and hand swelling in premenopausal breast cancer survivors. Cancer Epidemiol Biomarkers Prev. 2007;16:775-82. doi: 10.1158/1055-9965.epi-06-0168
10. Boyages J, Kalfa S, Xu Y, Koelmeyer L, Mackie H, Viveros H, Taksa L, Gollan P. Worse and worse off: the impact of lymphedema on work and career after breast cancer. Springerplus. 2016;5:1-8. doi: 10.1186/s40064-016-2300-8
11. Vignes S, Fau-Prudhomot P, Simon L, Sanchez-Bréchot ML, Arrault M, Locher F. Impact of breast cancer-related lymphedema on working women. Support Care Cancer. 2020;28:79-85. doi: 10.1007/s00520-019-04804-2
12. Mehnert A. Employment and work-related issues in cancer survivors. Crit Rev Oncol Hematol. 2011;77(2):109-30. doi: 10.1016/j.critrevonc.2010.01.004
13. Sun Y, Shigaki CL, Armer JM. The influence of breast cancer related lymphedema on women's return-to-work. J Women's Health. 2020;16. doi: 10.1177/1745506520905720
14. Huang Z, Zu S. Acceptance of disability, coping style, perceived social support and quality of life among patients with chronic lymphedema: a cross-sectional study. Support Care Cancer. 2022;30(5):4099-108. doi: 10.1007/s00520-022-06855-4

15. Kalfa S, Koelmeyer L, Taksa L, Winch C, Viveros H, Gollan PJ, MackieH, Boyages J. Work experiences of Australian cancer survivors with lymphoedema: a qualitative study. Health Soc Care Community. 2019;27(4):848-55. doi: org/10.1111/hsc.12698
16. Ruggieri R, Gabanelli P, Belluccio C, Giorgi I, Fiabane E. Carcinoma mammario e reinserimento lavorativo: barriere e facilitatori. G Ital Med Lav Erg. 2021;43(1):66-73.
17. Magnavita N, Di Prinzio RR, Meraglia I, Vacca ME, Arnesano G, Merella M, Mauro I, Iuliano A, Terribile DA. Supporting return to work after breast cancer: a mixed method study. Healthcare. 2023;11(16):2343. doi: 10.3390/healthcare11162343
18. Fiabane E, Dordoni P, Perrone C, Bernardo A, Corsi F, Gabanelli P. What really matters for returning to work after breast cancer? A 6-month exploratory study. Women & Health. 2024;64(4):298-307. doi:10.1080/03630242.2024.2324312
19. Mak C, Waller C, Barfoot J, Whittingham K. Psychological flexibility, professional quality of life and psychological adjustment in workers in the disability sector. J Workplace Behav Health. 2025;40(2):178-94. doi: 10.1080/15555240.2024.2432334
20. Bandura A. Health promotion from the perspective of social cognitive theory. In Bandura A (Ed). Understanding and changing health behaviour. East Sussex (UK): Psychology Press; 2013. p. 299-339.
21. Rosbjerg R, Hansen DG, Zachariae R, Hoejris I, Lund T, Labriola M. The predictive value of return-to-work self-efficacy for return to work among employees with cancer undergoing chemotherapy. J Occup Rehabil. 2020;30(4):665-78. doi: 10.1007/s10926-020-09882-2
22. Wolvers MDJ, Leensen MCJ, Groeneveld IF, Frings-Dresen MHW, De Boer AGEM. Predictors for earlier return to work of cancer patients. J Cancer Surviv. 2018;12(2):169-77. doi: 10.1007/s11764-017-0655-7
23. Matthews KA, Räikkönen K, Sutton-Tyrrell K, Kuller LH. Optimistic attitudes protect against progression of carotid atherosclerosis in healthy middle-aged women. Psychosom Med. 2004;66:640-4. doi: 10.1097/01.psy.0000139999.99756.a5
24. Hart SL, Vella L, Mohr DC. Relationships among depressive symptoms, benefit-finding, optimism, and positive affect in multiple sclerosis patients after psychotherapy for depression. Health Psychol. 2008;27:230-8. doi: 10.1037/0278-6133.27.2.230
25. Geers AL, Wellman JA, Fowler SL, Helfer SG, France CR. Dispositional optimism predicts placebo analgesia. J Pain. 2010;11:1165-71. doi: 10.1016/j.jpain.2010.02.014
26. Myhren H, Ekeberg Ø, Stokland O. Health-related quality of life and return to work after critical illness in general intensive care unit patients: a 1-year follow-up study. Crit Care Med. 2010;38(7):1554-61. doi:10.1097/CCM.0b013e3181e2c8b1
27. Scheier MF, Carver CS. Dispositional optimism and physical health: A long look back, a quick look forward. Am Psychol. 2018;73(9):1082. doi: 10.1037/amp0000384
28. Bandura A, Wessels S. Self-efficacy. Cambridge: Cambridge University Press; 1997.
29. Judge TA, Bono JE. Relationship of core self-evaluations traits-self-esteem, generalized self-efficacy, locus of control, and emotional stability-with job satisfaction and job performance: a meta-analysis. J Appl Psychol. 2001;86:80-92. doi: 10.1037/0021-9010.86.1.80
30. Patton MQ. Qualitative evaluation and research methods. Thousand Oaks (CA): SAGE Publications; 1990.
31. Chiesi F, Galli S, Primi C, Innocenti Borgi P, Bonacchi A. The Accuracy of the Life Orientation Test-Revised (LOT-R) in measuring dispositional optimism: Evidence from item response theory analyses. JPA. 2013;95(5):523-9. doi: 10.1080/00223891.2013.781029
32. Hackman JR, Oldham GR. Development of the job diagnostic survey. J Appl Psychol. 1975;60(2):159. doi: 10.1037/h0076546
33. Gjengedal RG, Lagerveld SE, Reme SE, Osnes K, Sandin K, Hjemdal O. The return-to-work self-efficacy questionnaire (RTW-SE): a validation study of predictive abilities and cut-off values for patients on sick leave due to anxiety or depression. J Occup Rehabil. 2021;31:664-73. doi: 10.1007/s10926-021-09957-8
34. Glaser BG, Strauss AL. Grounded theory. 1998. Strategien qualitativer Forschung. Bern: Huber; 1998.
35. Cortini M, Tria S. Triangulating qualitative and quantitative approaches for the analysis of textual materials: An introduction to T-lab. Soc Sci Comput Rev. 2014;32:561-8. doi: 10.1177/0894439313510108
36. 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
37. Critical Appraisal Skills Programme. CASP qualitative checklist. Cambridge: CASP; 2018. Available from: https://casp-uk.net/wp-content/uploads/ 2018/01/CASP-Qualitative-Checklist-2018.pdf.
38. Hayes AF. Mediation, moderation, and conditional process analysis. Introduction to mediation, moderation, and conditional process analysis: A regression-based approach. New York NY: The Guilford Press; 2018.
39. Rasmussen HN, Wrosch C, Scheier MF, Carver CS. Self-regulation processes and health: the importance of optimism and goal adjustment. Journal of Personality. 2006;74(6):1721-48. doi:10.1111/j.1467-6494.2006.00426.x
40. Fu MR, Ridner SH, Hu SH, Stewart BR, Cormier JN, Armer JM. Psychosocial impact of lymphedema: a systematic review of literature from 2004 to 2011. Psycho-Oncology. 2013;22:1466-84. doi: https://doi.org/10.1002/pon.3201
41. Fantinelli S, Di Fiore T, Marzuoli A, Galanti T. Self-perceived employability of workers with disability: a case study in an educational farm. Frontiers in Psychology. 2022;13:871616.

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 293-300
DOI: 10.4415/ANN_25_04_08

Examining the "worried well" phenomenon: insights from Italy's AIDS and STIs Helpline

Matteo Schwarz[1], Pietro Gallo[1], Anna Colucci[1], Emanuele Fanales Belasio[1], Rudi Valli[1], Rosa Dalla Torre[1], Camilla Gallo[2] and Anna D'Agostini[1]

[1] *Unità Operativa Ricerca Psico-Socio-Comportamentale, Comunicazione, Formazione, Dipartimento Malattie Infettive, Istituto Superiore di Sanità, Rome, Italy*
[2] *Media, Comunicazione Digitale e Giornalismo, Sapienza Università di Roma, Rome, Italy*

Abstract

Background. The fear of having contracted HIV or another sexually transmitted infection (STI), even in the absence of significant risk factors, is a globally observed phenomenon across diverse cultural, social, and healthcare settings. Helplines serve as a valuable observatory for this pattern, often described as "worried well" (WW). This study investigates the WW phenomenon with the objective of assessing whether the COVID-19 pandemic has acted as a compounding factor in its intensification.

Methods. AIDS and STIs Helpline of the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) extracted data from a structured database and analyzed patterns related to callers' concerns.

Results. Between 2018 and 2023, 4,703 calls were analysed, showing how WWs represent 8.1% of all users and questions asked by WWs accounted for 7.8% of the total number of questions received by the AIDS and STIs Helpline.

Conclusions. While the COVID-19 pandemic may have contributed to an intensification of the WW phenomenon, its origins are more deeply rooted in factors such as psychological distress and limited health literacy.

Key words
- HIV
- AIDS
- STIs
- counselling
- worried well

INTRODUCTION

Over the years, several health services specializing in sexually transmitted infections have documented and examined the phenomenon commonly referred to in the literature as the "worried well" (WW).

Worried well individuals are those who experience excessive distress or anxiety concerning their health and who engage in frequent, often repetitive, health-related searches on the Internet, which tend to exacerbate rather than alleviate their concerns. In the context of HIV, AIDS, and other sexually transmitted infections (STIs), this phenomenon is particularly salient, as it often manifests as a pronounced form of health anxiety that can significantly impair daily functioning, occupational performance, and overall psychosocial well-being [1]. In the scientific literature, these subjects are often referred to as "worried well people" or as subjects suffering from venerophobia [2-5].

The terminology may imply the absence of pathological conditions; however, the state referred to as "worried well" can be profoundly debilitating for the individual.

It is inappropriate to dismiss anxiety associated with such conditions as clinically irrelevant solely due to the absence of identifiable risk factors, as this anxiety may in fact reflect an underlying pathological condition warranting clinical attention [6].

Evidence of this phenomenon has been documented by the Dutch AIDS Information Helpline, where individuals classified as "worried well" frequently utilize telephone-based services related to sexually transmitted infections. Notably, in approximately half of the calls received, users assessed their own risk profile as greater than that estimated by the operator, with the most commonly sought form of assistance being reassurance regarding the absence of risk. [7].

Based on the experience of the AIDS and STIs Helpline of the Italian National Institute of Health (Istituto Superiore di Sanità, ISS), these users repeatedly and insistently return to the same questions and/or specific topics, despite having already received comprehensive information and guidance during their initial call. Some of these individuals report no actual risk behaviors or, in cases where a potential risk factor is present, express fear of undergoing diagnostic testing

Address for correspondence: Matteo Schwarz, Unità Operativa Ricerca Psico-Socio-Comportamentale, Comunicazione, Formazione – UO RCF – Dipartimento Malattie Infettive, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: matteo.schwarz@iss.it.

or skepticism regarding the validity of previous negative test results.

These users require a significant investment of time and resources from the helpline professionals, who must therefore be adequately trained to implement telephone interventions grounded in specific counselling competencies.

Although the number of studies published on this phenomenon remains limited, it is nonetheless evident that the issue has assumed global dimensions, impacting both clinical and organizational aspects within counselling and screening services for infectious diseases, as well as in the fields of psychiatry and behavioral disorders. Moreover, it is important to highlight that this behavior can be observed across a wide range of contexts worldwide, varying significantly in terms of cultural, economic, and healthcare management systems, and it cannot be considered confined to specific health, socioeconomic, or environmental conditions.

This article presents the findings of a study conducted over three consecutive two-year periods (2018-2019, 2020-2021, 2022-2023), aimed at determining whether the COVID-19 pandemic has exacerbated the phenomenon of pathological fear of STIs. This was assessed by comparing data across the three periods, defined respectively as pre-pandemic, pandemic, and post-pandemic. The study also seeks to identify the socio-demographic and behavioral characteristics, as well as the underlying motivations, of individuals who repeatedly contacted the AIDS and STIs Helpline of the Istituto Superiore di Sanità.

METHODS

The AIDS and Sexually Transmitted Infections Helpline (800 861061) – operated by the Istituto Superiore di Sanità and active since 1987 – delivers effective interventions aimed at the primary and secondary prevention of HIV, AIDS, and other sexually transmitted infections (STIs).

The service is situated within the Communication Division of the Operational Unit for Psycho-Socio-Behavioral Research, Communication, and Training (Unità Operativa Ricerca Psico-Socio-Comportamentale, Comunicazione, Formazione - UO RCF) of the Department of Infectious Diseases (Dipartimento Malattie Infettive, DMI).

Case definition: the Authors analyzed calls made by individuals who placed two or more calls to the TV AIDS and STIs Helpline within a 30-day period, exhibiting an unfounded fear of HIV and other STIs throughout the counseling intervention. Despite not presenting any significant risk factors for HIV or STIs in general, these individuals nevertheless fear being infected to the extent that they limit their social, relational, and sexual lives.

The telephone intervention is structured around the core competencies of counselling and is organized into phases according to the Communicative-Relational Operating Model. A dedicated data-entry interface and ad hoc software enable the storage and analysis of data collected during counselling activities.

Researchers from the UO RCF have developed the Communicative-Relational Operating Model (MO), based on the fundamental skills of counselling. This model facilitates the development of effective telephone communication with users, allowing for personalized responses through the integration of technical-scientific knowledge and relational-communicative competencies [8].

Data collection is carried out in a structured manner using a database specifically designed to ensure the security of large-scale information, whether stored on the institution's internal servers or in the cloud. In particular, cloud storage is configured to preserve data confidentiality, with data managed through a standardized data collection form.

Instruments: for each call, data are collected across various sections, including: frequency of calls per user (based on self-reported information), age, gender, personal characteristics either self-reported by the user or inferred by the operator from the context of the call, type of situation (real or hypothetical), topics of the questions – specifically modes of transmission, symptoms, questions about testing, emotional state, misinformation, and access to Pre-exposure prophylaxis (PrEP) and Post-exposure prophylaxis (PEP). A descriptive analysis of the aggregate data collected during the telephone interventions was performed using Access 365 software.

Data analysis/Results

The general data regarding calls made by WW users in the study period extending from 2018 to 2023 (4,703 out of a number of questions equal to 16,401), compared with the overall number of calls received by the service in the same period of time (53,068 out of a number of questions equal to 192,667) show how calls from WW represent 8.87%, and questions asked by WW users accounted for 8.51% of the total number of questions received by the AIDS and STIs Helpline (*Table 1*).

Sample characteristics

The data relating to age highlight that the population represented by the WW has a higher median age (41 years – IQR 33-47) compared to the general user population (35 years – IQR 28-42).

Analyzing the distribution of calls between the two genders, it emerges that women represent a significantly higher percentage among the WW (19.3%) compared to the percentage of women in the general user population (15.0%).

In 24.8% of calls from WW, users declare having already carried out more than one HIV test, compared to a percentage of 46.6% in the general user population. Just 12.2% of WW declare that they have never had an HIV test compared to a percentage of 38.3% in the calls of the general population.

Data highlight that calls made by WW users show the absence of risk factors in a percentage of 96.3%, whereas in calls from the general users population such percentage amounts to 76.9%.

The total number of questions formulated by the WW amounted to 16,401 compared to a number of 192,667 in the general user population. From the analysis of the requests formulated by the two population groups, we can observe that the incidence of questions relating to the infectious potential and resistance of pathogens (17.1% in the WW group and only 5.4% in the general user population) shows significant statistical differences.

The differences found in the calls made by the two compared groups of users were statistically significant (p value<0.001) (*Table 1*).

The gender analysis carried out on calls by WW highlights how in 27.3% of cases the questions related to misinformation are asked by female users, while the requests on this topic by men represent 25%. As regards questions relating to the contagiousness and survival of pathogens, 18% of the requests were made by female users while 16.9% were made by male users. As for questions on the ways of transmission, male users are prevalent (18%) compared to female users, who represent 15% of calls. With regards to psycho-social aspects, female users return to being prevalent over male users (16.3% *vs* 15.8%). Finally, 17.1% of women and 15.6% of men ask for specific information on the diagnostic test (*Figure 1*).

RESULTS

Comparison between the numbers relating to calls from WW users in the three two-year periods of study

Analyzing the data relating exclusively to calls from WW users in the three periods under study, it emerges that there is a progressive increase in the median age (from 40 in the first two-year period to 42 in the third). This increase in age is particularly accentuated in the

Table 1

Table comparing call characteristics between worried well and general callers (without worried well)

	General calls without worried well		**Calls of worried well**			
	n=53,068		**n=4,703**			
Variables					**p-value**	**method**
N questions (means)	**192,667** (average of questions per call=3.9)		**16,401** (average of questions per call=3.5)			
Gender					0.000	chi square
Male	45,104	85.0%	3,794	80.7%		
Female	7,953	15.0%	909	19.3%		
Not binary	11	0.0%	0	0.0%		
Age						
Means age	35.8		40.9		0.0001	t-test indipendent samples
Median age	35		41			
IQR	(28-42)		(33-47)			
HIV in the past					0.000	chi square
No	20,343	38.3%	576	12.2%		
Yes	24,726	46.6%	1,595	33.9%		
Not indicated	7,999	15.1%	2,532	53.8%		
Questions with Risk factor for STI/HIV					0.000	chi square
No	52,131	76.9%	2,745	96.3%		
Yes	15,672	23.1%	105	3.7%		
Type of question					0.000	chi square
Ways of transmission	67,803	35.2%	2,850	17.4%		
Information on tests	56,632	29.4%	2,613	15.9%		
Psyco-social aspects	22,568	11.7%	2,609	15.9%		
Misinformation	14,703	7.6%	4,180	25.5%		
Contagiousness and survival of pathogens	10,487	5.4%	2,806	17.1%		
Prevention	7,749	4.0%	219	1.3%		
Symptoms	5,723	3.0%	281	1.7%		
Therapy and research	2,937	1.5%	136	0.8%		
Other	4,065	2.1%	707	4.3%		
Total	**192,667**		**16,401**			

IQR: interquartile range; STI: sexually transmitted diseases.

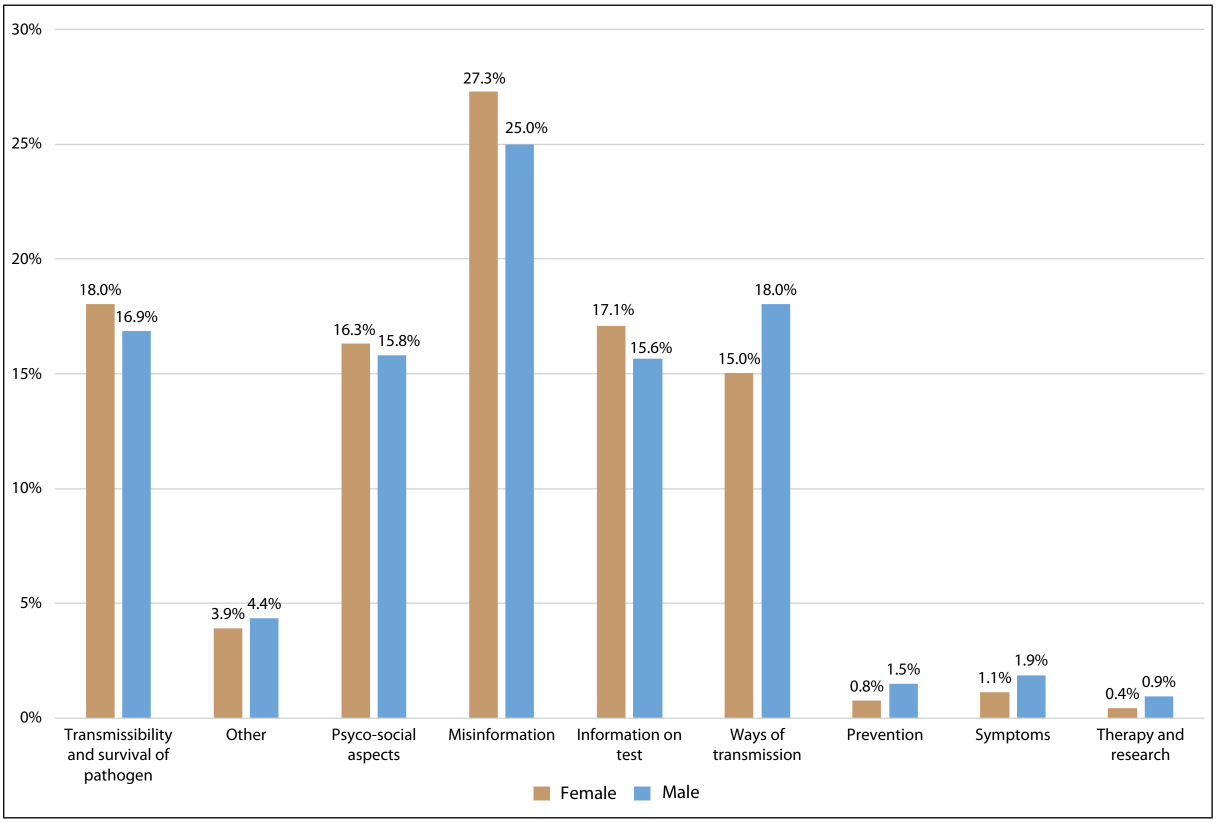


Figure 1
Gender analysis of calls by worried well (WW).

over 50 age group, raising from 15.0% in the first two years to 19.3% in the second and reaching 27.1% in the third two years period (*Table 2*).

In terms of geographical origin, there was an increase in calls from WW users declaring to live in the southern regions throughout the second and third two-year periods (35.1% in the second two-year period, 31.5% in the third, compared to 27.8% in the first).

The distribution of calls by users' gender shows an increase in calls from male users between the first and third two-year period (from 80.0% to 84.0%). As regards calls from women, the increase is significant in the second two-year period (21.0% compared to of 20.0% in the first), decreasing significantly in the third (16.0%).

The trend in the frequency of calls from WW in the three periods highlights a significant increase in the number of calls from individuals who repeatedly contact the Helpline (even more than 15 times), going from 34.7% in the first two years to 57.6% in the second, decreasing to 51.7% in the third.

The data relating to the number of HIV tests carried out shows that the percentage of calls from WW users who declare that they have never carried out the test drops from 13.9% in the first two years to 7.3% in the last, while the calls from WW who have carried out multiple tests pass from 22.9% in the first two years to 29.4% in the last.

On the other hand, there were no significant variations in the type of questions asked by WW users, with the exception of a modest increase, during the three two-year periods, in the number of questions relating to psycho-social aspects.

The data trends observed across the three analyzed periods suggest a likely significant association between the environmental conditions induced by the pandemic and the incidence of Helpline calls from users who may be classified as WW.

Over the course of the three two-year periods, the number of individuals contacting the AIDS and STIs Helpline due to an irrational fear of having contracted HIV, or of having been at risk of doing so, followed a trend that clearly highlights the complete absence of any actual risk factors in the majority of cases. Notably, there is a persistent subset of callers who, even after receiving scientifically accurate and up-to-date information about HIV transmission and the lack of any risky behavior, continue to seek further reassurance through repeated calls (*Table 2*).

DISCUSSION

The present study analyzes the characteristics of phone calls made by WW users across three two-year periods, highlighting the specific features of this group of calls and examining their quantitative and qualitative variations before, during, and after the COVID-19 pandemic.

The data show that the pandemic amplified the fears expressed by the study sample. The end of the pandemic only partially mitigated this effect, without returning to pre-pandemic levels.

Table 2
Comparison between the numbers relating to calls from WW users in the three two-year periods of study

Variables	**Years 2018-2019**		**Years 2020-2021**		**Years 2022-2023**		**Total**	
Geographical area	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
North	774	38.3%	501	33.2%	417	35.6%	1,692	36.0%
Centre	530	26.2%	359	23.8%	324	27.7%	1,213	25.8%
South	562	27.8%	529	35.1%	369	31.5%	1,460	31.0%
Islands	155	7.7%	118	7.8%	61	5.2%	334	7.1%
Not indicated	2	0.1%	1	0.1%	1	0.1%	4	0.1%
Total	2,021	100.0%	1,507	100.0%	1,171	100.0%	4,703	100.0%
Gender	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Men	1,618	80.0%	1,191	79.0%	985	84.0%	3,794	80.7%
Women	405	20.0%	317	21.0%	187	16.0%	909	19.3%
Not binary	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Total	2,023	100.0%	1,508	100.0%	1,172	100.0%	4,703	100.0%
Age	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
From 10 to 19	9	0.4%	6	0.4%	1	0.1%	16	0.3%
From 20 to 29	279	13.8%	213	14.1%	151	12.9%	643	13.7%
From 30 to 39	691	34.2%	424	28.1%	333	28.4%	1,448	30.8%
From 40 to 49	740	36.6%	573	38.0%	362	30.9%	1,675	35.6%
Above 50	303	15.0%	291	19.3%	318	27.1%	912	19.4%
Not indicated	1	0.0%	1	0.1%	7	0.6%	9	0.2%
Total	2,023	100.0%	1,508	100.0%	1,172	100.0%	4,703	100.0%
Call frequency	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
More than 15 calls	702	34.7%	868	57.6%	606	51.7%	2,176	46.3%
More than 5 calls	995	49.2%	487	32.3%	374	31.9%	1,856	39.5%
From 2 to 5 calls	326	16.1%	153	10.1%	192	16.4%	671	14.3%
Total	2,023	100.0%	1,508	100.0%	1,172	100.0%	4,703	100.0%
Previous HIV test	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
No	282	13.9%	208	13.8%	86	7.3%	576	12.2%
Not indicated	1,090	53.9%	809	53.6%	633	54.0%	2,532	53.8%
Yes, more than one	463	22.9%	357	23.7%	345	29.4%	1,165	24.8%
Yes	188	9.3%	134	8.9%	108	9.2%	430	9.1%
Total	2,023	100.0%	1,508	100.0%	1,172	100.0%	4,703	100.0%
Questions' topic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Misinformation	1,725	26.0%	1,380	25.0%	1,076	25.3%	4,181	25.5%
Total	6,632	100.0%	5,524	100.0%	4,245	100.0%	16,401	100.0%

Notably, the median age reported in calls from WW users is significantly higher than that reported in calls from non-WW users.

Moreover, only 3.7% of WW calls report the presence of one or more risk factors, compared to 23.1% of calls from the non-WW user population. This suggests that the perception of infectious risk within the study sample is significantly more influenced by emotional factors and a distorted perception of reality than in calls made by non-WW individuals. This interpretation is supported by the fact that in 33.9% of calls from WW, users reported having undergone HIV testing despite the absence of identifiable risk factors.

These findings highlight how the use of diagnostic services without actual exposure to risk is highly prevalent within the analyzed sample, where both misinformation and emotional responses play a markedly disruptive role.

Misinformation was identified in 25.5% of calls from WW users, a significantly higher proportion compared to only 7.6% in calls from non-WW users. This finding is particularly noteworthy, as calls from WW clearly indicate a tendency to engage in obsessive online searches for detailed information about risk factors. However, this behavior does not appear to result in a genuine increase in awareness regarding the transmission and prevention of STIs.

It thus appears that the combination of limited health literacy – commonly observed in calls from both WW and non-WW users – and the distinctive emotional and personality traits characteristic of WW users renders this group of Helpline callers clearly identifiable. These observations are consistent with findings from multiple studies conducted over time on the WW phenomenon in various global contexts.

A number of observational studies, conducted in India and Nepal between 2017 and 2020, within clinical settings dedicated to dermatology and venereology [2-5], describe the characteristic traits of venerophobia, consisting of an irrational fear of having contracted a sexually transmitted disease (STD) following single or repeated sexual intercourse. This condition can have serious consequences on the good health and well-being of those affected.

The phenomenon has been observed mainly among young males and is often a consequence of sexual relationships with sex workers or of extramarital sexual relationships that are associated with feelings of guilt and shame.

In such cases, the altered emotional state and persistent anxiety are not necessarily associated with a complete absence of risk factors. However, a defining characteristic of these individuals is a persistent tendency to undergo repeated diagnostic testing for sexually transmitted infections (STIs), accompanied by a lack of trust in test results. This behavior is driven by an ongoing, obsessive monitoring of presumed venereal symptoms, either localized to the external genitalia or presenting at a systemic level.

The marked predominance of male subjects among individuals exhibiting such behaviors can be partly attributed to the higher frequency of occasional sexual encounters with sex workers within this group. Additionally, male individuals are more likely to directly observe presumed alterations or symptomatic manifestations of pathological conditions on their own genitalia.

The Authors of these studies underline how, in such cases, a dismissive approach on the part of the clinician in excluding any potential infectious risk, could result ineffective in overcoming the obsessive approach of the patient, no matter how clear the absence of risk factors is.

These studies also highlight a high incidence, in the group of patients analyzed, of anxiety and depression disorders associated with a wrong perception of potential infectious risks. This misperception is often linked to arbitrary interpretations of STD-related contents found online.

In a study reported online on Cambridge University Press in 2020 [9], the phenomenon of HIV worried well was analyzed in the European context by a group of professionals working within a clinical structure dedicated to psychiatry and mental health in the city of Porto, Portugal.

What emerges from the study highlights how the management of HIV-related WW people represents an extremely complex aspect from a psychiatric point of view, since these subjects, despite solid evidence regarding the absence of an infection and/or of concrete risk factors, continue to access healthcare facilities to carry out tests and other health checks, fearing that healthcare personnel may have made diagnosis errors.

Different kinds of painful and traumatic experiences are often found in the past history of these individuals: addictions, serious relational and family problems, psychiatric precedents, alongside with a poor ability to read and interpret informative materials on HIV and AIDS found online.

It should be emphasized that the incidence of various types of psychiatric disorders was found to be very high.

It is clear, however, that the phenomenon has assumed a global dimension over time, albeit with some specific traits in the different territorial, health and cultural contexts in which it is observed.

In this framework, it is noteworthy that in the Canadian province of Ontario, the Hassle Free Clinic – a network providing free medical and counselling services for sexually transmitted infections (STIs) and a key access point for anonymous HIV testing – found it necessary to implement specific counselling guidelines. These guidelines are directed at counsellors, healthcare providers conducting the tests, and educators, with the aim of facilitating the management of interactions with users exhibiting high levels of HIV-related anxiety despite having minimal or no actual risk exposure [10].

An additional aspect that warrants attention is the concern over the potential impact of an HIV-positive diagnosis on individuals' relational and social lives. In some cases, this concern appears to outweigh fears related to the physical health implications of the diagnosis, underscoring the enduring influence of HIV-related stigma, rooted in decades of stigma-laden media discourse.

In this connexion, it is useful to investigate whether the COVID-19 pandemic may have further accentuated anxious states and obsessive behaviors such as those described in the abovementioned studies, and whether the communication campaigns on infectious risks, the restrictions on people's freedom of movement and, in general, all the measures adopted to restrict the contagion, may have aggravated these conditions, where preexisting, and/or expanded the number of people with a similar profile, thus favoring the emergence of latent frailties.

The extant scientific literature indicates that social isolation, pandemic-related socio-economic challenges, uncertainties regarding transmission pathways, and fear of contagion have contributed to a marked increase in health-related anxiety disorders. In this context, the extensive experience accumulated over decades in addressing HIV infection and its associated stigma constitutes a valuable precedent for the design and implementation of targeted interventions. These interventions should aim to facilitate the referral of individuals to counseling and mental health services, thereby enabling effective mitigation of phenomena such as health-related anxiety and suicidal ideation [11].

Restricting the analysis to the European context (EU and EEA countries), an assessment of the consequences of COVID-19 on mental health highlighting a stronger impact of the pandemic on the population, in terms of increase in the incidence of anxiety and depressive symptoms, is contained in the document titled "*Public health and social measures for health emergencies and pandemics in the EU/EEA: recommendations for strengthening preparedness planning*", published by the European Center for Disease Prevention and Control (ECDC) in March 2024 [12], in which it is stated: "*…In addition, the pandemic impacted on the mental health of the population in most European countries, reflected by increases in reported anxiety and depressive disorders…*".

Limitations

The limitations of this study were already taken into consideration in designing the statistical analysis.

They can be summed up as follows:

- telephone calls are anonymous, therefore users cannot be easily identified and followed over time, although the service operators, working as a team, are in most cases able to recognize the behavioral patterns and distinctive traits of most WW users;
- all the information collected during the counselling interview is self-reported by the user and there is no possibility of carrying out any objective checks or direct observations;
- it is not always possible to recognize users who call repeatedly, as the information they provide regarding their age, geographic origin, etc., can be modified by them over time. Nevertheless, teamwork and the recurrence of behavioural patterns greatly assist operators in identifying the origin of the WW calls;
- the telephone interview only allows the detection of the verbal and paraverbal elements of the communication, while the relevant non-verbal aspects in the relationship between the expert and the user are missing.

CONCLUSIONS

A significant finding emerging from the analysis of telephone calls made by WW users to the AIDS and STIs Helpline is the widespread lack of adequate cognitive and interpretive tools necessary to effectively filter, comprehend, and contextualize the extensive amount of online information available on STIs.

In this regard, it could be useful to interpret the phenomenon under study by also placing it in a broader framework. For many years now, the scientific community has been wondering about the extent of the effects produced by the inability of some individuals to recognize their incompetence with respect to certain subjects and the consequent construction of false beliefs in that field.

The effect of this unawareness is twofold: on the one hand, these people often reach erroneous conclusions, on the other hand, their unconscious incompetence deprives them of the metacognitive ability to recognize their own errors [13].

This lack of cognitive tools is actually found in a much larger number of users than that represented by the WW sample, and it might constitute an important indicator of a substantial absence of structured sexual education programs in school curricula.

As a matter of fact, though it is undeniable that the discomfort expressed by WW people often finds its most direct cause in traumas and problematic personal experiences which heavily influence the way in which sexuality is perceived and experienced by the individual, it can be assumed that improving quality education through the integration of sexual education and prevention of STIs programs into compulsory school curricula, would represent a valuable action to enhance good health and well-being and combat, or at least mitigate, the misinformation and the fallacious interpretation of scientific contents found online, of which the WW phenomenon represents a problematic fallout.

Nonetheless, it is crucial to point out that AIDS and STIs Helpline operators, upon identifying a call from a WW user, consistently endeavor to prompt the individual to reflect on the potential benefits of confronting their fears and cognitive distortions through engagement in a psychotherapeutic process.

Finally, as previously noted, the cultural perception of HIV infection – far more so than other sexually transmitted infections – has been deeply shaped over the years by media communication, as well as by cinema, literature, and social media. This layered cultural framing has significantly hindered efforts to combat the persistent stigma associated with the virus. Concurrently, the heightened attention and fear surrounding HIV complicate the ability of healthcare professionals to effectively communicate preventive information regarding other STIs [14].

Funding

The study was conducted with the resources of the Unità Operativa Ricerca Psico-Socio-Comportamentale, Comunicazione, Formazione – UO RCF – and did not receive any third-party funding.

Availability of data and material

The collection of the relevant data gathered during the counselling interventions is based on a data-entry software, through which information relating to both the user calling and to the topic areas covered within the counselling intervention is anonymously collected and stored.

Code availability (software application or custom code)

The descriptive analysis of the aggregate data collected during the telephone interventions was carried out using the Access 365 software.

Authors' contributions

All Authors contributed significantly to the study design and interpretation of results and critically reviewed and approved the final version of the manuscript.

Conflict of interest statement

No potential conflict of interest was reported by the Authors.

Received on 23 April 2025.
Accepted on 22 October 2025.

REFERENCES

1. Miller D, Acton TMG, Hedge B. The worried well: their identification and management. J R Coll Physicians Lond. 1988;22(3):158-65.
2. Mahajan BB, Shishak M. An approach to venerophobia in males. Indian J Sex Transm Dis AIDS. 2017;38:103-6. doi: 10.4103/0253-7184.203441
3. Chowdhry S, Jaiswal P, Souza PD, Dhali TP. Venerophobia – Sexually transmitted disease. J Emerg Dis Virol. 2018;4(1). doi: 10.16966/2473-1846.139
4. Shekhar KC, Adhikary M, Karn D. Clinical scenario of venerophobia in patients presenting in outpatient department. J Nepal Health Res Counc. 2020;18(3):483-7. doi: 10.33314/jnhrc.v18i3.2764
5. Hafi B, Uvais NA, Latheef EN, Razmi MT, Afra TP, Aysha S. Venereophobia – a cognitive deception? Case reports with literature review. Our Dermatol Online. 2020;11(e):e138.1-e138.5. doi: 10.7241/ourd.2020e.138
6. Spence D. Bad medicine: the worried hell. Br J Gen Pract. 2016;66(651):526. doi: 10.3399/bjgp16X687361
7. Mevissen FE, Eiling E, Bos AE, Tempert B, Mientjes M, Schaalma HP. Evaluation of the Dutch AIDS STI information helpline: differential outcomes of telephone versus online counseling. Patient Educ Couns. 2012;88(2):218-23. doi: 10.1016/j.pec.2012.04.007
8. Luzi AM, Colucci A, Gallo P, De Mei B, Mastrobattista L, De Santis M, et al. The communicative-relational operating model of the Italian National Institute of Health for an effective telephone intervention in public health, structured on basic counselling skills. Ann Ig. 2023;35(4):379-402. doi: 10.7416/ ai.2023.255
9. Marinho M, Covelo V, Marques J, Braganca M. HIV/AIDS "worried well" – When the "virus" leads to a significant illness, even in its absence. Eur Psychiatry. 2017;41(Suppl.):S170-S237. doi: 10.1016/j.eurpsy.2017.01.2256
10. Hassle Free Clinic. Counselling guidelines – Clients with high HIV anxiety and no/low risk. Hassle Free Clinic; 2021. Available from: https://hivtestingontario.ca/wp-content/uploads/2021/12/HANLR.pdf.
11. Kini G, Karkal R, Bhargava M. All's not well with the "worried well": understanding health anxiety due to COVID-19. J Prev Med Hyg. 2020;61(3):E321-3. doi: 10.15167/2421-4248/jpmh2020.61.3.1605
12. European Centre for Disease Prevention and Control. Public health and social measures for health emergencies and pandemics in the EU/EEA: recommendations for strengthening preparedness planning. Stockholm: ECDC; 2024. doi: 10.2900/253991
13. Kruger J, Dunning J. Unskilled and unaware of it: how difficulties in recognizing one's own incompetence lead to inflated self-assessments. J Pers Soc Psychol. 1999;77(6):1121-34. doi: 10.1037//0022-3514.77.6.1121
14. Vallorani N. Corpi estranei. Linguaggi medici e artistici nella rappresentazione dell'AIDS. Studi Culturali, Rivista Quadrimestrale. 2010;2:261-78. doi: 10.1405/32427

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 301-314
DOI: 10.4415/ANN_25_04_09

Worldwide prevalence of tattoos with a focus on younger age groups: a literature review

Francesca Palese and Francesca Valent

SOC Igiene e Sanità Pubblica, Dipartimento di Prevenzione, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

Abstract

Background. From 11.7% to 31.5% of the population in Western countries has tattoos. Given the potential health implications, it is important to obtain reliable estimates of the prevalence of the tattooed population.

Objective. To estimate the prevalence of tattoos in the general population and among younger age groups worldwide, and the settings in which tattoos are performed.

Methods. We conducted a literature review by searching MEDLINE, Scopus, and Web of Science for relevant articles published between January 1, 2000, and September 17, 2025. Studies were included if they reported data on the prevalence of tattoos and/or the settings in which tattooing occurred, drawn from the general population or specific age groups and students.

Results. From the 7,921 potential articles identified, 86 were included in our review. We found a global prevalence ranging from 0.18% to 63.9% (from 5.2% to 35.3% in developed countries), with a significantly increasing trend. The data revealed a higher tattoo prevalence among younger individuals. In Western countries, from 64% to 93.9% of the samples got their tattoos in authorized parlours.

Conclusions. The data demonstrate a clear increase in tattooing worldwide. This represents a matter of concern from a public health perspective, as it is likely to be accompanied by a corresponding increase in health risks and requests for tattoo removal.

Key words
- tattoo
- body art
- prevalence
- worldwide
- young

INTRODUCTION

In recent years, body art practices, most commonly tattooing and piercing, have become popular, particularly in Western countries, with 11.7% to 31.5% of the population estimated to be tattooed [1]. In parallel, the literature on this subject has grown, with adolescents being the most frequently studied population segment [2-10]. Publications about tattooed persons explore various aspects of the phenomenon, including epidemiology [1, 11-19], psychological implications [7, 12, 20, 21], associations with risky behaviours [22-24], and health consequences [25].

Tattoos involve the permanent colouration of the skin through the insertion of inks. They can be classified into five main categories: professional (created by expert tattooists), amateur (done by non-professional individuals), traumatic (unintentional tattoos caused by foreign bodies embedded in the dermis), cosmetic (primarily used for permanent makeup), and medical (performed by healthcare professionals for purposes such as nipple reconstruction, scar concealment, and as markers in radiation therapy) [26]. From a public health perspective, professional and, to a lesser extent, amateur tattoos are particularly significant. The rising global trend of individuals getting tattoos has raised concerns among health professionals regarding potential risks to both clients and tattooists. Issues such as microbiological contamination during tattooing and the presence of potentially hazardous chemicals in tattoo inks can lead to various adverse health effects. These may include infections, allergic reactions, and the development of neoplastic conditions (such as melanoma, basal cell carcinoma, and squamous cell carcinoma), along with non-neoplastic lesions (like sarcoidosis and granulomatous reactions). Other possible complications include hypertrophic scars, keloids, pain, and intense itching caused by the involvement of cutaneous nerve branches, as well as photosensitization [25].

In Italy, tattooing is not currently regulated by specific national legislation. The only national reference consists of the circulars issued by the Ministry of Health, which contain the guidelines for performing tattooing

Address for correspondence: Francesca Palese, Dipartimento di Prevenzione, Azienda Sanitaria Universitaria Friuli Centrale, Via Trento Trieste 4, 33038 San Daniele del Friuli (UD), Italy. Email: francesca.palese@asufc.sanita.fvg.it.

and piercing procedures under safe conditions [27]. The ministerial circulars provide guidance on hygiene requirements for performing tattoos safely, address the risks of transmitting infections, and the potential toxic effects of the substances used for dermal pigmentation. They also include, among the final recommendations, proper training for tattoo artists and the need to inform clients about the risk of infectious disease transmission. At the subnational level, some Italian Regions have issued specific laws to regulate the sector. For example, the Tuscany Region promulgated a regional law in 2004 [28] and the subsequent regulation detailing the specific hygienic and sanitary requirements of the parlours, the permitted equipment and materials, and training requirements for tattooists [29]; the same was done by Friuli Venezia Giulia Region [30, 31]. Analogous laws and resolutions were issued in the Veneto Region [32], in the Marche Region [33], in the Lazio Region [34, 35], and in the Lombardy Region [36].

Based on current regulations, the hygiene and public health services of the Prevention Departments within Local Health Authorities deliver hygienic-sanitary evaluations and carry out inspection activities for tattoo businesses that are properly registered. However, there remains an unquantified proportion of unauthorized or "amateur" tattooists who evade health inspections. Oversight of these tattooing activities might seem of relatively minor importance compared to other healthcare activities. For this reason, it is advisable to determine the prevalence of tattoos to measure the magnitude of the phenomenon, the population involved, and the actual impact this phenomenon could have on public health. This information can support health authorities, lawmakers, potential clients, and professionals in implementing measures to protect both the general population and tattoo workers. It is also of interest to understand whether tattoos performed outside authorized centres – potentially at greater risk of adverse effects since they are not subject to health inspections – truly represent a significant public health issue or not.

The main aim of this literature review is to assess the existing evidence on tattoo prevalence in the general population and younger age groups across various countries worldwide. The secondary objective is to present the retrieved data about the settings in which tattoos are typically performed.

METHODS

Search strategy

We employed the CoCoPop framework to develop our search query and to establish our inclusion and exclusion criteria. Our research focused on the following question: What is the prevalence of tattooed individuals (Condition) in various countries worldwide (Context), specifically within the general population and among young people or students (Population)? We conducted a search of MEDLINE, Scopus, and Web of Science to identify relevant articles published between January 1, 2000, and September 17, 2025 (the date of our last consultation). The query string used in our search among the three databases was: ((tattoo) AND (population)) OR ((tattoo) AND (epidemiology)) OR ((tattoo) AND (prevalence)). The limits applied were: full text availability (for MEDLINE), restriction to English and Italian languages (for the three databases), and exclusion from the search of books, book chapters, corrections, and retracted articles (for the three databases).

Inclusion and exclusion criteria

Studies were included if they reported data on the prevalence of tattoos and/or the settings in which tattooing occurred, drawn from the general population, specific age groups within the general population, students, or adolescents. Additionally, studies estimating the prevalence of hepatitis C virus (HCV), hepatitis B virus (HBV), and human immunodeficiency virus (HIV) infections (for which tattooing is considered a risk factor), or addressing other issues related to tattoos that encompassed information on tattoo epidemiology were also included. Conversely, the exclusion criteria were as follows: studies conducted in specific contexts, such as clinics or hospital admissions/visits, or restricted to particular population subgroups (e.g., pregnant women, inmates, blood donors, farmers, psychiatric patients, veterans); studies that did not provide sufficient information to calculate tattoo prevalence; duplicate publications; grey literature; websites; abstracts without accompanying full texts; and studies focused on traumatic, cosmetic, or medical tattooing. Critical reviews were retained for background information but were excluded as sources of original data.

Data extraction

In the first stage, all study titles and abstracts obtained from the database search were reviewed for eligibility by one of the Authors (FP). Papers that successfully passed this stage were appraised in full, and those meeting the inclusion criteria were selected for data extraction, independently of their size, by the same author. Any doubts regarding the eligibility of studies were resolved through discussion with the other Author (FV). Extracted information, reported on a spreadsheet, included citation details (authors, publication year), study period, population characteristics (country, age group), prevalence of tattooed population, and the percentage of individuals who underwent tattoos in different settings (e.g., authorized parlour, at home). References of all the included studies and relevant reviews were also screened to identify any additional eligible publications.

To validate our search, we checked if relevant publications that we were already aware of were included in the results list.

Data analysis

Measures of prevalence and the number of individuals who have received tattoos in various settings are presented as percentage values. Whenever possible, we verified the data for potential errors based on the number of tattooed individuals and the size of the population sample. We calculated prevalence estimates when they were not reported in the studies. Results were presented by country and population category (all ages, young people, and students). If a paper provided age-stratified prevalence data, we extrapolated the data for younger age groups (<40 years), if available. Within each country and category, we also analysed sex-based differences in prevalence. In cases where multiple studies used the same dataset and time frame, only the most comprehensive articles were included. Additionally, if a single study reported prevalence measures for the tattooed population from different databases or populations, all relevant results were presented.

RESULTS

Initially, we identified 7,921 potential articles. After applying inclusion and exclusion criteria, and adding 12 additional references from bibliographies, we included a total of 86 articles in our review (*Figure 1*).

The selected literature consisted mainly of cross-sectional studies, often utilizing convenience sampling. These studies employed structured questionnaires, which were either self-administered (including online formats) or administered by trained interviewers.

Overall prevalence

A limited number of studies specifically aimed to estimate the absolute prevalence of tattooing in general populations across different countries [1, 11-19]. However, by combining data from these studies with figures extracted from publications regarding HCV [37-52], HBV [43-45, 50, 53-57], and HIV [58, 59] seropositivity in selected populations and other related topics (e.g., the association of tattooing and personality traits [19-21, 60-65], tobacco consumption [66], hazardous sexual behaviours [67, 68], awareness of the related risks [8, 15, 69-71], etc.), we found a global prevalence that varied widely, ranging from 0.18% [51] to 63.9% [50] (as shown in *Table 1*). In developed countries, tattoo prevalence ranged from 5.2% [54] to 35.3% [72], with a substantially increasing trend.

Age- and sex-based differences

Findings regarding sex-based differences in tattoo prevalence were inconsistent. In contrast, research consistently shows a higher tattoo prevalence among younger individuals (*Table 2*), with a peak of 45.6% among

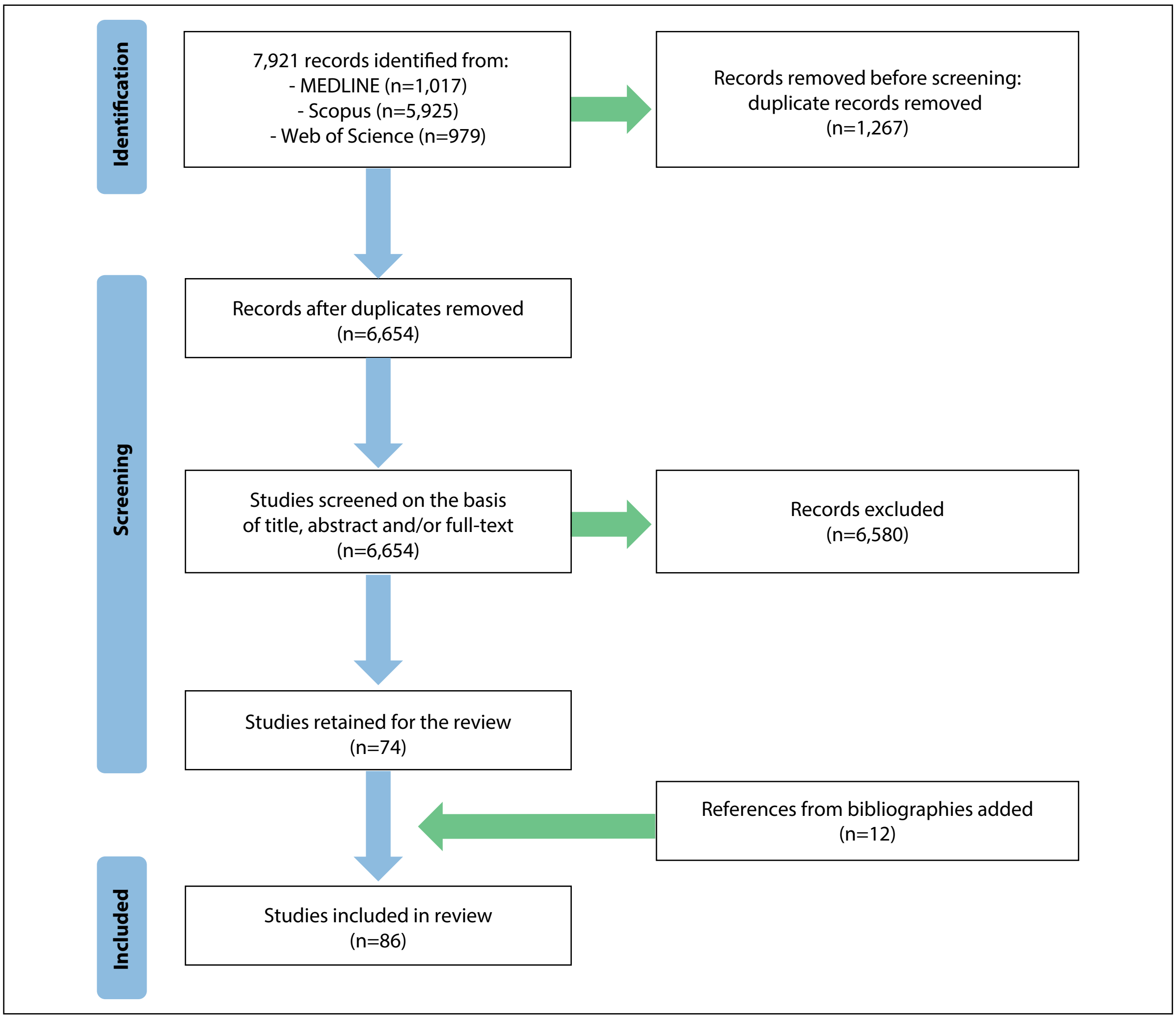


Figure 1
Flowchart of the study selection for inclusion in the literature review about the worldwide prevalence of tattoos.

Table 1
Worldwide prevalence of tattoos in general populations

Continent	Country	Study	Time	Age§	Sample number	Overall (%)	Men (%)	Women (%)
North America	USA	Laumann, Derick 2006 [75]	2004	18-50	500	24.0	26.0	22.0
	USA	Karagas, Wasson 2012 [13]	2008	14-69	452	-	16-18	7-29
	USA	Mortensen *et al.* 2019 [23]	2016	18-65	2,008	32.1	23.2	36.7
	USA	Morlock *et al.* 2023 [72]	2017	>18	3,033	35.3	29.4	41.1
	USA	Kluger *et al.* 2019 [1]	2018-2019	≥18	2,008	31.5	27.8	35.1
	USA (Utah)	McCarty *et al.* 2024 [19]	2020-2021	≥18	18,687	-	22	26
Europe	Denmark	Bjerre *et al.* 2018 [79]	2006	24-76	2,212	14.2	17.8	11.0
	France	Kluger *et al.* 2019 [1]	2017	≥15	5,000	16.8	14.4	19.1
	France	Kluger *et al.* 2019 [1]	2018-2019	≥18	2,048	17.8	19.5	16.2
	Italy	Renzoni *et al.* 2018 [15]	2015	≥12	7,608	12.8	11.7	13.8
	Austria and Southern Germany	Stieger *et al.* 2010 [6]	NA	≥16	440	15.2	12.4	17.8
	Austria and Southern German-speaking area of Central Europe	Swami *et al.* 2012 [62]	NA	Mean: 31.4 (SD: 13.7)	540	22.2	20.3	23.8
	Austria and Southern German-speaking area of Central Europe	Swami *et al.* 2016 [64]	NA	18-76	1,006	19.1	17.6	20.3
	Germany	Lahousen *et al.* 2019 [18]	2009	14-94	2,512	-	14.1	10.2
	Germany	Ernst *et al.* 2022 [98]	2016	14-44	1,060	32.0	-	-
	Germany	Stirn *et al.* 2006 [12]	NA	14-93	2,043	8.5	-	-
	Netherlands	Dillingh *et al.* 2020 [103]	2013	NA	5,215	9.8	-	-
	Norway	Sagoe *et al.* 2017 [14]	NA	16-91	15,654	20.8	17.9	23.8
	Romania	Gheorghe *et al.* 2013 [54]	2006-2008	18-68	12,125	5.2	-	-
	Russia	Kluger *et al.* 2019 [1]	2018-2019	≥18	2,010	11.7	15.0	8.9
	Spain (Catalonia)	Domìnguez *et al.* 2001 [37]	1996	≥5	2,142	17.2	-	-
	UK (Greater London)	Swami *et al.* 2015 [63]	2014-2015	20-58	378	25.7	-	-
South America	Southern Brazil (Porto Alegre)	Kvitko *et al.* 2013 [42]	2009	≥20	3,391	16.2	-	-
	Southern Brazil (Cássia dos Coqueiros municipality)	Melo *et al.* 2015 [45]	2011-2013	≥18	1,001	6.8	-	-
	Brazil (Amazon)*	Vasconcelos *et al.* 2024 [50]	2015	≥0	430	63.9	-	-
	Brazil	Kluger *et al.* 2019 [1]	2018-2019	≥18	2,003	22.3	20.0	24.4
	Puerto Rico (San Juan)	Pérez *et al.* 2005 [39]	2001-2002	21-64	964	12.4	-	-
Asia	Armenia	Demirchyan *et al.* 2024 [49]	2021	≥18	3,380	10.4	-	-
	Eastern China (Jiangsu province)	Huang *et al.* 2015 [51]	2011-2012	≥0	149,175	0.18	-	-
	China	Kluger *et al.* 2019 [1]	2018-2019	≥18	3,010	12.2	12.1	12.2
	Georgia	Hagan *et al.* 2019 [48]	2015	≥18	6,014	10.2	-	-
	Southern India (Andhra Pradesh)	Dandona *et al.* 2008 [58]	2004-2005	15-49	12,617	11.2	7.8	14.5
	Western Iran (Kermanshah)	Sayad *et al.* 2008 [52]	2006	15-64	1,721	10.6	-	-
	Southern Iran (Bandar Abbas)	Makiani *et al.* 2014 [43]	2012	15-45	2,000	8.4	-	-
	Western Iran (Kermanshah province)	Alavian *et al.* 2012 [57]	NA	6-65	1,979	21.3	-	-
	Southern India (area of Puducherry)	Rajalatchumi *et al.* 2025 [56]	2021-2022	≥18	5,169	4.0	-	-

Continues

Table 1
Continued

Continent	Country	Study	Time	Age§	Sample number	Overall (%)	Men (%)	Women (%)
	Western-central India (Maharashtra state)	Bhate *et al.* 2015 [44]	NA	≥5	1,833	4.0	-	-
	South-western Iran	Moezzi *et al.* 2015 [46]	2013	≥15	3,000	10.4	-	-
	Southern Iran (Qeshim Island)	Holakouie *et al.* 2015 [59]	2013-2014	NA	1,500	4.6	-	-
	Central Iran (Qom)	Ghadir *et al.* 2012 [53]	NA	NA	3,690	4.54	-	-
	Pakistan (Balochistan province)	Ahmed *et al.* 2012 [41]	2007-2009	≥18	2,000	7.5	-	-
	Central Thailand	Wasitthankasem *et al.* 2017 [47]	2015	30-64	3,077	12.9-17.9	-	-
	Northern Vietnam (Thai Binh province)	Nguyen *et al.* 2007 [40]	2002	16-82	837	4.5	-	-
Oceania	Australia	Makkai, McAllister 2001 [11]	1998	≥14	10,340	10.1	11.9	8.5
	Australia	Tranter, Grant 2018 [99]	2009	≥18	1,525	12.6	-	-
	Australia	Heywood *et al.* 2012 [73]	2004-2005	16-64	8,656	14.5	15.4	13.6
Africa	Southwest Ethiopia	Belay *et al.* 2020 [55]	2017-2018	≥18	612	43.1	-	-

SD: standard deviation; NA: not available; §expressed in years; *sample extracted from the indigenous general population.

people aged 18 to 44 years, according to a recent a US study [72]. Out of the 86 studies reviewed, 40 focused on tattoo prevalence and related issues among younger age groups, primarily within schools, universities, and colleges (*Table 2*).

Tattooing setting

Eight publications reported data on the locations where tattoos were obtained (*Table 3*). In Western countries, the majority of the samples (64%-93.9%) received their tattoos in authorized parlours [3, 15, 73-

Table 2
Worldwide prevalence of tattoos among younger age groups and students

Continent	Country	Study	Time	Age§	Sample type	Sample number	Overall (%)	Men (%)	Women (%)
North America	Canada (Outaouais Region in Quebec)	Deschesnes *et al.* 2006 [3]	2002	12-18	High school students	2,180	7.7	5.6	9.8
	USA	Roberts, Ryan 2002 [24]	1995-1996	11-21	Adolescents from general population	5,837	4.5	4.8	4.2
	USA	Drews *et al.* 2000 [87]	1999	Mean: 19.3 (SD: 1.2)	Undergraduate college students	235	12.3	8.9	14.3
	USA	Mayers *et al.* 2002 [88]°	2001	Mean: 21.0	Undergraduate university students	446	23.8	21.6	25.9
	USA	Laumann, Derick 2006 [75]	2004	18-29	General population	140	26.0	-	-
	USA	French *et al.* 2016 [104]	2008-2009	24-32	General population	15,189	10.9	12.3	9.7
	USA	Karagas, Wasson 2012 [13]	2008	14-49	General population	-	-	18	29
	USA	Morlock *et al.* 2023 [72]	2017	18-44	General population	1,678	45.6	-	-
	USA	Kluger *et al.* 2019 [1]	2018-2019	18-24	General population	-	40.2	-	-
	USA	Kluger *et al.* 2019 [1]	2018-2019	25-34	General population	-	42.8	-	-
	USA (Colorado)	Dukes, Stein 2011 [83]	2007	13-19	High school students	1,462	18	19	17

Continues

Table 2
Continued

Continent	Country	Study	Time	Age§	Sample type	Sample number	Overall (%)	Men (%)	Women (%)
	USA (NY State)	Mayers, Chiffriller 2008 [4]°	2006	Mean: 21.2	Undergraduate university students	650	21.8	23.0	21.0
	USA (Utah)	McCarty *et al.* 2024 [19]	2020-2021	18-24	General population	1,575	27.4	22	32
	USA (Utah)	McCarty *et al.* 2024 [19]	2020-2021	25-29	General population	1,214	37.5	34	45
	USA (Utah)	McCarty *et al.* 2024 [19]	2020-2021	30-39	General population	2,758	33.2	31	39
	USA	Lipscomb *et al.* 2008 [90]	NA	18-62 (median: 21)	Undergraduate college students	496	19.5	16.4	23.2
	Mid-western USA	King, Vidourek 2013 [74]	NA	Mean: 21.92 (SD: 5.37)	Undergraduate college students	998	29.6	-	-
	South-western USA	Forbes 2001 [60]	NA	Male-mean: 22.5 (SD: 5.6); Female-mean: 23.8 (SD: 7.5)	Undergraduate university students	302	18.5	14.7	21.0
	South-western USA	Armstrong *et al.* 2002 [84]	NA	≥18	Undergraduate college students	514	18.9	20.9	17.5
	South-western USA	Koch *et al.* 2005 [67]	NA	Mean: 20.9 (SD: 4.5)	Undergraduate university students	450	22.2	-	-
	South-western USA	Owen *et al.* 2013 [91]	NA	NA	Undergraduate college students	595	21.0	-	-
	USA (Colorado)	Manuel, Sheehan 2007 [65]	NA	17-37 (mean: 20.0)	Undergraduate university students	210	31.9	30.4	32.3
	USA (Tennessee)	Tate, Shelton 2008 [20]	NA	Mean: 21.92 (SD: 5.37)	Undergraduate and graduate university students	1,375	26.3	27.3	25.8
Europe	Croatia	Zrno *et al.* 2015 [92]		19-30	Undergraduate university students	100	35.0	-	-
	Denmark	Bjerre *et al.* 2018 [79]	2006	24-39	General population	486	27.4	-	-
	France	Kluger *et al.* 2019 [78]Σ	2017	15-18	General population	175	10.3	12.8	6.1
	France	Kluger *et al.* 2019 [17]	2017	15-34	General population	1,592	25.3	-	-
	France	Kluger *et al.* 2019 [1]	2018-2019	18-24	General population	-	22.0	-	-
	France	Kluger *et al.* 2019 [1]	2018-2019	25-34	General population	-	30.5	-	-
	France (Brittany)	Guéguen 2012 [68]	NA	Mean: 20.84 (SD: 1.35)	Undergraduate university students	2,080	14.5	7.8	19.8
	France (Brittany)	Guéguen 2013 [66]	NA	Mean: 20-22	Undergraduate university students	2,587	12.2	10.4	14.4
	Greece (Athens)	Notara *et al.* 2022 [102]	NA	18-30	General population	629	31.3	27.6	32.5
	Italy (Padua and its province)	Bosello *et al.* 2010 [21]	2003	Mean: 16.5 (SD: 1.6)	High school students	818	4.0	-	-
	Italy (Grosseto and Scansano, Tuscany Region)	Boncompagni *et al.* 2005 [2]	2003-2004	14-20	High school students	496	4.8	3.0	6.0
	Italy (Cagliari)	Preti *et al.* 2006 [93]	2004	15-19	High school students	820	8.5	14.5	5.4

Continues

Table 2
Continued

Continent	Country	Study	Time	Age§	Sample type	Sample number	Overall (%)	Men (%)	Women (%)
	Italy (Veneto Region)	Cegolon *et al.* 2010 [94]†	2007	13-21	High school students	4,277	6.0	-	-
	Italy (Veneto Region)	Clerici, Meggiolaro 2011 [95]	2007	14-18	High school students	4,213	-	5.9-7.3	4.5-8.8
	Italy (Naples province)	Gallè *et al.* 2011 [69]	2008-2009	Mean: 16.1 (SD: 1.3)	High school students	9,322	11.3	11.7	11.0
	Italy (Naples province)	Gallè *et al.* 2011 [69]	2008-2009	Mean: 21.6 (SD: 4.1)	Undergraduate university students	3,610	24.5	-	-
	Italy (Bari)	Quaranta *et al.* 2011 [70]	2009-2010	17-58	Freshmen university students	1,598	9.6	9.1	9.8
	Italy (Veneto Region)	Majori *et al.* 2013 [8]	2009-2010	13-22	High school students	2,843	6.4	5.3-7.8	3.3-9.5
	Italy	Renzoni *et al.* 2018 [15]	2015	12-17	General population	-	7.7	-	-
	Italy	Renzoni *et al.* 2018 [15]	2015	18-24	General population	-	22.1	-	-
	Italy	Renzoni *et al.* 2018 [15]	2015	25-34	General population	-	22.7	-	-
	Italy (Palermo)	Sidoti *et al.* 2010 [5]	NA	Mean: 21.1-21.4 (SD: 3.5-4.3)	Undergraduate university students	1,200	31.8	43.5	17.6
	Italy	Gallè *et al.* 2021 [76]*	2020-2021	NA	Undergraduate university students	2,985	27.9	-	-
	Italy	Protano *et al.* 2021 [96]*	2020-2021	Mean: 23.15 (SD: 3.99)	Undergraduate university students	3,005	27.9	-	-
	Italy (L'Aquila)	Scatigna *et al.* 2022 [85]	NA	Mean: 21.5 (SD: 4.1)	Undergraduate university students	575	30.5	24.4	33.1
	Austria and Southern Germany	Stieger *et al.* 2010 [6]	NA	16-20	General population	81	0.9	-	-
	Austria and Southern Germany	Stieger *et al.* 2010 [6]	NA	21-25	General population	222	7.5	-	-
	Austria and Southern Germany	Stieger *et al.* 2010 [6]	NA	26-30	General population	109	6.4	-	-
	Austria and Southern German-speaking area of central Europe	Swami *et al.* 2012 [62]	NA	Mean: 31.4 (SD: 13.7)	General population	540	22.2	20.3	23.8
	Germany	Lahousen *et al.* 2019 [18]	2009	25-34	General population	-	-	26	25.5
	Germany	Ernst *et al.* 2022 [98]	2016	14-44 (mean: 30.47, SD: 8.41)	General population	1,060	32.0	-	-
	Germany	Stirn *et al.* 2006 [12]	NA	14-44 (mean: 31.1)	General population	864	15	-	-
	Norway	Sagoe *et al.* 2017 [14]	NA	16-19	General population	1,310	7.9	-	-
	Norway	Sagoe *et al.* 2017 [14]	NA	20-29	General population	4,358	26.2	-	-
	Norway	Sagoe *et al.* 2017 [14]	NA	30-39	General population	2,809	27.6	-	-

Continues

Table 2
Continued

Continent	Country	Study	Time	Age[§]	Sample type	Sample number	Overall (%)	Men (%)	Women (%)
	Poland	Rogowska *et al.* 2017 [82]	2015-2016	Mean: 22±2.5	Undergraduate university students	1,199	27.0	-	-
	Russia	Kluger *et al.* 2019 [1]	2018-2019	18-24	General population	-	15.0	-	-
	Russia	Kluger *et al.* 2019 [1]	2018-2019	25-34	General population	-	19.4	-	-
	Sweden	Röhrl, Stenberg 2010 [105][#]	2000-2004	14.9-23.4	Upper secondary school children	6,095	4.8	3.0	6.0
	Sweden	Fors *et al.* 2012 [106][#]	2000-2004	14.9-23.4	Upper secondary school children	6,095	5.1	3.4	6.2
South America	Brazil	Kluger *et al.* 2019 [1]	2018-2019	18-24	General population	-	21.9	-	-
	Brazil	Kluger *et al.* 2019 [1]	2018-2019	25-34	General population	-	30.3	-	-
Asia	China	Kluger *et al.* 2019 [1]	2018-2019	18-24	General population	-	12.3	-	-
	China	Kluger *et al.* 2019 [1]	2018-2019	25-34	General population	-	20.7	-	-
	South India (Area of Puducherry)	Rajalatchumi *et al.* 2025 [56]	2021-2022	≥18	General population	5,169	4.0	-	-
	Myanmar (Mandalay Region)	Show *et al.* 2019 [71]	2015	18-24	General population	198	22.2	-	-
	Myanmar (Mandalay Region)	Show *et al.* 2019 [71]	2015	25-35	General population	203	16.7	-	-
	Central Taiwan (Taishi township)	Lee *et al.* 2004 [38]	1999	13-16	Junior high school students	1,999	1.7	-	-
	Southern Taiwan	Yen *et al.* 2012 [7]	2004	12-17	High school students	9,755	1.0	-	-
	Turkey (Istanbul)	Balci *et al.* 2015 [22]	2009-2010	Mean: 21.69 (SD: 1.55)	Undergraduate university students	1,303	4.3	-	-
	Turkey (Istanbul)	Ekinici *et al.* 2012 [61]	NA	Mean: 17.42 (SD: 0.92)	High school students	607	4.8	-	-
	Turkey (Istanbul)	Wise, Akınkoç 2022 [100]	NA	18-25	Undergraduate university students	430	32.6	-	-
Oceania	Australia	French et at. 2016 [104]	2001-2002	24-32	General population	4,279	20.4	20.8	19.9
	Australia	Heywood *et al.* 2012 [73]	2004-2005	16-19	General population	367	5.4	-	-
	Australia	Heywood *et al.* 2012 [73]	2004-2005	20-29	General population	737	22.3	-	-
	Australia	Heywood *et al.* 2012 [73]	2004-2005	30-39	General population	810	23.2	-	-
	Australia (Queensland)	Tranter, Grant 2018 [99]	2013	19-20	High school students	2,206	14.3	-	-
Africa	Tanzania (Dar es Salaam)	Chacha, Kazaura 2015 [9]	2014	Mean: 23.9 (SD: 4.5)	Undergraduate medical university students	536	7.5	6.8	8.6

SD: standard deviation; NA: not available; [§]expressed in years; [°]the same samples involved in the studies by Mayers *et al.* (2002) [88] and by Meyers and Chiffriller (2008) [4] are analysed in the Meyers and Chiffriller (2007) [89] publication (not reported in the *Table*); [Σ]the study sample was extracted from the study population analysed by Kluger *et al.* (2019) [17]; [†]the same samples involved in the study by Cegolon *et al.* (2010) [94] are analysed in the publication by Cegolon *et al.* (2010) [97] (not reported in the *Table*); [*#]the two studies focus on the same sample.

Table 3
Settings where tattoos are performed according to literature

Study	Authorized parlour (%)	Beauty salon/ piercing studio (%)	At home (%)	Other (%)
Balci *et al.* 2015 [22]	80.4		-	-
Deschenes *et al.* 2006 [3]	90.4	-	9.6	
Gallè *et al.* 2021 [76]	93.9	0.5	4.3	1.3
Heywood *et al.* 2012 [73]	90.7	-	3.6	3.2
King, Vidourek 2013 [74]	87.6	10.7	6.7	-
Laumann, Derick 2006 [75]	64	-	26	
Oinam *et al.* 2019 [10]	10.8	-	68.6	16.6
Renzoni *et al.* 2018 [15]	76.1	9.1	4.4	10.2

76], whereas a study involving Indian school students revealed that 68.6% of them were tattooed at home by friends [10].

DISCUSSION

To our knowledge, this is the first literature review that focuses exclusively on global tattoo prevalence. While one prior critical review [16] and one literature review (https://www.cieh.org/media/1982/tattoo-toolkit_part-e_-literature-review.docx) [77] have addressed prevalence as part of broader discussions on tattoo-related topics, we are not aware of any other studies that focus on where tattoos are done. Over the last 25 years, few studies have specifically addressed tattoo prevalence [1, 11-19]. Nevertheless, the literature shows a substantially increasing trend worldwide, which is expected to be accompanied by an increase in adverse reactions and tattoo removal requests as well.

Tattoo complications, removal requests, and public health concerns

The prevalence of tattoo-related complications in the general population is substantially uncertain, as they have been reported to range from 0% to 67% [4, 25, 69, 72, 75, 78, 79], with 5.6% of them requiring medical treatment [79]. While serious adverse effects are expected to be uncommon, the popularity of tattoo practices and the potential for complications to arise long after the procedure could create a considerable strain on healthcare services for many years ahead.

It has been estimated that up to 50% of tattooed persons experience regret about their tattoos [80], and some of them will attempt to erase one of their tattoos. Tattoo removal methods include surgical excision techniques (often used for small tattoos), dermatome shaving, salabrasion, and chemical removal, all of which carry the risk of scarring and dyspigmentation. Laser removal is usually preferred, but it can be painful, requires a large number of sessions, and is expensive. Additionally, it poses a risk that residues or degradation products released in the dermis as a result of the thermophotolysis process may lead to unforeseen long-term immune responses and carcinogenic effects. Further secondary effects include burns, pigmentary disruptions (hypopigmented skin areas alternated with hyperpigmented zones), and paradoxical darkening. Notably, complete removal by laser is not always accomplished, even when performed by experienced dermatologists and plastic surgeons, especially for multicoloured tattoos [16, 81].

The increase in tattoo removal requests has led to an unregulated market for such procedures, operated by beauticians, body artists, nurses, and non-specialized physicians, as well as to cheaper over-the-counter options [16].

Other matters of concern from a public health perspective are that tattoos, especially larger ones, can interfere with the performance of certain diagnostic and therapeutic procedures. Tattoos may hinder the diagnosis of various skin lesions, such as melanoma and other kinds of skin cancer. Moreover, the inks used for tattooing often contain metal filings, which can generate an electric current during magnetic resonance imaging. This reaction may cause a rise in local skin temperature, leading to discomfort, pain or even skin burns [82].

Tattoos may be performed in non-professional parlours by unlicensed personnel or even at home, possibly using low-quality and non-sterile equipment. The growth of these practices has been facilitated by the internet, which allows for easy purchase of tattoo kits and pigments and offers tutorials that claim to teach how to perform tattoos. Although studies indicate that the proportion of individuals in Western countries who receive amateur tattoos remains relatively low [3, 15, 73-76], this aspect is of relevant concern for public health and should be carefully considered due to the limited capacity to control health risks in non-professional settings. In addition, home tattooing increases the risk of low-quality tattoos, which may lead to an increased demand for tattoo removal procedures [16].

European legislation on ink safety and public health agencies' actions

The European Council adopted on February 20, 2008 the European Resolution called ResAP(2008)1 (https://search.coe.int/cm?i=09000016805d3dc4), which outlines important criteria for ensuring the safety of tattoo inks and permanent makeup (PMU). This resolution addresses several key aspects, including the labeling and composition of these products, the risks associated with substances used in tattoo inks and PMU, and the hygienic conditions that must be upheld during tattooing and PMU procedures. It also emphasizes the obligation to inform individuals about potential health risks linked to tattoos and PMU. The resolution's annexes feature a list of banned chemical substances in tattoo ink and in PMU formulations due to their carcinogenic and mutagenic properties, along with a list specifying substances that have maximum concentration limits and information on their permissible limits. Furthermore, it requires that inks be sterile and preferably in disposable packaging.

Italy maintains an active system for surveillance and monitoring to ensure adherence to health and hygiene standards, as well as compliance with ministerial regulations and guidelines. This system operates at various levels: inspections at the local level are conducted by the Local Health Authorities (Aziende Sanitarie Locali, ASL) and Regional Environmental Protection Agencies (Agenzie Regionali per la Protezione dell'Ambiente, ARPA), which focus on performing analytical tests on substances like inks. At the national level, oversight is handled by the Carabinieri's Anti-Adulteration Units (Nuclei Antisofisticazioni e Sanità, NAS) and the Maritime, Air, and Border Health Offices (Uffici di Sanità Marittima, Aerea e di Frontiera, USMAF). The Italian National Institute of Health (Istituto Superiore di Sanità, ISS) plays a key role in coordinating the laboratory network and in conducting confirmatory analyses of analytical data.

A crucial tool in this framework is the European Union's Rapid Exchange of Information System (RAPEX), designed to address products that present serious risks to health. Through this system, Member States inform the European Commission without delay about any measures taken in response to hazardous products. RAPEX facilitates swift information sharing across Member States, detailing the product concerned and the associated risks, while outlining restrictive measures such as market withdrawal. Notifications through RAPEX are publicly accessible on specific pages of the European Union's official website (https://ec.europa.eu/safety-gate-alerts/screen/search).

In cases where tattoo products in Italy are found to contain chemical substances posing significant health risks, the Ministry of Health issues a "Consumer Alert". This alert, published on its official website (https://www.salute.gov.it/new/it/avvisi/allarmi-consumatori-e-reazioni-notifiche-di-prodotti-non-alimentari-pericolosi/), provides detailed information about the product, its potential dangers, and the actions being implemented to protect public health.

Tattoo professionals as a source of information

Research from Italy [69, 76], has highlighted that most tattooed students who had prior knowledge of health risks cited the tattoo artist as their primary source of information. This suggests that body art professionals have the potential to serve as valuable conduits for educating clients about health risks. By providing clear and essential aftercare instructions, tattooists can guide customers effectively, helping to prevent complications. Therefore, equipping tattoo artists with comprehensive health-related knowledge could significantly reduce avoidable risks associated with body art practices.

Limitations

Research has predominantly focused on specific population groups, mainly adolescents and students [2-10, 78, 83-97], often relying on convenience samples. Studies conducted within high school and university or college settings frequently face selection bias due to the voluntary nature of student participation, the disproportionate representation of individuals from higher socio-economic and cultural backgrounds, and sex imbalances (e.g., humanistic faculties often have a higher percentage of female students). As a result, these studies are not representative of the general population and tend to be geographically limited and fragmented, which makes estimating national prevalences challenging. However, the available data illustrate a clear and sustained rise in tattooing, reflecting an increase in societal acceptance of the practice. This upward trend complicates comparisons of prevalence across studies conducted in different time periods.

Although the literature from Europe and North America is relatively well-established, there is a notable scarcity of data regarding tattoo prevalence in Oceania, Africa, and South America - Brazil being a partial exception. Many studies predominantly focused on unrelated primary topics, such as addressing sociological [7, 18, 84, 85, 87, 97-102] and labour market-related issues [103, 104], or investigating blood infection rates [37-59] and allergic reactions prevalence [105, 106] within specific populations, offering only limited insights into tattoo epidemiology (e.g., differences in prevalence between males and females or among different age groups).

To compare tattoo prevalence among young people in different countries, we also extracted youth-specific data from general population studies when available. However, differences among studies in age group definitions make precise comparisons across countries difficult.

CONCLUSIONS

As tattooing practices gain popularity in the general population, a corresponding increase in associated health risks can be expected, particularly if tattoos are performed in unlicensed settings. However, as the prevalence estimates of tattoo-related adverse reactions in the general population are unreliable, their magnitude remains unknown.

Together with the number of tattooed people, practices aimed at tattoo removal are also expected to rise. As professional interventions aimed to remove tattoos are expensive, practices performed by laypersons, using cheaper and unsafe instruments bought on the internet, or even at home using do-it-yourself products, are becoming more common. This situation requires the attention of policymakers, lawmakers, and public health agencies to issue and enforce regulations governing these activities.

The collaboration between health authorities and law enforcement agencies regarding the surveillance of inks and materials used for tattooing is of utmost importance.

As body artists and their parlours appear as fundamental in preventing the avoidable health consequences of tattoos and in counselling actual and potential customers, local health authorities, such as the Prevention Departments, should play a central role in monitoring tattoo practices, ensuring compliance with hygiene standards, providing training for safe practices, and exercising regulatory oversight of parlour environments.

According to the literature, knowledge about the contraindications and health risks associated with tattooing and tattoo removal is not always satisfactory, especially among young people [10, 15, 69, 70, 82, 86, 96, 102]. As a consequence, Prevention Departments' involvement in educational programs addressing tattoo-related risks and complications, as well as in promoting public awareness campaigns at a local level, is highly recommended.

Data availability statement

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

Authors' contributions

FP: data curation, writing-original draft preparation, conceptualization, methodology; FV: writing-original draft preparation, conceptualization, methodology, supervision.

Conflict of interest statement

None declared.

Received on 18 July 2025.
Accepted on 22 October 2025.

REFERENCES

1. Kluger N, Seité S, Taieb C. The prevalence of tattooing and motivations in five major countries over the world. J Eur Acad Dermatol Venereol. 2019;33(12):e484-6. doi: 10.1111/jdv.15808
2. Boncompagni G, Lazzeri G, Martiello MA, Incandela L, Santori R, Spinelli GM, et al. Related risks of tattooing and body piercing: prevalence study in a convenience sample. J Prev Med Hygiene. 2005;46:153-8.
3. Deschesnes M, Demers S, Finès P. Prevalence and characteristics of body piercing and tattooing among high school students. Can J Public Health. 2006;97(4):325-9. doi: 10.1007/BF03405614
4. Mayers LB, Chiffriller SH. Body art (body piercing and tattooing) among undergraduate university students: "then and now". J Adolesc Health. 2008;42(2):201-3. doi: 10.1016/j.jadohealth.2007.09.014
5. Sidoti E, Paolini G, Tringali G. Prevalence, knowledge, attitudes and practices towards body art in university students: body art as an indicator of risk taking behaviours? Ital J Public Health. 2010;7(4):386-94.
6. Stieger S, Pietschnig J, Kastner CK, Voracek M, Swami V. Prevalence and acceptance of tattoos and piercings: a survey of young adults from the southern German-speaking area of Central Europe. Percept Mot Skills. 2010;110(3 Pt. 2):1065-74. doi: 10.2466/pms.110.C.1065-1074
7. Yen CF, Hsiao RC, Yen JY, Yeh YC, Wang PW, Lin HC, et al. Tattooing among high school students in southern Taiwan: the prevalence, correlates and associations with risk-taking behaviors and depression. Kaohsiung J Med Sci. 2012;28(7):383-9. doi: 10.1016/j.kjms.2011.10.008
8. Majori S, Capretta F, Baldovin T, Busana M, Baldo V, Collaborative Group. Piercing and tatooing in high school students of Veneto region: prevalence and perception of infectious releated risk. J Prev Med Hyg. 2013;54(1):17-23.
9. Chacha CE, Kazaura MR. Body-art practices among undergraduate medical university students in Dar es Salaam, Tanzania, 2014. Indian J Dermatol. 2015;60(2):212. doi: 10.4103/0019-5154.152567
10. Oinam J, Singh AB, Singh YN. Prevalence of tattooing and knowledge about health risk associated with it among adolescent school students in Manipur, North-eastern India: a cross-sectional study. Int J Community Med Public Health. 2019;6(2):774-9. doi: 10.18203/2394-6040.ijcmph20190205
11. Makkai T, McAllister I. Prevalence of tattooing and body piercing in the Australian community. Commun Dis Intell Q Rep. 2001;25(2):67-72. doi: 10.33321/cdi.2001.25.14
12. Stirn A, Hinz A, Brähler E. Prevalence of tattooing and body piercing in Germany and perception of health, mental disorders, and sensation seeking among tattooed and body-pierced individuals. J Psychosom Res. 2006;60(5):531-4. doi: 10.1016/j.jpsychores.2005.09.002
13. Karagas MR, Wasson JH. A World Wide Web-based survey of nonmedical tattooing in the United States. J Am Acad Dermatol. 2012;66(1):e13-4. doi: 10.1016/j.jaad.2010.11.038
14. Sagoe D, Pallesen S, Andreassen CS. Prevalence and correlates of tattooing in Norway: a large-scale cross-sectional study. Scand J Psychol. 2017;58(6):562-70. doi: 10.1111/sjop.12399. PMID: 29105125
15. Renzoni A, Pirrera A, Novello F, Lepri A, Cammarata P, Tarantino C, et al. The tattooed population in Italy: a national survey on demography, characteristics and perception of health risks. Ann Ist Super Sanità. 2018;54(2):126-36. doi: 10.4415/ANN_18_02_08
16. Kluger N. Epidemiology of tattoos in industrialized countries. Curr Probl Dermatol. 2015;48:6-20. doi: 10.1159/000369175
17. Kluger N, Misery L, Seité S, Taieb C. Tattooing: a national survey in the general population of France. J Am Acad Dermatol. 2019;81(2):607-10. doi: 10.1016/j.jaad.2018.10.059
18. Lahousen T, Linder MD, Gieler U, Hofmeister D, Trapp EM, Borkenhagen A, et al. Body modification in Germany: prevalence, gender differences and attitude towards cosmetic surgery. G Ital Dermatol Venereol. 2019;154(6):646-9. doi: 10.23736/S0392-0488.18.06172-2
19. McCarty RD, Trabert B, Millar MM, Kriebel D, Grieshober L, Barnard ME, et al. Associations of demographic, health, and risk-taking behaviors with tattooing in a population-based cross-sectional study of ~18,000 US adults. Res Sq [Preprint]. 2024:rs.3.rs-4838597. doi: 10.21203/rs.3.rs-4838597/v1
20. Tate JC, Shelton BL. Personality correlates of tattooing and body piercing in a college sample: the kids are alright. Pers Individ Differ. 2008;45(4):28155. doi: 10.1016/j.paid.2008.04.011
21. Bosello R, Favaro A, Zanetti T, Soave M, Vidotto G,

Huon G, et al. Tatuaggi e piercing negli adolescenti: correlati familiari e temperamentali [Tattoos and piercings in adolescents: family conflicts and temperament]. Riv Psichiatr. 2010;45(2):102-6.
22. Balci S, Sari E, Mutlu B. Comparison of risk-taking behaviour and frequency of piercing and tattooing among university students. J Pak Med Assoc. 2015;65(6):587-92.
23. Mortensen K, French MT, Timming AR. Are tattoos associated with negative health-related outcomes and risky behaviors? Int J Dermatol. 2019;58(7):816-24. doi: 10.1111/ijd.14372
24. Roberts TA, Ryan SA. Tattooing and high-risk behavior in adolescents. Pediatrics. 2002;110(6):1058-63. doi: 10.1542/peds.110.6.1058
25. Chalarca-Cañas D, Caviedes-Cleves MA, Correa-Londoño LA, Ospina-Gómez JP, Velásquez-Lopera MM. Tattoos: risks and complications, clinical and histopathological approach. An Bras Dermatol. 2024;99(4):491-502. doi: 10.1016/j.abd.2023.07.004
26. Choudhary S, Elsaie ML, Leiva A, Nouri K. Lasers for tattoo removal: a review. Lasers Med Sci. 2010;25(5):619-27. doi: 10.1007/s10103-010-0800-2
27. Ministero della Salute. Linee guida del Ministero della Sanità per l'esecuzione di procedure di tatuaggio e piercing in condizioni di sicurezza. Circolare n. 2.9/156, 5 febbraio1998.
28. Regione Toscana. Legge regionale 31 maggio 2004, n. 28. Disciplina delle attività di estetica e di tatuaggio e piercing. Bollettino Ufficiale della Regione Toscana n. 21, parte prima, 7 giugno 2004.
29. Regione Toscana. Testo coordinato del DPGR 2 ottobre 2007, n. 47/R. Regolamento di attuazione della legge regionale 31 maggio 2004, n. 28 (Disciplina delle attività di estetica e di tatuaggio e piercing). Bollettino Ufficiale della Regione Toscana n. 27, 8 agosto 2008.
30. Regione autonoma Friuli Venezia Giulia. Legge regionale 12 aprile 2012, n. 7. Disciplina delle attività di tatuaggio, di piercing e delle pratiche correlate. Bollettino Ufficiale della Regione autonoma Friuli Venezia Giulia n. 16, 18 aprile 2012.
31. Regione Autonoma Friuli Venezia Giulia. Decreto del Presidente della Regione 14 aprile 2014, n. 64. Regolamento recante la disciplina di attuazione della legge regionale 12 aprile 2012, n. 7 (Disciplina delle attività di tatuaggio, di piercing e delle pratiche correlate). Bollettino Ufficiale della Regione autonoma Friuli Venezia Giulia n. 17, 23 aprile 2014.
32. Regione Veneto. Deliberazione della Giunta Regionale n. 11 del 09 gennaio 2013. Revisione della DGR n. 2401 del 14/10/2010 in materia di tatuaggio e piercing. Nuovi indirizzi regionali per tutelare la salute della popolazione in connessione alle attività di tatuaggio e piercing. Bollettino Ufficiale della Regione Veneto n. 10, 25 gennaio 2013.
33. Regione Marche. Legge regionale 18 novembre 2013, n. 38. Disciplina dell'attività di tatuaggio e piercing. Bollettino Ufficiale della Regione Marche n. 93, 28 novembre 2013.
34. Regione Lazio. Legge Regionale 3 marzo 2021, n. 2. Disposizioni relative alle attività di tatuaggio e piercing. Bollettino Ufficiale della Regione Lazio n. 23, 4 marzo 2021.
35. Regione Lazio. Deliberazione Giunta Regionale 3 maggio 2022, n. 270. Disposizioni attuative dell'art. 9, comma 1, della LR 3 marzo 2021, n. 2, "Disposizioni relative alle attività di tatuaggio e di piercing" e successive modifiche ed integrazioni. Bollettino Ufficiale della Regione Lazio n. 40, 10 maggio 2022.
36. Regione Lombardia. Legge Regionale 23 luglio 2021, n. 13. Disciplina delle attività di tatuaggio e piercing. Bollettino Ufficiale della Regione Lombardia n. 30, Supplemento del 27 luglio 2021.
37. Domínguez A, Bruguera M, Vidal J, Plans P, Salleras L. Community-based seroepidemiological survey of HCV infection in Catalonia, Spain. J Med Virol. 2001;65(4):688-93. doi: 10.1002/jmv.2091
38. Lee PL, Wang JH, Tung HD, Lee CM, Lu SN. A higher than expected recovery rate from hepatitis C infection amongst adolescents: a community study in a hepatitis C-endemic township in Taiwan. Trans R Soc Trop Med Hyg. 2004;98(6):367-72. doi: 10.1016/j.trstmh.2003.10.013
39. Pérez CM, Suárez E, Torres EA, Román K, Colón V. Seroprevalence of hepatitis C virus and associated risk behaviours: a population-based study in San Juan, Puerto Rico. Int J Epidemiol. 2005;34(3):593-9. doi: 10.1093/ije/dyi059
40. Nguyen VT, McLaws ML, Dore GJ. Prevalence and risk factors for hepatitis C infection in rural north Vietnam. Hepatol Int. 2007;1(3):387-93. doi: 10.1007/s12072-007-9008-3
41. Ahmed F, Irving WL, Anwar M, Myles P, Neal KR. Prevalence and risk factors for hepatitis C virus infection in Kech District, Balochistan, Pakistan: most infections remain unexplained. A cross-sectional study. Epidemiol Infect. 2012;140(4):716-23. doi: 10.1017/S0950268811001087
42. Kvitko DT, Bastos GA, Pinto ME. Prevalence of risk factors for hepatitis C and associated factors: a population-based study in southern Brazil. Arq Gastroenterol. 2013;50(2):117-22. doi: 10.1590/s0004-28032013000200020
43. Makiani MJ, Davoodian P, Abedi F, Hossini M, Zare S, Rahimi S, et al. AIDS and hepatitis B and C high risk behaviors among 15 to 45 years old individuals in Bandar Abbas (Iran) in 2012. Electron Physician. 2014;6(3):884-9. doi: 10.14661/2014.883-889
44. Bhate P, Saraf N, Parikh P, Ingle M, Phadke A, Sawant P. Cross sectional study of prevalence and risk factors of hepatitis B and hepatitis C infection in a rural village of India. Arq Gastroenterol. 2015;52(4):321-4. doi: 10.1590/S0004-28032015000400013
45. Melo LV, Silva MA, Perdoná Gda S, Nascimento MM, Secaf M, Monteiro RA, et al. Epidemiological study of hepatitis B and C in a municipality with rural characteristics: Cássia dos Coqueiros, State of São Paulo, Brazil. Rev Soc Bras Med Trop. 2015;48(6):674-81. doi: 10.1590/0037-8682-0222-2015
46. Moezzi M, Imani R, Karimi A, Pourheidar B. Hepatitis C seroprevalence and risk factors in adult population of Chaharmahal and Bakhtiari Province of Iran in 2013. J Clin Diagn Res. 2015;9(10):LC13-7. doi: 10.7860/JCDR/2015/14986.6694
47. Wasitthankasem R, Vichaiwattana P, Siripon N, Posuwan N, Auphimai C, Klinfueng S, et al. Assessment of hepatitis C virus infection in two adjacent Thai provinces with drastically different seroprevalence. PLoS One. 2017;12(5):e0177022. doi: 10.1371/journal.pone.0177022
48. Hagan LM, Kasradze A, Salyer SJ, Gamkrelidze A, Alkhazashvili M, Chanturia G, et al. Hepatitis C prevalence and risk factors in Georgia, 2015: setting a baseline for elimination. BMC Public Health. 2019;19(Suppl. 3):480. doi: 10.1186/s12889-019-6784-3
49. Demirchyan A, Mozalevskis A, Sahakyan S, Musheghyan L, Aslanyan L, Muradyan D, et al. Seroprevalence of hepatitis C virus and factors associated with it in Armenia,

2021. Viruses. 2024;16(9):1446. doi: 10.3390/v16091446

50. Vasconcelos MPA, Sánchez-Arcila JC, Peres L, de Sousa PSF, Castro-Alves J, Albuquerque HG, et al. Seroprevalence of hepatitis B, C, and D and associated factors in the semi-isolated Yanomami Amazonian indigenous community. BMC Infect Dis. 2024;24(1):15. doi: 10.1186/s12879-023-08928-z
51. Huang P, Zhu LG, Zhai XJ, Zhu YF, Yue M, Su J, et al. Hepatitis C virus infection and risk factors in the general population: a large community-based study in eastern China, 2011-2012. Epidemiol Infect. 2015;143(13):2827-36. doi: 10.1017/S0950268814003719
52. Sayad B, Fatemeh S, Keyvani H, Mansour R, Tannaz A, Vaziri S, et al. Seroepidemiology of Hepatitis C in Kermanshah (West of Iran, 2006). Hep Mon. 2008;8(2):141-6.
53. Ghadir MR, Belbasi M, Heidari A, Jandagh M, Ahmadi I, Habibinejad H, et al. Distribution and risk factors of hepatitis B virus infection in the general population of Central Iran. Hepat Mon. 2012;12(2):112-7. doi: 10.5812/hepatmon.822
54. Gheorghe L, Csiki IE, Iacob S, Gheorghe C. The prevalence and risk factors of hepatitis B virus infection in an adult population in Romania: a nationwide survey. Eur J Gastroenterol Hepatol. 2013;25(1):56-64. doi: 10.1097/MEG.0b013e328358b0bb
55. Belay AS, Abateneh DD, Yehualashet SS, Kebede KM. Hepatitis B virus infection and associated factors among adults in Southwest Ethiopia: community-based cross-sectional study. Int J Gen Med. 2020;13:323-32.
56. Rajalatchumi A, Chinnakali P, Dhodapkar R, Olickal JJ, Subramanian S, Kar SS, et al. Prevalence of hepatitis B infection and its associated factors in rural South India. Indian J Gastroenterol. 2025;44(4):517-24. doi: 10.1007/s12664-025-01768-6
57. Alavian SM, Tabatabaei SV, Nourizad S, Mansouri F, Khademi N, Amini Kafi-abad S, et al. Seroepidemiology of HBV infection in Kermanshah- West of Iran; a population-based study. Jundishapur J Microbiol. 2012;5(4):564-9. doi: 10.5812/jjm.4156
58. Dandona L, Dandona R, Kumar GA, Reddy GB, Ameer MA, Ahmed GM, et al. Risk factors associated with HIV in a population-based study in Andhra Pradesh state of India. Int J Epidemiol. 2008;37(6):1274-86. doi: 10.1093/ije/dyn161
59. Holakouie N, Kargar Kheirabad A, Sajjadi MJ, Gouklani H. Prevalence of HIV disease between Qeshm Island people during 2013-2014, Iran. J Med Life. 2015;8(Spec Iss 3):190-4.
60. Forbes GB. College students with tattoos and piercings: motives, family experiences, personality factors, and perception by others. Psychol Rep. 2001;89(3):774-86. doi: 10.2466/pr0.2001.89.3.774
61. Ekinci O, Topcuoglu V, Sabuncuoglu O, Berkem M, Akin E, Gumustas FO. The association of tattooing/body piercing and psychopathology in adolescents: a community-based study from Istanbul. Community Ment Health J. 2012;48(6):798-803. doi: 10.1007/s10597-012-9509-y
62. Swami V, Pietschnig J, Bertl B, Nader IW, Stieger S, Voracek M. Personality differences between tattooed and non-tattooed individuals. Psychol Rep. 2012;111(1):97-106. doi: 10.2466/09.07.21.PR0.111.4.97-106
63. Swami V, Gaughan H, Tran US, Kuhlmann T, Stieger S, Voracek M. Are tattooed adults really more aggressive and rebellious than those without tattoos? Body Image. 2015;15:149-52. doi: 10.1016/j.bodyim.2015.09.001
64. Swami V, Tran U, Kuhlmann T, Stieger S, Gaughan H, Voracek M. More similar than different: tattooed adults are only slightly more impulsive and willing to take risks than non-tattooed adults. Pers Individ Diff. 2016;88:40-4. doi: 10.1016/j.paid.2015.08.054
65. Manuel L, Sheehan E. Getting inked: tattoos and college students. Coll Stud J. 2007;41:1089-97.
66. Guéguen N. Tattoo, piercing, and adolescent tobacco consumption. Int J Adolesc Med Health. 2013;25(1):87-9. doi: 10.1515/ijamh-2013-0012
67. Koch JR, Roberts AE, Armstrong ML, Owen DC. College students, tattoos, and sexual activity. Psychol Rep. 2005;97(3):887-90. doi: 10.2466/pr0.97.3.887-890
68. Guéguen N. Tattoos, piercings, and sexual activity. SBP. 2012;40(9):1543-8. doi: 10.2224/sbp.2012.40.9.1543
69. Gallè F, Mancusi C, Di Onofrio V, Visciano A, Alfano V, Mastronuzzi R, et al. Awareness of health risks related to body art practices among youth in Naples, Italy: a descriptive convenience sample study. BMC Public Health. 2011;11:625. doi: 10.1186/1471-2458-11-625
70. Quaranta A, Napoli C, Fasano F, Montagna C, Caggiano G, Montagna MT. Body piercing and tattoos: a survey on young adults' knowledge of the risks and practices in body art. BMC Public Health. 2011;11:774. doi: 10.1186/1471-2458-11-774
71. Show KL, Le Win L, Saw S, Myint CK, Than KM, Oo YTN, et al. Knowledge of potential risk of blood-borne viral infections and tattooing practice among adults in Mandalay Region, Myanmar. PLoS One. 2019;14(1):e0209853. doi: 10.1371/journal.pone.0209853
72. Morlock R, Morlock A. Think before you ink: perception, prevalence, and correlates of tattooing and tattoo regret in US adults. Cureus. 2023;15(11):e48167. doi: 10.7759/cureus.48167
73. Heywood W, Patrick K, Smith AM, Simpson JM, Pitts MK, Richters J, et al. Who gets tattoos? Demographic and behavioral correlates of ever being tattooed in a representative sample of men and women. Ann Epidemiol. 2012;22(1):51-6. doi: 10.1016/j.annepidem.2011.10.005
74. King KA, Vidourek RA. Getting inked: tattoo and risky behavioral involvement among university students. Soc Sci J. 2013;50(4):540-6. doi: 10.1016/j.soscij.2013.09.009
75. Laumann AE, Derick AJ. Tattoos and body piercings in the United States: a national data set. J Am Acad Dermatol. 2006;55(3):413-21. doi: 10.1016/j.jaad.2006.03.026
76. Gallè F, Valeriani F, Marotta D, De Giorgi A, Bargellini A, Bianco A, et al. What about your body ornament? Experiences of tattoo and piercing among Italian youths. Int J Environ Res Public Health. 2021;18(23):12429. doi: 10.3390/ijerph182312429
77. Aiyedun V. Literature review on the epidemiology of tattooing and its complications. Colindale: Health Protection Agency; 2013.
78. Kluger N, Misery L, Seité S, Taieb C. Tattoos and body-piercings among French teenagers. Forum for Nord Derm Ven. 2019;24(4):115-6.
79. Bjerre RD, Ulrich NH, Linneberg A, Duus Johansen J. Adverse reactions to tattoos in the general population of Denmark. J Am Acad Dermatol. 2018;79(4):770-2. doi: 10.1016/j.jaad.2018.03.038
80. Laux P, Tralau T, Tentschert J, Blume A, Dahouk SA, Bäumler W, et al. A medical-toxicological view of tattooing. Lancet. 2016;387(10016):395-402. doi: 10.1016/S0140-6736(15)60215-X
81. Breuner CC, Levine DA; AAP Committee on Adolescence. Adolescent and young adult tattooing, piercing, and scarification. Pediatrics. 2017;140(4):e20171962.
82. Rogowska P, Szczerkowska-Dobosz A, Kaczorowska R, Słomka J, Nowicki R. Tattoos: evaluation of knowledge about health complications and their prevention among

students of Tricity universities. J Cosmet Dermatol. 2017;17(1):27-32. doi: 10.1111/jocd.12479

83. Dukes RL, Stein JA. Ink and holes: correlates and predictive associations of body modification among adolescents. Youth Soc. 2011;43(4):1547-69. doi: 10.1177/0044118X10396638
84. Armstrong ML, Owen DC, Roberts AE, Koch JR. College students and tattoos. Influence of image, identity, family, and friends. J Psychosoc Nurs Ment Health Serv. 2002;40(10):20-9. doi: 10.3928/0279-3695-20021001-07
85. Scatigna M, Masotta V, Cesarini V, Renzetti P, Petrucci C, Lancia L, et al. Sociocultural overview and predisposing factors of body art in a health promotion perspective: survey on a sample of Italian young adults. Ann Ig. 2022;34(5):439-52. doi: 10.7416/ai.2021.2497
86. Cegolon L, Miatto E, Bortolotto M, Benetton M, Mazzoleni F, Mastrangelo G; VAHP Working Group. Body piercing and tattoo: awareness of health-related risks among 4,277 Italian secondary school adolescents. BMC Public Health. 2010;10:73. doi: 10.1186/1471-2458-10-73
87. Drews DR, Allison CK, Probst JR. Behavioral and self-concept differences in tattooed and nontattooed college students. Psychol Rep. 2000;86(2):475-81. doi: 10.2466/pr0.2000.86.2.475
88. Mayers LB, Judelson DA, Moriarty BW, Rundell KW. Prevalence of body art (body piercing and tattooing) in university undergraduates and incidence of medical complications. Mayo Clin Proc. 2002;77(1):29-34. doi: 10.4065/77.1.29
89. Mayers L, Chiffriller S. Sequential survey of body piercing and tattooing prevalence and medical complication incidence among college students. Arch Pediatr Adolesc Med. 2007;161(12):1219-20. doi: 10.1001/archpedi.161.12.1219-b
90. Lipscomb TJ, Jones MA, Totten JW. Body Art: prevalence, search and evaluation among University Business students. Serv Mark Q. 2008;29(4):42-65. doi: 10.1080/15332960802218745
91. Owen DC, Armstrong ML, Koch JR, Roberts AE. College students with body art: well-being or high-risk behavior? J Psychosoc Nurs Ment Health Serv. 2013;51(10):20-8. doi: 10.3928/02793695-20130731-03
92. Zrno M, Frencl M, Degmečić D, Požgain I. Emotional profile and risk behaviours among tattooed and non-tattooed students. Med Glas (Zenica). 2015;12(1):93-8.
93. Preti A, Pinna C, Nocco S, Mulliri E, Pilia S, Petretto DR, et al. Body of evidence: tattoos, body piercing, and eating disorder symptoms among adolescents. J Psychosom Res. 2006;61(4):561-6. doi: 10.1016/j.jpsychores.2006.07.002
94. Cegolon L, Xodo C, Mastrangelo G; VAHP Working Group. Characteristics of adolescents who expressed indifference or no interest towards body art. BMC Public Health. 2010;10:605. doi: 10.1186/1471-2458-10-605
95. Clerici R, Meggiolaro S. The context of body art: body piercing and tattooing among High School students in a Northeastern Italian Region. SAGE Open. 2011;1(3). doi: 10.1177/2158244011425833
96. Protano C, Valeriani F, Marotta D, Bargellini A, Bianco A, Caggiano G, et al. Assessing undergraduates' perception of risks related to body art in Italy: the SUPeRBA multicenter cross-sectional study. Int J Environ Res Public Health. 2021;18(17):9233. doi: 10.3390/ijerph18179233
97. Cegolon L, Mastrangelo G, Mazzoleni F, Majori S, Baldovin T, Xodo C; VAHP Working Group. Body art in 4,277 Italian secondary school adolescents: prevalence and associations with personal and family characteristics. Fam Med. 2010;42(4):273-9.
98. Ernst M, Borkenhagen A, Fegert JM, Brähler E, Plener PL. The association of childhood abuse and neglect with tattoos and piercings in the population: evidence from a representative community survey. BMC Psychol. 2022;10(1):105. doi: 10.1186/s40359-022-00811-x
99. Tranter B, Grant R. A class act? Social background and body modifications in Australia. J Sociol. 2018;54(3):412-28. doi: 10.1177/1440783318755017
100. Wise RM, Akınkoç İ. Tattoos, risk-taking behaviors, and religiosity among young adults in Turkey. JPER. 2022;30(2):53-70.
101. Huxley C, Grogan S. Tattooing, piercing, healthy behaviours and health value. J Health Psychol. 2005;10(6):831-41. doi: 10.1177/1359105305057317
102. Notara V, Gnardellis C, Sakellari E, Soultatou P, Petratou E, Dragomanovits K, et al. Health knowledge and motives on tattooing: a community-based cross-sectional study in Greece. J Cosmet Dermatol. 2022;21(2):720-8. doi: 10.1111/jocd.14119
103. Dillingh R, Kooreman P, Potters J. Tattoos, lifestyle, and the labor market. Labour. 2020;34(2):191-214.
104. French MT, Maclean JC, Robins PK, Sayed B, Shiferaw L. Tattoos, employment, and labor market earnings: is there a link in the ink? Sout Econ J. 2016;82(4):1212-46. Available from: https://www.jstor.org/stable/26632314.
105. Röhrl K, Stenberg B. Lifestyle factors and hand eczema in a Swedish adolescent population. Contact Dermatitis. 2010;62(3):170-6. doi: 10.1111/j.1600-0536.2009.01679.x
106. Fors R, Persson M, Bergström E, Stenlund H, Stymne B, Stenberg B. Lifestyle and nickel allergy in a Swedish adolescent population: effects of piercing, tattooing and orthodontic appliances. Acta Derm Venereol. 2012;92(6):664-8. doi: 10.2340/00015555-1305

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 315-319
DOI: 10.4415/ANN_25_04_10

Sodium oxybate and acamprosate association for maintenance of alcohol abstinence: a case series

Fabio Caputo[1], Martina Lombardi[2], Caterina Trevisan[2], Anna Loffreda[3], Alberto Casabianca[4], Lisa Lungaro[5], Anna Costanzini[5], Giacomo Caio[1], Gianni Testino[6], Stefano Volpato[2] and Roberto De Giorgio[1]

[1]Centro Universitario per lo Studio ed il Trattamento delle Patologie Alcol-Correlate (PACC), Dipartimento di Medicina Traslazionale, Università degli Studi di Ferrara, Ferrara, Italy
[2]Dipartimento di Scienze Mediche, Università degli Studi di Ferrara, Ferrara, Italy
[3]UOSD Alcolismo, Dipartimento Dipendenze, Azienda Sanitaria Locale Caserta, Caserta, Italy
[4]Dipartimento di Medicina Interna, Ospedale SS. Annunziata, Università degli Studi di Ferrara, Cento, Ferrara, Italy
[5]Dipartimento di Medicina Traslazionale, Università degli Studi di Ferrara, Ferrara, Italy
[6]Struttura Complessa Patologie delle Dipendenze ed Epatologia Alcol correlata, ASL3, Ospedale Policlinico San Martino, Genoa, Italy

Abstract

Background. Disulfiram, acamprosate (ACM), naltrexone, and nalmefene are medications currently approved for the treatment of Alcohol Use Disorder (AUD). Baclofen and sodium oxybate (SO) have been approved for the treatment of AUD and alcohol withdrawal syndrome in France and Italy, respectively. However, concerning the effectiveness of combined therapies for AUD, data from the current literature are contrasting.
Aims. To investigate the outcomes of combined therapy of SO and ACM for the maintenance of alcohol abstinence.
Methods. A sample of 48 AUD patients consecutively enrolled and treated with SO (50-100 mg/kg of body weight, t.i.d.) plus ACM (666 mg three times daily; with dosage reduced in patients with body weight <60 kg) was observed for 12 weeks.
Results. At the 3-month visit, continuous abstinence from alcohol was maintained by 34 patients (70.8%). Fifteen patients (31.3%) reported side effects like nausea, dizziness, and abdominal pain, with no significant differences between abstinent and not abstinent patients.
Conclusion. SO plus ACM may be an effective and safe pharmacological combination for maintaining alcohol abstinence in AUD patients. Future *ad hoc* clinical trials are needed to test this therapeutic association for AUD treatment.

Key words
- alcohol use disorder
- combined pharmacological treatment
- acamprosate
- sodium oxybate

INTRODUCTION

Alcohol consumption is responsible for 5.9% of all deaths (3.3 million), accounting for 5.1% of the global disease burden [1]. Alcohol Use Disorder (AUD) has a European and US adult population prevalence of 7-10% [1]. Currently, disulfiram, acamprosate (ACM), and naltrexone are medications approved by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA), while nalmefene has been approved only by EMA for the treatment of AUD [2]. In addition, baclofen has been authorized by the French agency for the treatment of AUD [2, 3], and sodium oxybate (SO) has been approved by the Italian agency for the treatment of alcohol withdrawal syndrome [4]. The actual efficacy of these combined pharmacological therapies raised debate among experts as these drugs yielded contrasting results [5].

SO, or the sodium salt of gamma-hydroxybutyrate, acts directly on the gamma-aminobutyric acid (GABA) system as a GABA$_B$ agonist and indirectly through SO-derived GABA [4, 6, 7], and exhibits an alcohol-mimicking effect. Compared to placebo, SO was effective in the treatment of alcohol withdrawal syndrome and in preventing relapses in previously detoxified participants [8].

ACM shows a neuroprotective effect, which can be explained through the antagonistic activity on the

Address for correspondence: Fabio Caputo, Centro Universitario per lo Studio ed il Trattamento delle Patologie Alcol-Correlate (PACC), Dipartimento di Medicina Traslazionale, Università degli Studi di Ferrara, Via Luigi Borsari 46, 44121 Ferrara, Italy. E-mail: fabio.caputo@unife.it.

N-methyl-D-aspartate (NMDA) glutamate receptor, and subsequent reduction of the excessive intracellular calcium flow [9]. This mechanism improves dysphoria, often identifiable in patients affected by AUD, and indirectly reduces alcohol craving and consumption [10].

So far, the few published studies involving SO in combination with other drugs showed positive results in the maintenance of alcohol abstinence and the prevention of relapse [11-14]. Similarly, limited evidence has been produced about ACM in association with other drugs [10]. However, no study examined the possible efficacy of the combination SO with ACM in patients with AUD. Therefore, our case series aimed to evaluate the outcomes of a combined therapy of SO plus ACM in maintaining alcohol abstinence in a cohort of patients with AUD.

METHODS

We enrolled 48 AUD patients consecutively admitted over 24 months to the Unit of Alcohol Addiction Treatment, SerD, Caserta and in the Centre for the Study and Treatment of Alcohol-Related Diseases, SS. Annunziata Hospital, Cento, Ferrara. AUD was defined according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria [15]. Patients with severe liver and/or renal failure were excluded. After the resolution of the acute phase of alcohol withdrawal syndrome [16], only patients with the persistence of symptoms of alcohol withdrawal were recruited. All recruited patients were treated with oral doses of SO (50-100 mg/kg of body weight, tid), and they needed the treatment with SO for at least 12 weeks. In addition, ACM (666 mg three times daily, reduced in those patients with a body weight <60 kg) was combined with SO for 12 weeks too. Each subject underwent weekly outpatient visits for 12 weeks, recording the degree of abstinence from alcohol and the amount of daily alcohol intake (expressed as standard US drinks; one standard US drink = 12 g of absolute alcohol) [1]. Complete abstinence was assessed based on interviews with patients and their relatives, and by measuring ethyl glucuronide in urine [17]. Laboratory parameters related to alcohol abuse – aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (GGT), and mean red blood cell volume (MCV) – were assessed at the beginning and after three months of treatment. An accurate investigation on the amount of abused SO was carried out with the assistance of patients and their family members to whom the SO had been entrusted. In addition to weekly counseling sessions and pharmacological therapy, self-help groups, such as Alcoholics Anonymous and social services, were recommended.

The study was performed in accordance with the ethical standards of the 1975 Declaration of Helsinki, as revised in 2013, and all participants gave verbal informed consent.

Statistical analysis

The characteristics of the study participants were expressed as median and interquartile range (IQR) for quantitative variables (due to the non-normal distribution) and as count and percentages for categorical variables. Sociodemographic and treatment-related variables were compared between participants who were abstinent *vs* those who were not abstinent at the end of the observation period using the Mann-Whitney U test and the Chi-square or Fisher test, as appropriate. Intra-individual changes in laboratory parameters from the start of treatment to the 12-week visit within the groups of abstinent and not abstinent individuals were assessed through the non-parametric Wilcoxon test for paired samples. All analyses were performed using the IBM SPSS version 25.0 statistical software. All analyses were two-tails, and a p-value <0.05 was defined as statistically significant.

RESULTS

The sample included 48 AUD patients (34 males and 14 females) with a median age of 47.5 years, whose clinical and demographic characteristics are shown in *Table 1*. Patients who resulted abstinent and those who were not abstinent at the 3-month visit did not differ in terms of age, education, baseline units of alcohol intake, duration of alcohol consumption, and laboratory markers of alcohol misuse, while the former group was more likely to use illegal drugs at the first visit *(Table 1)*.

At the 3-month visit, continuous abstinence from alcohol was maintained by 34 patients (70.8%). During the observation period, all laboratory markers of alcohol misuse significantly decreased both in abstinent and not abstinent patients *(Table 2)*. Concerning side effects *(Table 3)*, 15 (31.3%) patients reported mainly nausea (20.8%), dizziness (8.3%), and abdominal pain (2.1%), without significant differences between abstinent and not abstinent patients. A significantly higher dropout rate was observed in patients who were not abstinent than abstinent (50% *vs* 5.9%). At the end of treatment, no patient developed cravings or episodes of abuse of SO, and none showed withdrawal symptoms at SO discontinuation. No additional sedative effects due to alcohol/SO interaction were observed in patients failing to maintain abstinence.

DISCUSSION

To our knowledge, this is the first case series that evaluated the outcomes of the combined therapy with SO and ACM for AUD. In particular, the present study suggests that the association of these drugs may be effective in maintaining complete alcohol abstinence in almost 70% of AUD patients. These results align with previous experiences of SO combined with other compounds. Indeed, we previously showed that the degree of abstinence ranged from 68% to 72% in patients treated with SO plus DF [12] and SO plus NTX [11], respectively. Moreover, the therapeutic combination between SO and ACM seems more promising than other pharmacological regimens. For instance, recent studies found that the abstinence rate was about 50% in patients treated with ACM plus NTX, while considering therapies with SO or ACM alone, it did not overcome 40% [18]. Of note, the high number of patients (almost two-thirds of the sample) achieving complete abstinence at the end of treatment exhibited a sig-

Table 1
Baseline characteristics of the patients in the sample as a whole and by treatment outcome

Characteristics	All (n=48)	Not abstinent (n=14, 29.2%)	Abstinent (n=34, 70.8%)	p-value
Age	47.5 (41.25-54)	47.5 (41.25-53)	47.5 (40.75-54.5)	0.81
Sex (male)	34 (70.8)	9 (64.3)	25 (73.5)	0.52
Scholarity				0.11
Primary	19 (39.6)	4 (28.6)	15 (44.1)	
Secondary	24 (50)	10 (71.4)	14 (41.2)	
Degree or above	5 (0.4)	0 (0)	5 (14.7)	
Pre-treatment UA/day	11.5 (8.25-16)	11 (8-16)	11.5 (9-16)	0.75
Duration of addiction (months)	18 (10-26.5)	16.5 (10.75-28.25)	18 (10-25)	0.75
Current or past substances use				0.02
Current	3 (6.3)	3 (21.4)	0 (0.0)	
Past	12 (25)	3 (21.4)	9 (26.5)	
Type of substance used				0.96
Heroin	3 (6.3)	1 (7.1)	2 (5.9)	
Cocaine	5 (10.4)	2 (14.3)	3 (8.8)	
Cannabis	7 (14.6)	3 (21.4)	4 (11.8)	
Psychiatric comorbidities	16 (33.3)	6 (42.9)	10 (29.4)	0.37
Biochemical parameters				
GGT	97.5 (55.75-188.75)	162.5 (59.5-573)	90.5 (54.5-167)	0.21
GPT	39.5 (23.25-78.25)	46 (30-77.75)	32 (22-81.5)	0.11
GOT	31 (22-78.25)	51 (29.75-80.75)	25.5 (20.75-82)	0.10
MCV	95.5 (92-102)	102 (94.75-107.25)	94.5 (91.8-100)	0.02

UA: unit of alcohol; GGT: γ-glutamyl transpeptidase; GPT: glutamic pyruvic transaminase; GOT: glutamic oxaloacetic transaminase; MCV: mean red blood cell volume.

Table 2
Changes in biochemical parameters and alcohol intake in abstinent (n=34) and not abstinent (n=14) individuals at the 3-month control

	Time 0	Time 1	ΔT1-T0	p-value
GOT				
Abstinent	25.5 (20.75-82.0)	16.5 (14.75-21.5)	-11.5 (- 56.75, -3)	<0.001
Not abstinent	51 (29.75-80.75)	22 (20-36)	-28 (- 44.25, -9.50)	0.001
GPT				
Abstinent	32 (22-81.5)	16.0 (13-22.25)	-14.5 (-49, -7)	<0.001
Not abstinent	46 (30-77.75)	26.5 (18.50-36.5)	-19 (-48, -12.5)	0.001
GGT				
Abstinent	90.5 (54.5-167)	28 (18.75-33)	-66 (-141.5, -27.25)	<0.001
Not abstinent	162.5 (59.5-573)	56 (28-112.75)	-60 (-468.25, -29.5)	0.001
MCV				
Abstinent	94.50 (91.75-100)	88 (86.75-91.25)	-5.50 (-8.25,-4)	<0.001
Not abstinent	102 (94.75-107.25)	95 (90.50-99)	-5.50 (-12.75,-3)	0.001
Alcohol (Unit/day)				
Abstinent	11.50 (9-16)	0 (0.0)	-11.5 (-16, -9)	<0.001
Not abstinent	11 (8-16)	2.00 (1.75-3.25)	-9.5 (-13.25, -6)	0.001

GGT: γ-glutamyl transpeptidase; GPT: glutamic pyruvic transaminase; GOT: glutamic oxaloacetic transaminase; MCV: mean red blood cell volume.

Table 3
Treatment outcomes of the patients involved

Treatment outcomes	All (n=48)	Not abstinent (n=14, 29.2%)	Abstinent (n=34, 70.8%)	p-value
Drop-out	9 (18.8)	7 (50)	2 (5.9)	<0.001
Side effects	15 (31.3)	5 (35.7)	10 (29.4)	0.669
Type of effects				0.662
Nausea	10 (20.8)	4 (28.6)	6 (17.6)	
Abdominal pain	1 (2.1)	0 (0)	1 (2.9)	
Dizziness	4 (8.3)	1 (7.1)	3 (8.8)	

nificant reduction of all laboratory markers of alcohol misuse. In the not abstinent group, we also observed a significant decrease in all laboratory markers of alcohol misuse confirming that the reduction of alcohol intake improved liver function too.

The high potential of the efficacy of this treatment is likely ascribable to the different actions of SO and ACM. These medications affect the two major signaling systems, i.e. GABA and NMDA both involved in AUD. SO has an alcohol-mimicking effect on GABA receptors and acts as a replacement therapy, while ACM is an antagonist of glutamate and modulates the upregulation of the NMDA system.

An important issue to be considered is craving and the potential abuse of SO [6, 7]. In our study none of the treated patients showed craving for SO. It is well known that both abuse of and craving for SO may limit the use of this drug, although clinical trials suggested that these effects are relatively rare at therapeutic doses [7, 19, 20]. Craving and the abuse of SO are more frequent in patients with psychiatric comorbidities or poly-drug use [19, 20]. In the case series herein reported, conversely to previous experience [19], craving and abuse were not documented although about one-third of patients experienced previous or current substance abuse.

A further aspect that needs to be considered is the prescription of SO. In Italy, SO has been used for over 30 years for the treatment of AUD in the absence of specific indications [21]. In 2018 the Italian Drug Agency (Agenzia Italiana del Farmaco, AIFA) modified the clinical prescription of SO leaving only the indication for the treatment of alcohol withdrawal syndrome, removing the indication for maintaining abstinence from alcohol and the prevention of relapse. For this reason, in the guidelines of the treatment of AUD recently published on the Italian National Guidelines System, SO has been included only with the indication for the treatment of alcohol withdrawal syndrome since it is an off-label medication for the maintenance of alcohol abstinence and the prevention of relapse [21]. Indeed, after the resolution of the acute phase of alcohol withdrawal syndrome [16], all reported patients in our case series showed the persistence of symptoms of alcohol withdrawal which allowed the treating physicians to use SO for at least 12 weeks. In favor of the safety and efficacy outside the specifically authorized use for the treatment of alcohol withdrawal syndrome, essential data on the use of SO for maintaining alcohol abstinence and relapse prevention have been recently published. At this regard, a meta-regression analysis showed that SO was more effective in AUD patients with higher severity, and undergone longer treatments [22].

In conclusion, this case series suggests that SO and ACM are safe and may be effective in patients with AUD. Well-designed, controlled clinical trials are needed to establish whether the combination of drugs might become a key step in the therapeutic approach to AUD.

Funding

The Authors report no involvement in the research by the sponsor that could have influenced the outcome of this work. FC and RDG receive constant support from the University of Ferrara (FAR 2024 and FIRD 2024 funds).

Conflict of interest statement

The Authors declare no conflict of interest.

Received on 6 August 2025.
Accepted on 3 November 2025.

REFERENCES

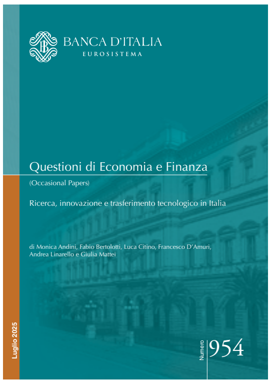
1. World Health Organization. Global status report on alcohol and health and treatment of substance use disorders. Geneva: WHO; 2024.
2. Haber PS. Identification and treatment of alcohol use disorder. N Engl J Med. 2025;392(3):258-66. doi: 10.1056/NEJMra2306511
3. Agabio R, Saulle R, Rösner S, Minozzi S. Baclofen for alcohol use disorder. Cochrane Database Syst Rev. 2023;1(1):CD012557. doi: 10.1002/14651858.CD012557.pub3
4. Guiraud J, van den Brink W. Sodium oxybate: A comprehensive review of efficacy and safety in the treatment of alcohol withdrawal syndrome and alcohol dependence. Int Rev Neurobiol. 2024;178:213-81. doi: 10.1016/bs.irn.2024.07.005
5. Naglich AC, Lin A, Wakhlu S, Adinoff BH. Systematic review of combined pharmacotherapy for the treatment of alcohol use disorder in patients without comorbid conditions. CNS Drugs. 2018;32(1):13-31. doi: 10.1007/s40263-017-0484-2

6. Antonelli M, Ferrulli A, Sestito L, Vassallo GA, Tarli C, Mosoni C, et al. Alcohol addiction - the safety of available approved treatment options. Expert Opin Drug Saf. 2018;17(2):169-77. doi: 10.1080/14740338.2018.1404025
7. Burnette EM, Nieto SJ, Grodin EN, Meredith LR, Hurley B, Miotto K, et al. Novel agents for the pharmacological treatment of alcohol use disorder. Drugs. 2022;82(3):251-74. doi: 10.1007/s40265-021-01670-3
8. Leone MA, Vigna-Taglianti F, Avanzi G, Brambilla R, Faggiano F. Gamma-hydroxybutyrate (GHB) for treatment of alcohol withdrawal and prevention of relapses. Cochrane Database Syst Rev. 2010;(2):CD006266. doi: 10.1002/14651858.CD006266.pub2
9. De Witte P, Littleton J, Parot P, Koob G. Neuroprotective and abstinence-promoting effects of acamprosate: elucidating the mechanism of action. CNS Drugs. 2005;19(6):517-37. doi: 10.2165/00023210-200519060-00004
10. Soyka M, Rösner S. Modern pharmacotherapy guidance for treating alcohol use disorders. Expert Opin Pharmacother. 2025;26(2):147-56. doi: 10.1080/14656566.2024.2445734
11. Caputo F, Addolorato G, Stoppo M, Francini S, Vignoli T, Lorenzini F, et al. Comparing and combining gamma-hydroxybutyric acid (GHB) and naltrexone in maintaining abstinence from alcohol: an open randomised comparative study. Eur Neuropsychopharmacol. 2007;17(12):781-9. doi: 10.1016/j.euroneuro.2007.04.008
12. Caputo F, Trevisan C, Vignoli T, Maremmani AGI, Montesano F, Carboni G, et al. Efficacy of sodium oxybate plus disulfiram for the maintenance of alcohol abstinence in treatment-resistant patients with alcohol use disorder: a multicentre retrospective study. Ann Ist Super Sanità. 2024;60(4):252-7. doi:10.4415/ANN_24_04_03
13. Maremmani AGI, Pani PP, Rovai L, Pacini M, Dell'Osso L, Maremmani I. Long-term γ-hydroxybutyric acid (GHB) and disulfiram combination therapy in GHB treatment-resistant chronic alcoholics. Int J Environ Res Public Health. 2011;8(7):2816-27. doi: 10.3390/ijerph8072816
14. Stella L, Addolorato G, Rinaldi B, Capuano A, Berrino L, Rossi F, et al. An open randomized study of the treatment of escitalopram alone and combined with gamma-hydroxybutyric acid and naltrexone in alcoholic patients. Pharmacol Res. 2008;57(4):312-7. doi: 10.1016/j.phrs.2008.03.001
15. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Fifth Edition. Washington DC: American Psychiatric Publishing; 2013.
16. Heilig M, Egli M, Crabbe JC, Becker HC. Acute withdrawal, protracted abstinence and negative affect in alcoholism: are they linked? Addict Biol. 2010;15(2):169-84. doi: 10.1111/j.1369-1600.2009.00194.x
17. Jones AW. Brief history of the alcohol biomarkers CDT, EtG, EtS, 5-HTOL, and PEth. Drug Test Anal. 2024;16(6):570-87. doi: 10.1002/dta.3584
18. Cheng HY, McGuinness LA, Elbers RG, MacArthur GJ, Taylor A, McAleenan A, et al. Treatment interventions to maintain abstinence from alcohol in primary care: systematic review and network meta-analysis. BMJ. 2020;371:m3934. doi: 10.1136/bmj.m3934
19. Caputo F, Francini S, Stoppo M, Lorenzini F, Vignoli T, Del Re A, et al. Incidence of craving for and abuse of gamma-hydroxybutyric acid (GHB) in different populations of treated alcoholics: an open comparative study. J Psychopharmacol. 2009;23(8):883-90. doi: 10.1177/0269881108094620
20. Caputo F, Francini S, Brambilla R, Vigna-Taglianti F, Stoppo M, Del Re A, et al. Sodium oxybate in maintaining alcohol abstinence in alcoholic patients with and without psychiatric comorbidity. European Neuropsychopharmacology. 2011;21(6):450-6. doi: 10.1016/j.euroneuro.2010.12.005
21. Centro di Riferimento Alcologico Regione Lazio, Dipartimento Salute Mentale ASL Roma 1, Dipartimento di Epidemiologia del Servizio Sanitario Regionale – Regione Lazio ASL Roma 1. Linee guida trattamento del disturbo da uso di alcol. Roma: Sistema Nazionale Linee Guida dell'Istituto Superiore di Sanità; 2024.
22. Guiraud J, Addolorato G, Aubin HJ, Bachelot S, Batel P, de Bejczy A, et al. Sodium oxybate for alcohol dependence: A network meta-regression analysis considering population severity at baseline and treatment duration. Alcohol Alcohol. 2023;58(2):125-33. doi: 10.1093/alcalc/agac070

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 320-321
DOI: 10.4415/ANN_25_04_11

BOOK REVIEWS, NOTES AND COMMENTS

Edited by
Federica Napolitani Cheyne



RICERCA, INNOVAZIONE E TRASFERIMENTO TECNOLOGICO IN ITALIA
Monica Andini, Fabio Bertolotti, Luca Citino, Francesco D'Amuri, Andrea Linarello, Giulia Mattei
Roma: Banca d'Italia Ed.; 2025.
Questioni di Economia e Finanza (Occasional Papers), n. 954 (07/2025)
106 p.
ISSN 1972-6643

Freely available online at https://www.bancaditalia.it/pubblicazioni/qef/2025-0954/index.html?dotcache=refresh

[Research, innovation and technology transfer in Italy]

This careful and comprehensive survey of the current state of Italian research, but above all of its short- and medium-term prospects, is a voluminous text that we strongly recommend to researchers, scholars, and even students. We recommend it to researchers active in industrial research, particularly in pharmacology and pharmaceuticals, or in the diverse world of biomedicine in general, including those who work exclusively or almost exclusively in clinical practice. This substantial "critical reflection" reveals and analyzes (especially through rigorous and thoughtful comparisons with other European countries) the main strengths, but also the weaknesses, that hinder or slow down our overall significant, and often excellent path in the development of biomedical and technological scientific research at the national level.

The discussion is based on a fundamental principle that frames the whole educational narrative, as is usual for Banca d'Italia, an institution that also, or maybe mainly, aims to give practical advice that goes way beyond mere economic or financial issues. In this case, it aims to critically review the whole higher education system, especially research, with a view to improving it. Public research plays a recognized central role, and the related reflections are well worth reading carefully, as they are likely to trigger collective reasoning. The stated intent is to "restore" the ecosystem for Italian innovation (analyzing its various elements separately and together), with the hope that they will gradually interact in an increasingly coordinated and synergistic manner.

Certainly, the limited availability of economic resources allocated to the Italian research system represents a long-standing structural problem that has not yet been fully overcome. Nevertheless, as repeatedly and firmly emphasized by the editors, the excellent performance of Italian scientific research emerges mainly when evaluated through scientific publications: growing in number in the STEM disciplines, i.e., science and technology, where between 2009 and 2023 the most cited publications grew by 60%. This is despite the emergence, and therefore the powerful challenge, of the People's Republic of China: our country has, in fact, maintained unchanged its share of publications in the world (3%). At the European level, we are second, just behind Germany, but we have long surpassed France and Spain. One wonders why this phenomenon persists despite the criticism of the mechanisms for allocating funding, which are not always considered fully meritocratic.

It should be added that the volume's curators probably underestimate the unfortunately growing weakness of the indicators of "scientific output" represented by the quantity/quality of scientific publications: a historically weak criterion, which has shown its limitations with the aggressive and rapid emergence of the so-called predatory journals [1, 2].

A second aspect deeply analyzed in the text is the fragility of our technology transfer, where Italy, when measured by the number of patents filed, although growing, remains at about half that of France and one-fifth that of Germany. On this subject, the former President of the CNR, biomedical engineer Maria Chiara Carrozza, recently identified the difficulties of the so-called scale-up phase: in other words, our research groups "invent" and perhaps come close to obtaining a patent, and sometimes they do but when there is a need to move from a prototype to a large-scale production, the overall ecosystem, which obviously includes the essential industrial component, structurally struggles perhaps due to its historically small, sometimes nuclear size.

The section that is likely to be of most interest to biomedical readers is the one dedicated to pharmacology, which in Italy has a long and prestigious history of excellence. Unfortunately, there have been painful examples of a subsequent decline in the ability to produce genuine innovation and development in this area, which should be addressed by the relevant public bodies, at least at the national level.

Overall, this "ecosystemic" analysis of the elements and problems involved, and of possible future remedies for this situation, make this publication an almost essential reading. Hopefully, it will lead to further seminars, workshops, or thematic conference sessions aimed at the institutions or, rather, at the scientific societies most directly involved in the delicate process of advancing technological knowledge and its applications (including for public health) and biomedicine in general, which has nevertheless implemented powerful means and methods to hyperbolically increase its output of publications. This last element deserves careful consideration, especially given the pressing need to promote evaluation standards that are more suited to the transformed context of scientific publishing and bibliometric practices.

Enrico Alleva, Stella Falsini and Andrea Piccioli
Istituto Superiore di Sanità, Rome, Italy
enrico.alleva@guest.iss.it

REFERENCES

1. Barbaro A. “Predatory” publishers: to recognize them is to avoid them. Journal of EAHIL. 2022;18(1):7-10. doi: 10.32384/jeahil18506
2. Frangipane M. “Superamento dei confini, ‘Slow science’ e libertà della ricerca”. Opening ceremony for the academic year 2023-2024, Accademia Nazionale dei Lincei. https://www.lincei.it/it/node/1320

FILOMENA NITTI
E IL NOBEL NEGATO
Carola Vai
With the contribution of
Maria Luisa Nitti
Soveria Mannelli (CZ):
Rubettino Editore; 2025
208 p.
16,00 €
ISBN 9788849884470

[Filomena Nitti and the denied Nobel prize]

Filomena Nitti and the denied Nobel prize is the result of a collaborative writing effort, in which the recollections of Maria Luisa Nitti, Filomena’s niece, form the narrative thread that journalist Carola Vai weaves into the story of Filomena Nitti, a twentieth-century scientist.

The narrative unfolds through social, historical, and personal events, intertwining the life of Filomena Nitti with that of Rita Levi-Montalcini – two scientists whose paths crossed at the Istituto Superiore di Sanità.

Through the comparison between these two figures and their distinct human and scientific journeys, the author highlights how the highest recognition in the scientific field – the Nobel Prize – was denied to Filomena Nitti.

The book is structured into chapters that trace the personal history of Filomena Nitti and of her family. The opening epigraph, a quote attributed to Filomena Nitti, encapsulates – according to the author – the essence of her character: a generous woman whose scientific and human qualities constantly supported the creativity of others, in particular that of her father, the statesman Francesco Saverio Nitti, and of her husband, the Nobel Prize winner for medicine Daniel Bovet:

“My destiny was marked by the good and bad fortune of having had two great people by my side (…) I loved and admired them both, but it was hard not to disappear in their shadow.” Filomena Nitti

It is precisely based on this interpretation of Filomena Nitti that the first chapter of the book focuses on her marriage to Daniel Bovet, a brilliant young researcher at the Pasteur Institute. The narrative of Filomena Nitti’s life unfolds through a family perspective – which we can guess belongs to her niece, Maria Luisa Nitti – and through the historical context in which the events of the Nitti and Nitti-Bovet families unfold. The description of the socio-cultural environment of the Nitti family, their twenty-two years of exile in France, and Filomena Nitti’s social and personal life is detailed and vividly rendered.

The two years of imprisonment of Francesco Saverio Nitti and the family’s return to Italy at the end of the war paint a picture of a supportive family, animated by strong democratic principles and a sense of belonging to an Italy they had been forced to abandon.

One chapter is devoted to Daniel Bovet’s Nobel Prize, awarded during his years of research at the laboratories of the Istituto Superiore di Sanità (Italian National Institute of Health), then directed by Domenico Marotta. The author describes the harmonious and collaborative working atmosphere fostered by Filomena Nitti, as well as the highly dynamic scientific environment of the Institute, where at the time also worked the German-born British biochemist Ernst Boris Chain, Nobel laureate in Medicine in 1945 for his studies on penicillin. Carola Vai emphasizes how the research conducted at the Istituto Superiore di Sanità led Daniel Bovet to the Nobel Prize, while his main collaborator, Filomena Nitti, despite having always carried out and co-signed scientific papers with him, was excluded from the award.

Overall, *Filomena Nitti and the denied Nobel prize* offers a personal and wide-ranging narrative of Filomena Nitti’s eighty-five years of life, as a scientist and as a protagonist of an era marked by deep family and scientific commitment. Recognition of Filomena Nitti’s role as a researcher is also reflected in the publication *Filomena Nitti: Scienziata del Novecento* (2024), issued by the Istituto Superiore di Sanità within the series *I beni storico-scientifici dell’Istituto Superiore di Sanità* [1]. This recent work, which focuses particularly on Filomena Nitti’s scientific activity, has inspired the renaming of the Institute’s conference hall – previously dedicated to Daniel Bovet – to honor both scientists as the *Nitti-Bovet Hall*.

Barbara Caccia
Istituto Superiore di Sanità, Rome, Italy
barbara.caccia@iss.it

REFERENCE

1. Caccia B, De Castro P, Morini G (Eds). Filomena Nitti: scienziata del Novecento. Roma: Istituto Superiore di Sanità; 2024. (I beni storico-scientifici dell’Istituto Superiore di Sanità, Quaderno 15).

Ann Ist Super Sanità 2025 | Vol. 61, No. 4: 322-324
DOI: 10.4415/ANN_25_04_12

PUBLICATIONS FROM INTERNATIONAL ORGANIZATIONS ON PUBLIC HEALTH

Edited by
Annarita Barbaro

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS (FAO)

The State of Food Security and Nutrition in the World 2025. Addressing high food price inflation for food security and nutrition. Rome: FAO, IFAD, UNICEF, WFP and WHO 2025; 234 p. ISBN 978-92-5-139937-8. The State of Food Security and Nutrition in the World 2025 highlights how elevated inflation in many countries has undermined purchasing power and, especially among low-income populations, access to healthy diets. The report documents how high food price inflation is associated with increases in food insecurity and child malnutrition. Vulnerable groups, including low-income households, women, and rural communities, can be particularly affected by food price inflation, risking setbacks in the fight against hunger and malnutrition. In response to these challenges and to prevent future price shocks, the report examines policy measures adopted by countries, and outlines what is necessary going forwards. It stresses the importance of coherent implementation of fiscal and monetary policies to stabilize markets, promote open and resilient trade, and protect vulnerable populations. Additionally, it calls for better data systems and sustained investment in resilient agrifood systems to build long-term food security and nutrition. These coordinated actions are vital to reignite progress towards ending hunger and malnutrition by 2030.

OECD-FAO Agricultural Outlook 2025-2034. Paris and Rome: FAO and OECD 2025; 166 p. ISBN 978-92-5-139957-6. The OECD-FAO Agricultural Outlook 2025-2034 provides a comprehensive assessment of the ten-year prospects for agricultural commodity and fish markets at national, regional, and global levels. Jointly produced by the OECD and FAO, in collaboration with their Members and international commodity organisations, the Outlook serves as a forward-looking reference to support evidence-based policy planning. This 21st edition examines the evolving landscape of global agriculture in the face of economic, political and environmental challenges and comprises three parts: part 1 outlining key projections and insights on challenges facing agrifood systems over the coming decade; part 2 describing recent market developments and medium-term projections for consumption, production, trade, and prices for the commodities covered in the Outlook; and part 3, a Statistical Annex, which presents projections for production, consumption, trade, and prices for agricultural commodities, fish, and biofuels, as well as macroeconomic and policy assumptions.

INTERNATIONAL SCIENCE COUNCIL (ISC)

Data and AI for Science. Key considerations. Paris: International Science Council 2025; 30 p. This paper provides an overview of the technical, ethical and environmental factors to consider when preparing scientific data for artificial intelligence (AI), and how these factors align with the ‘Open Science’ movement. The information presented is relevant to researchers, data practitioners, scientific bodies and policymakers for science. The first section introduces the foundational concepts and discusses the advantages and challenges of making scientific data AI-ready. The second section examines the key considerations for data readiness for AI, and conversely, AI to curate data. The third section discusses data readiness within the framework of Open Science, presents two case studies that illustrate how Open Science practices can support AI-readiness for scientific research.

UNITED NATIONS ENVIRONMENT PROGRAMME (UNEP)

Climate Technology Progress Report 2025. Advancing biobased technologies in the bioeconomy. Copenhagen: United Nations Environment Programme Copenhagen Climate Centre 2025; 116 p. This Report examines how advancing the climate and nature agenda through the integration of technology and sustainable biobased solutions can offer a comprehensive and cost-effective pathway to achieving both objectives simultaneously. It emphasizes the importance of protecting and restoring ecosystems, halting deforestation, and investing in joint mitigation and adaptation approaches highlighting the key roles of both domestic policies, including clear and inclusive regulatory and legal frameworks, and international cooperation and financing. Structured to provide both global and regional perspectives, the report’s hybrid format reflects the diversity of challenges and opportunities across geographies. The report is intended as a resource for policymakers, practitioners, and stakeholders seeking to advance integrated, effective, and equitable climate and nature action in the lead-up to COP 30 and beyond.

Sustainable Procurement Guidelines for Data Centres and Servers. Paris: United Nations Environment Programme 2025; 77 p. ISBN: 978-92-807-4221-

3. Data centres in developing countries are set to grow rapidly due to economic expansion, rising data demand and increasing data sovereignty needs. However, these facilities are highly energy intensive. Despite efficiency improvements, regulations remain insufficient, with the EU still drafting its first Data Centre Regulation. UNEP's United for Efficiency (U4E) initiative has developed this set of technical specifications as a reference for establishing requirements for the procurement of data centres. These guidelines are designed to help organisations set robust criteria and processes that improve the energy efficiency of their current or upcoming facilities. They offer recommendations on several key performance criteria and operating conditions that are most relevant and impactful for selecting energy-efficient data centres and computer servers. The criteria cover indicators such as power usage effectiveness, water usage effectiveness, IT equipment energy efficiency, and cooling effectiveness ratio. In addition to public procurement, these Guidelines can be used as a starting point for other types of data centre procurement (such as through the private sector) and the basis of government regulations. These Guidelines were developed in a consultative process meant to reflect current global best practices, with the understanding that their contents should be adapted to local circumstances rather than applied verbatim based on generalized recommendations.

EUROPEAN FOOD SAFETY AUTHORITY (EFSA)

EFSA (European Food Safety Authority), Bonatti M, Lenzi P, Lewandowska A, Munoz Guajardo IP, Papadopoulou N, Raffaello T, Sánchez-Brunete E. **Literature horizon scan for new scientific data on plants and their products obtained by new genomic techniques (January 2022 to May 2025)**. EFSA Journal 2025;23(8):e9619. This report presents the outcome of the pilot literature search on new scientific data on plants and products thereof obtained by New Genomic Techniques (NGTs), performed as described in the protocol made available for public consultation in May-June 2025. The report describes search strategies and inclusion/exclusion criteria applied for the literature review and presents the results of the assessment performed for new scientific data (January 22 to May 25) on plants and their products obtained by NGTs. The report discusses the limitations of the search and provides recommendations for improvement. EFSA concluded that none of the studies retrieved by the literature search contained new hazards or risks not previously considered in EFSA scientific opinions.

EFSA (European Food Safety Authority), Barthélémy E, Cariou R, Castle L, Crebelli R, Di Consiglio E, Hemy Dumas T, et al. **Literature review on micro- and nanoplastic release from food contact materials during their use**. EFSA Journal 2025;22(10):9733E. To search for evidence of micro- and nanoplastics (MNP) release during the uses of food contact materials (FCM), a structured literature review was carried out on studies published between 2015 and 20th January 2025. It identified 1711 publications of which 122 were selected for data extraction. Eight additional publications were added to provide more context. Most studies concern microplastics, while data on nanoplastics are almost entirely absent. Despite the large number of publications investigating the release of MNP from FCM, the available evidence concerning the characteristics and quantities of released MNP from FCM remains limited. Results show that (i) there is evidence of microplastics released during the uses of FCM, (ii) this release is due to mechanical stress, such as abrasion or friction, or due to materials with open or fibrous structures, (iii) despite the uncertainties, the actual release is much lower than the results presented in many publications. In view of all this, there is no sufficient basis at this stage to estimate MNP exposure from FCM during their uses. This review identifies methodological shortcomings and data gaps and makes recommendations on related future research needs.

WORLD HEALTH ORGANIZATION (WHO)

Country preparedness for the introduction and appropriate use of antibiotics: operational guidance. Geneva: World Health Organization 2025; 204 p. ISBN 978-92-4-011109-7 (electronic version) ISBN 978-92-4-011110-3 (print version). This operational guidance supports countries to appropriately introduce an antibiotic for the first time. It aims to ensure timely access, appropriate use and optimal patient outcomes, while minimizing the potential of emerging resistance, by offering guidance on how to introduce an antibiotic into national health care systems. It primarily focuses on Watch and Reserve antibiotics, which are typically used as second- and third line treatments in hospital settings. Such antibiotics are essential for treating multidrug resistant organisms (MDROs), but often face specific access challenges, especially in low- and middle-income countries (LMICs). This guidance outlines an approach to planning the introduction and implementation of these products, considering their unique characteristics and associated needs, with the goal of enhancing treatment access for patients and promoting appropriate overall antibiotic use.

Malaria surveillance, monitoring and evaluation: a reference manual, second edition. Geneva: World Health Organization 2025; 222 p. ISBN 978-92-4-011247-6 (electronic version) ISBN 978-92-4-011248-3 (print version). This reference manual provides comprehensive guidance on integrating malaria surveillance as a core intervention across all malaria transmission settings, aligning with the principles of the Global technical strategy for malaria 2016-2030. It emphasizes the importance of transforming surveillance into a dynamic tool that informs programmatic decision-making, resource allocation and intervention planning. Key components of the guidance include the establishment of robust surveillance systems capable of detecting malaria cases, monitoring intervention coverage, and evaluating programme performance. The document outlines methodologies for data collection, analysis and reporting tailored to varying transmission intensities. It also provides strategies for integrating surveillance data with broader health information systems, ensuring sustainability and responsiveness to emerging challenges, such as climate change and drug resistance. Practical tools, including standardized indicators, data visualization methods and case studies, are included to support implementation at national and subnational levels. The manual addresses persistent gaps such as inadequate data quality, incomplete case detection and insufficient preparedness, and offers solutions that emphasize collaboration, capacity-strengthening and innovation to reduce malaria burden, accelerate towards elimination and sustain malaria-free status.

Mental health atlas 2024. Geneva: World Health Organization 2025; 98 p. ISBN 978-92-4-011448-7 (electronic version) ISBN 978-92-4-011449-4 (print version). WHO's Mental Health Atlas is a periodic survey and report of countries' mental health policies and programmes, laws, information systems, financing, workforce and services. The 2024 edition, the seventh in a series that started in 2001, draws on data from 144 countries and includes several new indicators on service delivery including telehealth and physical health, community-based care, and data monitoring. This latest report provides an overview of global mental health systems and services, tracks progress towards the targets of WHO's Comprehensive Mental Health Action Plan 2013–2030, and identifies key gaps in mental health service development across the world.

Acknowledgements to Referees

Annali ISS would like to thank the following individuals for their contributions as referees for the articles published in the four issues of 2025. Our success as a scientific journal depends on the quality of our peer-reviewers. We are grateful to all of them.

Agrimi Umberto, *ISS, Rome, Italy*
Alfò Marco, *Sapienza Università di Roma, Rome, Italy*
Alleva Enrico, *ISS, Rome, Italy*
Biffoni Mauro, *ISS, Rome, Italy*
Borgi Marta, *ISS, Rome, Italy*
Brusaferro Silvio, *ASU Friuli Centrale, Udine, Italy*
Busani Luca, *ISS, Rome, Italy*
Calamandrei Gemma, *ISS, Rome, Italy*
Camoni Laura, *ISS, Rome, Italy*
Cedri Sabina, *ISS, Rome, Italy*
Cerabona Vito, *Università degli studi di Perugia, Perugia, Italy*
Corea Francesco, *ASL, Viterbo, Italy*
Crestini Alessio, *ISS, Rome, Italy*
D'Angiò Mariella, *ISS, Rome, Italy*
Diana Lorenzo, *Swiss Paraplegic Research, Nottwil, Swiss*
Di Giacomo Silvia, *ISS, Rome, Italy*
Di Giulio Paola, *Università degli Studi di Torino, Turin, Italy*
Di Sotto Antonella, *Sapienza Università di Roma, Rome, Italy*
Facchinetti Gabriella, *ISS, Rome, Italy*
Ferrara Fulvio, *ISS, Rome, Italy*
Forresi Barbara, *Sigmund Freud University, Milan, Italy*
Francia Nadia, *ISS, Rome, Italy*
Gainotti Sabina, *ISS, Rome, Italy*
Gandin Claudia, *ISS, Rome, Italy*
Giuliani Alessandro, *ISS, Rome, Italy*
Giuliani Massimo, *IFO, Rome, Italy*
Grassi Maria Caterina, *Sapienza Università di Roma, Rome, Italy*
Ippoliti Ilaria, *ISS, Rome, Italy*
Kingdon Carol, *University of Liverpool, Liverpool, UK*
Kodra Yllka, *ISS, Rome, Italy*
Lavazza Andrea, *Centro Universitario Internazionale, Arezzo, Italy*
Lombardo Camilla, *ASL1 Abruzzo, L'Aquila, Italy*
Macrì Simone, *ISS, Rome, Italy*
Magnani Nadia, *AUSL Toscana sud est, Arezzo, Italy*
Marconi Matteo, *ISS, Rome, Italy*
Mariani Costantini Renato, *Università degli Studi "Gabriele d'Annunzio", Chieti-Pescara, Italy*
Mayer Flavia, *ISS, Rome, Italy*
Minelli Giada, *ISS, Rome, Italy*
Mirabella Fiorino, *ISS, Rome, Italy*
Orzi Francesco, *Sapienza Università di Roma, Rome, Italy*
Palamara Anna Teresa, *ISS, Rome, Italy*
Palanza Paola, *Università degli studi di Parma, Parma, Italy*
Palazzani Laura, *LUMSA, Rome, Italy*
Panza Costantino, *AUSL Reggio Emilia, Reggio Emilia, Italy*
Pezzotti Patrizio, *ISS, Rome, Italy*
Pirrera Antonia, *ISS, Rome, Italy*
Pizzarelli Scilla, *ISS, Rome, Italy*
Politi Cecilia, *FADOI, Rome, Italy*
Pompili Maurizio, *Sapienza Università di Roma, Rome, Italy*
Popoli Patrizia, *ISS, Rome, Italy*
Rossi Barbara, *ISS, Rome, Italy*
Scaravelli Giulia, *ISS, Rome, Italy*
Scattoni Maria Luisa, *ISS, Rome, Italy*
Stacchini Paolo, *ISS, Rome, Italy*
Stanganelli Ignazio, *Università degli Studi di Parma, Parma, Italy*
Toccaceli Virgilia, *ISS, Rome, Italy*
Vanacore Nicola, *ISS, Rome, Italy*

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 requirements 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

Extended quotations and illustrative material taken from other publications must be accompanied by the original permission granted by the authors and by the publisher or in accordance with the copyright policy of the original publication and the Creative Commons.

Responsibility for the contents and opinions expressed on this journal rests solely with the author(s).

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/