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Editorial

Violence against health workers

Massimo di Giannantonio, Enrico Zanalda

Past President SIP

Società Italiana di Psichiatria

Massimo di Giannantonio

Enrico Zanalda

Between 2016 and 2020, more than 12,000 cases of work-related injuries were ascertained by INAIL in health and social care, of which 46% were concentrated in the National Health Service, 28% in residential social care services and 26% in non-residential social care. Almost three quarters of the injured are women, half of whom are victims of violence in hospitals and nursing homes. The most affected professions are nurses and professional educators in services with minors, drug addicts, alcoholics, prisoners, the disabled, psychiatric patients and the elderly. They are followed with 25% of the cases by socio-medical workers (OSS) and with 15% by carers and attendants. In 5% of the cases of assault in the health sector the victims are 'doctors' of the National Health Service. It is, however, difficult to find the actual data because health workers often mistakenly refrain from reporting, yet among health personnel almost one in 10 injuries is due to aggression.

The WHO reports that about a quarter of health workers will experience physical violence in the course of their careers. Many more are threatened, exposed to verbal aggression and social stigma. In the crisis due to COVID-19, staff shortages and growing social tensions have increased the level of violence against health workers and attacks against facilities and emergency vehicles. Every year in Italy there are 1200 acts of aggression against healthcare workers. Among the top assault scenarios are emergency rooms, wards, outpatient departments, Psychiatric wards, intensive care units, 118 ambulances, nursing homes and prisons. As a type of violence, 60% are threats, 20% beatings, 10% armed violence and the remaining 10% vandalism. The perpetrators are 49% patients, 30% family members, 11% relatives and 8% users in general. The times most at risk are the evening and night shifts. Communication difficulties are recognised by 33% of the sample as the most frequently encountered difficulty in dealing with risk situations. From a survey it results that all the operators complain of negative psychological and emotional effects as a consequence of the violence suffered: anger and frustration are the most experienced feelings. According to 90% of the professionals interviewed the experience of the violence suffered worsens the quality of the victim's subsequent health services. Attacking those who work for health worsens the quality of the assaulted person's subsequent performance. I recall how the enormous increase in criminal and civil cases against doctors, over the last 20 years has led first to the phenomenon of defensive medicine with a considerable increase in unnecessary examinations for patients, and then to the phenomenon of obedience medicine resulting in the frequent relinquishment of positions of responsibility and flight from the National Health Service.

Recently we had the news of the murder of two doctors, one in Sicily and one in Milan, by patients dissatisfied with the service they received. These individuals, who are probably psychically fragile, and partially induced to such a gesture by the cultural climate. The easy accessibility to large amounts of information on pathologies and their treatment with which fragile people can identify and consequently act out their anger over a denied certificate or an alleged failure to recover. Health is the main good of all individuals, and to achieve and

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defend it we are willing to make any sacrifice, but if we feel our expectations are somehow unfulfilled, we can become aggressive. Emotionality connected to our wellbeing or that of our loved ones is very high, so that when we rightly or wrongly feel that we have been wronged in this area, we react strongly emotionally and sometimes even in anger or aggression. The doctor is the one who holds the power of well-being and failure to achieve it, regardless of the cause, is intolerable today. It is therefore crucial to communicate adequately with patients, motivating diagnostic and therapeutic choices, and not failing to foresee possible failures or worsening. It is unfortunate that the increased dissemination of health news and positive medical results may lead to greater distrust and aggression towards health professionals; knowing that even some serious illnesses respond to treatment does not mean that all of them do.

The right diagnosis and the right therapy are prerequisites for a good outcome, but no one can give a guarantee of an excellent result. We psychiatrists who use the relationship as a therapeutic tool have a better chance of understanding the patient's emotional condition during the course of treatment and directing it positively, but we must not underestimate inferring factors or persons as well as the lack of disease awareness of some of them. In such cases, having to impose ourselves as caregivers presents risks of switching to the act or of sudden contrary reactions that sometimes surprise us. The pandemic has made the relationship between healthcare personnel and the patient difficult. Healthcare workers have been called upon to manage highly emotional and socially uncomfortable relationships with users and their relatives – who have suffered badly from the centrally decided restrictions against the spread of the COVID-19 virus – as well as having to manage the highly interactive relationship with Coronavirus patients and other diseases during healthcare provision. Lastly, the campaigns against vaccines carried out by a large proportion of the population were also to the discredit of the work of health personnel due to bad information spread in bad faith to denigrate the official government positions of the Ministry of Health. L. 113/2020 defines the following legal framework: serious injuries inflicted on health personnel in the performance of their duties are punishable by imprisonment (from four to ten years) and very serious injuries (by imprisonment from eight to sixteen years). The provision aims to ensure enhanced protection of health personnel in the performance of their duties, due to the peculiarity of the activity performed. Two years after the approval of the law, the preventive benefit of the rule is not yet evident, but further study is needed to better understand how far this rule has succeeded in reducing, if not in number then at least in severity, assaults on health workers.

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Review

Società Italiana di Psichiatria

The implementation of evidence-based therapies for borderline personality disorder in Mental Health Services

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Michele Sanza

Summary

Objectives. This work address the implementation of the effective therapies for borderline personality disorder, with particular regard to the settings of public Mental Health Services. The objective of this review is to illustrate how to date Evidence-Based (EB) and non-EB treatments have been implemented within the framework of the possibilities and resources available.

Methods. 85 published researches have been identified and then selected on the basis of criteria of relevance to the objectives of the review. In particular, meta-analyzes, systematic reviews and RCTs were privileged. Small sample studies were excluded or cited with specification of sample component number.

Results. The critical factors of the implementation of the EB treatments for BPD (DBT, MBT, ST and TFT) in European countries, are placed on three levels: (1) the professionals involved; (2) the methodology of the treatment and (3) the level of management and organization of services. On the level of the professionals characteristics, the primary positive factors are: the non-judgmental attitude, the positive approach towards BPD, the presence of a strong and supportive leadership, the possibility of accessing supervision. The commonly encountered obstacles in the application of manual treatments are: the duration and cost of training, the continuous updates of the manuals that require frequent re-adaptations; the difficulty of applying telephone coaching, the treatment time required for each individual patient on a weekly basis. To meet the needs of psychotherapy implementation of BPD in the public mental health settings, more flexible and pragmatic approaches, like Stepped Care or Good Psychiatric Management, must be developed.

Conclusions. The need to adopt effective intervention modalities for BPD in public Mental Health Services suggests the use of pragmatic approaches that focus on the common factors of EB therapies, the modular use of the parts that can be considered effective alone. Even in absence of the complete structure of the therapy, the stepped care approach, takes the least invasive intervention as the elective one at the different stages of severity of the disorder. Finally, the dissemination of reference values (non-judgmental services), should be the general framework of treatment of BPD.

Key words: borderline personality disorder, dialectical behavioral therapy, mentalization based therapy, transference focused therapy, schema therapy, general psychiatric management, stepped care, implementation

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Conflict of interest
The authors declare that they have no conflict of interest nor that they have received compensation from third parties for the creation of this article.

Introduction

Borderline Personality Disorder (BPD) is characterized by a pervasive pattern of instability in interpersonal relationships, affects, identity and marked impulsiveness that begins in early adulthood and is expressed in various contexts [1]. Surveys estimates hypothesize the prevalence of BPD around 1.6% of the general population and 20% in the clinical population [2]. BPD has long been considered resistant to any treatment, a bias that has contributed to widespread therapeutic pessimism. However, research in recent years has not only shown that BPD can be treated, but it has also provided several manualized and empirically validated psychotherapeutic treatments [3], while no psychopharmacological treatment has been shown to be more than moderately effective [4]. Moreover, longitudinal observational studies have made it clear that patients with BPD, even without intensive treatment, experience high rates of remission within ten years [5-8]. With the availability of validated and proven therapies, the question of treating BPD may seem to be resolved, but unfortunately, access to adequate care remains a problem as most Evidence Based (EB) therapies are highly specialized and require intensive training and many resources. If effectively implemented, EB treatments compared to generic psychiatric treatments currently provided, would reduce the direct and indirect health costs of BPD which is one of the psychiatric disorders that requires most economic resources [9]. Unfortunately, despite the range of existing treatment options, the demand for treatment far exceeds supply [10]. This work aims to address the issue of implementing effective therapies for borderline personality disorder, with particular regard to the operational settings of public Mental Health Services. The aim of this review is to illustrate how to date EB and non-EB treatments have been implemented within the framework of the possibilities and resources available to the services.

Methods

Using PubMed, we have identified studies carried out in Europe or in countries such as Australia and Canada, where specialist mental health care is mainly provided by public services. This criterion was adopted because the second objective of the research is the analysis of adaptations that favour a greater diffusion of EB therapies, through the definition of standards of care compatible: (1) with the resources of public services; and (2) with a stepped care principle whereby even patients who are not eligible for standardized therapies can receive quality interventions based on the principles of effective therapies. On the other hand, the studies carried out in the United States were not included in the review, because the access of mental health services are conditioned by the insurance systems and the public offer remains limited in the context of emergency urgency.

To extract the works, the following search strings were used to query the PubMed search engine:

- ((dialectical behavioral therapy) AND (borderline personality disorder)) AND (implementation))
- ((mentalization based therapy) AND (borderline personality disorder)) AND (implementation))
- ((transference focused therapy) AND (borderline personality disorder)) AND (implementation))
- ((schema therapy) AND (borderline personality disorder)) AND (implementation))
- ((general psychiatric management) AND (borderline personality disorder)) AND (implementation))
- ((stepped care) AND (borderline personality disorder)) AND (implementation)).

In this way, 85 papers published between ANNO 2005 and ANNO 2022 were identified and then selected on the basis of criteria of relevance to the objectives of the review. In particular, meta-analyzes, systematic reviews and RCTs were privileged. Small sample studies were excluded or cited with specification of sample component number.

The obstacles to the implementation of EB therapies for BPD

Dialectical Behavioral Therapy

The best known and most available EB therapy is Dialectical Behavioral Therapy (DBT), initially developed by Marsha Linehan [11] for highly suicidal patients who did not respond as expected to standard cognitive behavioral interventions. The DBT treatment includes individual psychotherapy, participation in the psychoeducational group of Skills Training and the possibility of using telephone coaching 24/24h. The success of DBT lies in the robust empirical support and the large amount of rigorous studies conducted on comparison with Treatment As Usual (TAU) [12-18].

DBT requires major organizational changes, such as weekly team meetings, skills training and a high level of team engagement; the coordination of these functions is crucial to ensure the success of its adoption. Despite the number of evidences supporting this therapy, there are many obstacles to the implementation of standard DBT in services. In fact, it requires many resources, especially in terms of both economic and therapy time and, even before, the training of therapists [10]: the 4 components of therapy (individual psychotherapy, Skills training group, telephone availability and regular therapist team sessions) require approximately 3-4 hours per week per patient. The training consists of two 5-day courses 12 months apart, separated by frequent team supervision with qualified teachers, and involves the study of manuals of over 1,000 pages in total. Considering the resources of the public health system, a model that foresees the generalization of the standard DBT with unlimited access possibilities is utopian, at least at present. In the last decade, numerous studies have been carried out on the development of DBT and both facilitating and hindering factors in the implementation process have

been identified. In particular, in the research by King et al. (2018) [19] and Swales et al. (2012) [20] on the survival of DBT programs in the UK, it was found that the factors that favoured implementation were individual characteristics of clinicians and organizational support, while the most cited obstacles were the high turnover rate and inadequate funding. Swales et al. (2010) [21] hypothesized that a *pre-treatment* at an organizational level is necessary, which includes the identification of objectives, the assessment of the organization's readiness to change and the achievement of a level of commitment by the organization. The study conducted in a community setting in Ireland by Flynn et al. (2020) [22], concludes that the clinicians participating in the study identified the lack of support from the telephone coaching system and the lack of time for the therapists dedicated to DBT as an obstacle. Toms et al. (2019) [23] categorize difficulties and facilitators and identify a *benign* approach to BPD and an optimal level of communication within the services as a precondition for the adoption of DBT. Furthermore, they emphasize the importance of the cognitive flexibility of the therapists who will make up the team and that their values are in line with those of the DBT, in particular that they share the non-judgmental point of view. Healthcare management, in the design phase of the DBT implementation, must provide for the possibility of supervision and, consider the time and personnel requirements required even before activating team training. The review by Flynn et al. (2021) [24] analyses the studies on the implementation of DBT in the public health system emphasizing the importance of financial support for team training, as well as the need for continuous supervision.

Recent studies [25,26] have highlighted the effectiveness of DBT interventions that offer only Skills Training, both as stepped care for less complex cases, and by applying the model in a prevention perspective [27]. The efficacy of the standard treatment components of DBT (standard DBT, DBT with Skills Training only, and DBT with Individual Therapy only) was investigated in a dismantling study [28] which concluded that standard DBT was not significantly more effective than the Skills Training associated with case management. The variants of the study that included skills training had significantly better results in terms of reducing self-injurious non-suicidal behaviors than the variant of DBT that did not include skills training. All three treatment variants showed comparable results regarding suicidal behavior in high-risk patients. A relevant aspect underlined by the study is that the variant of DBT which included only the Skills Training required an average time of 31.7 hours against 55.3 hours of the standard DBT.

The effectiveness of Skills Training alone was also confirmed by the Australian study by Heerebrand et al. (2021) [29] on adult patients with BPD who received Skills Training together with general psychiatric treatment. The conclusions highlighted the reduction in maladaptive behaviors, the decrease in psychological and depressive symptoms, as well as the decreased use of health services.

Finally, recent research [30] has shown positive results of Skills Training also in the management of co-occurring symptoms of substance abuse in patients with BPD. The DBT, even in the modality of Skills Training alone, has a favorable cost/benefit ratio in the short term [31]. Further studies are used to investigate the result in the long term.

Mentalization Based Therapy

Mentalization-Based Therapy (MBT) is a dynamic approach treatment developed by Bateman and Fonagy and aims to stabilize a person's mentalization skills in stressful situations when the attachment system is activated [32]. MBT focuses on the development of mentalizing skills and does not involve homework. The basic training lasts three days and is reinforced by continuous supervision. A limitation of MBT is that few training centers exist. The fact that it is not intensely structured and does not consist of various parts such as the teaching of skills and phone coaching typical of DBT, has both disadvantages and advantages, since, although it does not require many resources to be learned, it could leave without reference points the less experienced therapists who need more guidance. The empirically tested version of MBT includes group therapy and a mentalizing team.

The factors responsible for the success or failure of the MBT implementation process in public mental health services were investigated in a study conducted in the Netherlands by Bales et al. (2017) [33]. Specifically, 6 mental health services and 7 MBT treatment programs were considered. It turned out that in two of seven programs the implementation could be considered successful, in two others the result was not entirely satisfactory and in three cases the implementation had failed. The difficulties were identified at the organizational, team and individual therapist level. Similarly, to what has already been observed for DBT, also in this case the facilitating factors were: organizational and economic support, strong leadership, the management of negative processes within the team, the selection of clinicians and the possibility of training. On the contrary, the lack, or the defect, of these factors was an impediment to implementation. It was observed, again by Bales et al. (2017) [34], that the success of MBT implementation, and its effectiveness, can be threatened by organizational changes: turnover, new inexperienced team members, renewed management, bad publicity, security risks. These are factors that impact adherence and the effectiveness of the treatment. In their study, the results of treatment before and after the aforementioned changes were compared, highlighting a worsening of the effectiveness of MBT.

Schema Therapy

Schema Therapy (ST) was developed on the basis of cognitive therapy and offers treatment for pervasive and lasting psychological disorders in which cognitive therapy has been less successful [35]. The ST format includes

cognitive therapy enriched with techniques from object relationship theories, attachment and Gestalt therapy. In the ST, attention is paid to the traumatic experiences of childhood and to an empathic and protective therapeutic relationship. Experiential techniques have been integrated into the model [36].

Some studies were considered that focused on the implementation of ST in public mental health service settings in Europe. In the Netherlands Nadort et al. (2009) [37] studied the factors promoting and hindering the implementation of ST for the treatment of BPD. In summary, the hindering factors were the length of the activation time, the high costs, the distance from the supervision site, and, finally, the need to offer telephone support to patients outside working hours. This particular aspect was studied by Nadort et al. (2009) [38] to facilitate the implementation of ST and there was no significant difference between the groups of patients who benefited from telephone coaching and those who did not, perhaps due to the particular organization of the Dutch health system that offers alternative options to telephone support as an intervention for crisis situations. As facilitating factors, the positive attention of the media towards ST and the evidence of effectiveness were identified. Another facilitating factor concerned the availability of audio-video materials for the training of clinicians. The result of this study suggests that ST can be successfully implemented in the Dutch public service and in countries with a comparable health system. The study found that ST is cost-effective and beneficial in the Netherlands and in countries with comparable health service organization [39].

Alternative models have also been proposed for ST, which reduce the costs of providing treatment. One of these is the Group Schema Therapy (GST) by Farrell and Shaw (2012) [40] authors of an 8-month RCT [41] study that showed efficacy in increasing the remission rate of BPD, reducing the severity of the disorder, improve psychosocial functioning, with a low dropout rate. Two German studies in small samples (n = 10, n = 9) [42,43] showed improvement in symptoms and general functioning in BPD patients with the same treatment modality.

Transference Focused Psychotherapy

Transference Focused Psychotherapy (TFP) is a psychoanalytically oriented treatment based on Kernberg's conception of the borderline personality organization he introduced in the 1960s. The characteristics, deriving from adverse temperamental and environmental factors, are: a widespread identity, confused internal operational models of relationships, unstable reality testing, variable empathy, hetero and self-directed aggression and the use of primitive defense mechanisms. The treatment consists of two sessions per week without group therapy and the patient's relational patterns are analyzed. TFP has proved useful in reducing aggression and improving mentalization [44,45]. As the work of Choi-Kain et al. (2016) suggests, TFP appears to be more suitable for clinicians experienced with psychodynamic training. Unfortunately, no studies on the implementation of TFP have been found.

Flexible intervention models for BPD

Stepped Care

Paris' (2013) [46] review which describes the use of Stepped Care as an alternative to the use of a routine extended treatment was considered. Paris starts from the observation that although BPD is a chronic disorder, there is no evidence that it benefits more from long-lasting interventions. Patients with BPD, in fact, show improvements even after short interventions within Stepped Care [47-50] models and closer to the resources actually available, also considering that duration is one of the obstacles to the availability of treatments. Stepped Care is a model for treating somatic and psychiatric disorders, which vary in intensity and prognosis, and consists of a spectrum of interventions ranging from minimal to very intense support, depending on the need and the level of severity. It does not aim at complete recovery, but recovery that allows the patient to self-manage and be monitored through, if necessary, follow-ups. This mode allows patients to contact services and obtain support tailored to the needs of the moment. An example of an algorithm [46,51] that depicts the possible steps proposed by Stepped Care, was drawn up in the article by Choi-Kain et al. (2016).

- In the "preclinical" stage, characterized by risk factors for BPD and some symptoms of the disorder that do not reach the threshold for diagnosis, the elective interventions, in a Stepped Care perspective, are psychoeducation (to the family and to the patient) psychological support and problem-solving interventions.
- In the early stage, with manifestations of the disorder reaching the threshold for diagnosis and self-harm, the suggested interventions are Case management, GPM and DBT ST.
- At a later stage, with self-harm and suicidality, GPM with medication management, DBT ST or EB treatment (MBT, DBT, TFP) is proposed.
- At the severe stage, characterized by potentially fatal suicide attempts, GPM medication management interventions, a higher level of care (residential treatment for example) or another EB therapy or an integration of EB therapies are proposed.
- In the case of a chronic and unresponsive level to previous treatments, GPM and supportive therapy is offered.

An example of an early intervention calibrated on the patient is the Helping Young People Early (HYPE) model studied in the RCT by Chanen et al. (2022) [52] which found good adhesion by users because it was tailored specifically on adolescents.

Any difficulties encountered in implementation, which are like those of other treatments, were also studied [53] for Stepped Care. Once again, they are divided into two levels: individual and organizational. In the first case, attitudes towards personality disorders and the opportunity to take part in training courses are crucial factors. While the organizational aspects particularly relevant to implementation were supportive leadership and organizational experience in managing change.

General Psychiatric Management

General Psychiatric Management [54] is a manualized treatment that Paul Link converted from John Gunderson's clinical guide for a treatment comparison study with DBT [12] which showed that GPM, a less intense and non-specialized intervention, had an outcome as much effective as the DBT also at one and two years of follow up [55] with a lower rate of drop out of patients who had a higher degree of comorbidity in Axis 1 [56]. This is not a model of psychotherapy in the strict sense, but a "good" psychiatric case management implemented by a doctor who has the basic knowledge of BPD and the vulnerabilities of patients with this diagnosis. Weekly psychotherapy is offered only to those who profit from it and those who show actual changes. Another important aspect of GPM is psychoeducation. The GPM focuses, in particular, on interpersonal sensitivity and aims to manage symptoms and comorbidities by optimizing the patient's functioning in relational dynamics. The central goal is to improve the quality of life. GPM training requires a one-day workshop and approximately 2.5 hours per week per patient [10]. With a Stepped Care perspective, the effectiveness of 10 sessions of GPM as a short intervention was studied [50]. Psychoeducation restores meaning to life events as a source of corrective experiences and growth rather than failure. At the beginning of the intervention, motivation and participation are promoted, and in subsequent sessions the criteria making up the diagnosis and any co-occurring disorders are evaluated. Throughout the entire treatment, the focus on the interpersonal hypersensitivity model is maintained, attributing meaning to the patient's life events and relationships. In the last sessions the clinical process and the understanding of the patient's difficulties are summarized, also involving other clinicians and family members. From here, short-term objectives can be formulated and possibly a "step up" or "step down" of the treatment in progress at that moment takes place. Generalist treatments such as GPM are not intended as an alternative to EB treatments, which remain the treatments of choice, but not in early stages of intervention.

Guideline Informed Treatment for Personality Disorders

Among the various approaches to the treatment of BPD, a particular reference should be made to the work of Hutsebaut et al. (2020) [57] presenting the Guideline Informed Treatment for Personality Disorders (GIT-PD). GIT-PD is an initiative of the Knowledge Center for Personality Disorders in the Netherlands and aims to develop high quality care for people with personality disorders as an alternative to regular and unstructured care. The background of this initiative is a twofold observation:

1. in the Netherlands only a minority of PD patients receive a treatment that follows multidisciplinary guidelines [58];
2. structuring the care according to an informed psychotherapeutic model leads to a significant improvement in quality (for example, Chanen et al. 2009). The principles of GIT-DP treatment derive from the common characteristics of EB treatments for BPD and the underlying idea is that the quality of care does not depend so much on the specific factors of the treatment program, but on generic ones, such as the attitude of basis of the therapists, the structure of the treatment program and the attention paid to the motivation and quality of the therapeutic relationship. The rationale for the development of GIT-PD is inherent in the contrast between the evidence supporting the centrality of psychotherapies for personality disorders and the low availability and accessibility of the same [58]. Valuing the experiences that show that non-evidence based structured psychotherapeutic interventions have similar results to those of EB specialized psychotherapy interventions, GIT-PD aims to provide treatment that is realistically applicable in public mental health services. It also provides a framework for clinician training and some evidence-based criteria for assessing the quality of care for people with PD.

Guidance of the Emilia-Romagna Region

The Guidelines of the Emilia-Romagna Region intend to promote the adaptation of the international guidelines of the BPD to the local context for the treatment of Serious Personality Disorders (SPD), since the BPD can be assimilated to the core symptoms of SPD. The LI investigate the configuration of the services, the functional integration with the Child-Adolescent Mental Health Services and the of the Mental Health Services for Adults, the characteristics of the therapeutic contract, the interventions on seizures, the diagnostic tools, the pharmacological therapies, the therapeutic interventions available in the services and those who can favour the therapeutic attitudes of the team towards the SPD.

The LI propose to foster the empowerment and autonomy of patients, as well as to establish a relationship based on trust and optimism regarding recovery. The LI are not anchored to a specific treatment, but establish the need to implement a step-by-step treatment, the stepped care.

Two levels of care intensity can be summarized as follows: There are two main programs: the simple and the complex treatment. The first consists in informed psychosocial intervention based on the principles of a non-judgmental attitude, patient empowerment and focuses on increasing personal resources in crisis management and emotional regulation; the second provides access to forms of spe-

cialized structured individual psychotherapy and/or the DBT Skills Training. The Guidelines of the Emilia Romagna Region envisaged the development of an expert function dedicated to SPD within the Mental Health Departments with the task of evaluating and treating people with SPD, training professionals, reducing stigma and implementing LI in the services of Mental Health Services, in the Addiction Units, and in the Child-Adolescents Mental Health Services, as well as to support them and develop a communication system between these services. It also has the task of involving patients and family members and informing them about the opportunities for support in services and in the sharing of information in the various Operating Units. In addition, promote social interventions and monitor the development of services for ethnic minorities.

Discussion

The analysis of the literature considered in this review leads to rather homogeneous conclusions. The critical factors of the implementation of EB treatments for BPD (DBT, MBT, ST and TFT) in European countries, are placed on three levels: 1) mental health professionals team; 2) methodology of the treatment; 3) management and organization of services. On the level of the characteristics of the professionals the necessary positive factors are: the non-judgmental attitude, the positive approach towards BPD, the presence of a strong and supportive leadership, the possibility of accessing supervision. The commonly encountered obstacles in the application of manual treatments are: the duration and cost of training, the continuous updates of the manuals that require frequent re-adaptations; the difficulty of applying telephone coaching, the treatment time required for each individual patient on a weekly basis. Finally, it must be considered that often, it is not necessary to offer extended EB treatment, but it is sufficient to offer some parts of it (e.g., psychoeducation or ST of DBT). The organizational obstacles that need to be addressed and possibly removed to facilitate the implementation of EB treatment for BPD are: scarcity of resources, staff turnover, clinician's resistance to change, weak involvement of health management on the Mental Health issues, a clinical governance lacking in flexibility, the difficulty in framing the necessary costs as investments in patient health and possible future savings. Furthermore, in the Guidelines, there is no indication for patients who are not motivated for treatment and, moreover, the Mental Health Services of European countries, which are generally public, must also give answers to patients who are not motivated or compliance with highly structured EB treatments. The GPM, the Stepped Care, the GIT-PD and the LI of the Emilia Romagna Region offer alternatives that overcome the limitations of the exclusive use of EB treatments and constitute the possibility of defining treatment standards for the totality of people with BPD who pertain to mental health services. Although very different between each other, these models have common characteristics in the reference values (non-judgmental attitude and patient empowerment), in the flexibility of formats, in the openness to EB therapies that patients could access after a phase of stabilization of symptoms or comorbidities (substance use disorders and mood disorders). Gunderson's GPM frames a phased treatment that uses psychoeducation and psychodynamic intervention to promote the search for the meaning of interpersonal experience in hypersensitive patients. It is arranged in phases of decreasing intensity and is open to the integration of modules of other therapies, such as the Skills Training of the DBT. It is a treatment that can also be carried out by educational staff, as well as by psychiatrists and psychologists, as long as they are properly trained. of Paris' Stepped Care is particularly interesting for the staging of 5 severity levels of BPD. Modular interventions of different and increasing intensity are identified, without neglecting the residual commitment to patients who are reluctant to treatments towards which to maintain an attitude of harm reduction. To avoid a worsening of patients' quality of life and for reasons of health economics, it is advantageous not to wait for the disease to require more intensive interventions, but act offering a lower level of care intensity when the disorder is adequately compensated or not serious. GIT-PD formulates a series of general treatment principles based on these common characteristics. The program is based on the characteristics of EB treatments, namely: a clear treatment framework, attention to the quality of the therapeutic relationship, active therapist, interventions aimed at improving self-reflection and interventions that increase motivation. Ensuring these commonalities may explain the most important effect in the treatment of PDs. The LI of the Emilia Romagna Region have in fact contextualized the international guidelines, proposing two levels of complexity and intensity of treatment that put the implementation of the Skills Training of the DBT at the centre of innovation in association with psychiatric treatment informed on the principles of EB treatments. These approaches, compared to EB treatments, are economical in terms of training, treatment time and human resources involved. They propose less intensive interventions for mild patients and do not require the adoption of a reference therapeutic paradigm. They consider the possibility of using "parts" of these EB treatments, proven in effectiveness, on their own but are not an alternative to therapies. The structure of these models, as verified in the Dutch experience and as suggested by unpublished data from the experience of Emilia Romagna, makes them an effective and reliable treatment for less experienced clinicians who have completed short training courses.

Conclusions

The need to adopt effective interventions for BPD in public Mental Health Services suggests the use of pragmatic approaches that focus on the common factors of EB therapies, the modular use of the parts that can be considered effective alone, even in the absence of the complete struc-

ture of the therapy, the stepped care approach which takes the least invasive intervention as the elective at the different stages of severity of the disorder; and finally the dissemination of reference values (non-judgmental services). This approach, certainly less expensive and more suited to the organizational logic of public services, still involves investments in planning, training and the use of time by clinicians. Current epidemiological trends see an increase in emotional regulation disorders in adolescents and young adults, often prodrome of BPD, which does not correspond to an equal increase in available resources. On the contrary, the resources allocated to Mental Health in Italy have decreased and in any case are concentrated more on the needs of residential care, a substitute for appropriate social and welfare interventions, on judicial processes, on urgent treatments. The implementation of treatments for personality disorders implies a paradigm shift that replaces the generalist psychiatric approach, centred on the pharmacotherapy of symptoms and the use of emergency services for crisis management. To do this it is necessary to overcome the doubts (OR worries?) of clinicians, remove organizational obstacles and ensure adequate resources for training and supervision. Research projects on the implementation of theoretical models and their adaptations in real-world clinical practice is needed to guide healthcare governance and clinicians with evidence of effectiveness.

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Review

Electroconvulsive therapy (ECT): a safe and effective treatment*

Andrea Conca

Electroconvulsive therapy (ECT) is a modern, effective and safe medical treatment for severe mental health conditions. There is a continuous need to inform mental health professionals regarding indications, benefits, risks, and side effects of ECT. For this purpose, the psychiatric associations of Germany, Switzerland, Austria, and Italy summarize the latest scientific knowledge.

Summary

This position paper aims to describe the current state of knowledge about ECT and, therefore, to facilitate the decision-making process for the use of ECT even in complex clinical cases, based on a risk-benefit assessment.
Specifically, the following points are covered:
Indications. ECT can be used for different psychiatric disorders in both acute treatment and to prevent relapses in the form of maintenance ECT. It is important to highlight that indications based on syndromes rather than diagnoses are gradually proving their validity in clinical practice.
Safety. ECT is one of the safest treatments performed under general anaesthesia and has been documented to cause no direct or indirect structural brain damage. On the contrary, recent studies have even highlighted an increase in the grey matter volume following ECT administration.
Side Effects. transient effects on cognitive function are the most relevant side effect of ECT. These are generally mild to moderate, and they usually resolve completely within a few days to a few weeks.
Mechanism of action. the proven effects of ECT are particularly evident in the areas of neuroplasticity, inflammation and functional connectivity.

Key word: electroconvulsive therapy (ECT), indications, safety, side effects; mechanism of action, risk-benefit assessment

Almost two decades respectively one decade have passed since the publication of the official recommendations for electroconvulsive treatment (ECT) by the German Medical Association (BÄK) in 2003 [1] and by the German (DGPPN), Swiss (SGPP) and Austrian Associations (ÖGPP) for Psychiatry and the regional Trentino-South Tyrol Italian Society of Psychiatry (SIP) [2] in 2012. Since then, important studies have been published regarding the indications for ECT. Evidence-based recommendations for the use of ECT have been included in the S3 guidelines for "Unipolar depression", "Schizophrenia" and "Diagnosis and therapy of bipolar disorders" [3-5]. Furthermore, ECT has been integrated into

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training curricula for psychiatrists in Germany and Austria. Moreover, additional reimbursement rates for ECT were integrated into the German reimbursement system for Psychiatry and Psychosomatic Medicine.

During the last 20 years, the number of ECT sessions in Germany nearly doubled [6], but this has only partially led to an improvement in the care of people with severe mental disorders, since the number of centres offering ECT has remained almost unchanged, although with an upward trend. An international survey has shown that German-speaking countries lag behind most industrialized countries in the use of ECT and that only about half of psychiatric clinics in Germany provide this therapeutic option.

Specific groups of patients, such as children and adolescents, people with intellectual disabilities, as well as forensic patients, have more difficulty accessing ECT, which has been repeatedly described as an ethically unacceptable limitation of the right of every individual to receive the best possible treatment [1,7].

This position paper aims to describe the current state of knowledge on indications for ECT and facilitate clinical decision-making even in difficult cases, based on risk-benefit analyses. It is crucial to highlight that indications based on syndromes rather than diagnoses are proving increasingly useful in clinical practice. For example, affective, psychotic and catatonic syndromes respond to ECT relatively independent of the etiology.

Indications for ECT

General indications for ECT described by the German Medical Association in 2003 remain substantially unchanged. ECT is basically indicated when:

- there is a need for rapid improvement due to the severity of the psychiatric disorder;
- risks of ECT are lower than alternative treatments,
- there is a known history of poor response to psychotropic medications (treatment resistance);
- there is a known history of good response to ECT;
- there have been episodes of intolerance and significant side effects to pharmacotherapy [1,8].

ECT is used as part of a broader treatment approach that includes a combination of appropriate pharmacotherapy and psychotherapy. In some urgent cases, ECT alone as a life-saving treatment may create the basis on which patients can subsequently be integrated into a more complex therapeutic concept.

Whether ECT is offered as first-line treatment or only after other treatments have failed depends less on the diagnosis than on the level of acuteness and severity of the disorder and the risks associated with the individual course of the disease. ECT is not the last resort (no “ultima ratio”) [2]. On the contrary, its early use during the course of treatment reduces suffering, disease duration, risk of chronicity and increases the likelihood of response to ECT [9].

For certain diagnoses, such as unipolar depression or schizophrenia, randomized controlled studies and meta-analyses, constituting the highest level of scientific evidence, have led to corresponding recommendations in national and international guidelines.

However, exclusively considering the level of meta-analytic evidence is too limited [10], since randomized controlled trials are not feasible for medical or ethical reasons in some seriously ill populations. In these cases, clinical experience (i.e. empirical evidence, for example based on case series, case-control studies, etc.) has to and can fill these evidence gaps in order not to deprive patients of a potentially highly effective and sometimes life-saving treatment.

There are various indications for ECT based on syndromes. Since response rates differ within the same syndrome (e.g. depressive syndrome) depending on the presence of certain clinical factors (e.g. age, chronicity, severity level, psychomotor symptoms, family history, etc.), no generalized hierarchical classification is made in terms of first or second choice treatment.

Table I shows existing indications with a selection of the relevant literature, with explicit reference to the recommendations of existing guidelines.

Table I. ECT indications.

Indications	References
Unipolar depression/depressive syndromes	S3 guidelines for unipolar depression [4,8]
Schizophrenia and schizoaffective syndromes	S3 guidelines for schizophrenia [3]
Bipolar disorder (including depressive and manic syndromes, mixed states, rapid cycling, delusional mania and delusional depression)	S3 guidelines for the diagnosis and treatment of bipolar disorders [5,11,12]
Catatonic syndromes (including malignant catatonia and neuroleptic malignant syndrome)	S3 guidelines for schizophrenia [3,13,16]
Organic/neuropsychiatric syndromes as in the lines 1-4	17-21
Treatment-resistant severe behavioural disorders (for example (auto) aggression) in neuropsychiatric disorders, dementia, autism spectrum disorders and other neurodevelopmental disorders	22-27
Autoimmune encephalitis (with severe and treatment resistant psychiatric symptoms)	28
Treatment resistant Parkinson’s disease (with motor and psychiatric symptoms)	17
Treatment resistant status epilepticus	29,30
Treatment-resistant delirium (including treatment-resistant benzodiazepine or barbiturate withdrawal delirium)	31-34

In addition to the well-established efficacy of ECT for acute treatment, there are now evidence-based strategies to prevent relapse using maintenance ECT [35-37]. This should be offered as a therapeutic option to all patients who do not achieve symptom stability or who relapse even with optimized pharmacological and psychotherapeutic treatment. The frequency and duration of maintenance ECT should be adapted according to the individual course of the illness. Even very long-term ECT maintenance therapies do not carry a cumulative risk of cognitive impairment [38], but instead have a positive effect on the long-term course of the disease.

Safety and impact on mortality and on suicidality

ECT is one of the safest treatment procedures performed under general anaesthesia. Until 2001, the mortality rate was approximately 1 per 50,000 treatment sessions; since then, this number has continued to decline, and it is lower than the mortality rate for comparable short-term surgical procedures [39]. The risk of treatment is therefore essentially the risk associated with anaesthesia.

It has been shown multiple times that there is no structural direct or indirect brain damage linked to ECT. On the contrary, over the last few years imaging studies have shown an increase in grey matter following ECT [40].

ECT has an anti-suicidal effect with a large effect size, even 3-6 months following an ECT series [41,42]. Even after one year, overall mortality of patients treated with ECT is approximately 50% lower compared to patients not treated with ECT [41].

Side effects

Transient effects on cognitive function are the most relevant side effect of ECT**.** Specifically, memory performance is mainly affected. Memory from before the ECT series and memory formation after the ECT series are only anecdotally affected. On the other hand, short-term cognitive side effects are common, usually mild to moderate, and they usually disappear completely within 15-30 days [43,44]. Over time there is an improvement in cognitive function when assessing the group of patients treated with ECT as a whole, since the impairments associated with the psychiatric disorder are reduced when responding to ECT. Effect size and side effects do not differ in a clinically relevant way between right unilateral and bilateral stimulation when dose is adjusted accordingly. Dosing using the "age method" also requires adjusting the dose according to age and electrode placement. Serious side effects (such as hemodynamically relevant cardiac arrhythmias, severe increases in blood pressure, prolonged apnoea with muscle relaxation, aspiration and tardive seizures) are rare and, moreover, generally acutely treatable 36. Postictal agitation on awakening occasionally occurs (immediately after the treatment) and can usually be avoided by optimizing the anaesthetic regimen. About one-third of patients may experience tension headaches following ECT, which can be treated effectively, even prophylactically, with analgesics. Nausea and vomiting after ECT/anaesthesia may occur and can also be prevented by prophylactic administration of antiemetics during anaesthesia. Performing an EEG prior to ECT is no longer considered mandatory. Following an ECT series, non-specific EEG changes often occur for several weeks and without any correlating clinical symptoms. Retrospectively patients rated ECT as "good to very good" [45].

Mechanism of action

The induction of a generalized seizure, meaning the synchronised activation of a group of cerebral neurons, is a necessary condition for the effectiveness of the treatment [46]. This seizure, along with the brain's ability to end the seizure "on its own" using a large variety of mechanisms, in turn, leads to the changes that contribute to the recovery of patients suffering from different severe psychiatric disorders [46]. Replicated effects of ECT, some of which have been meta-analytically confirmed, concern neuroplasticity (increase in neuronal growth factors and regional grey matter increases) [40,47,48], inflammation (reduction of inflammatory mediators) [49], functional connectivity (normalization of pathologically altered brain functions) [50,51] and anticonvulsant effect (increase in GABA levels and change of GABA/glutamate ratio) [46,52].

Risk-benefit assessment

Depending on the severity and acuteness of the psychiatric disorder, there are no absolute contraindications to ECT. A more detailed risk-benefit assessment is needed for patients with severe pre-existing somatic comorbidities. Hence, an individual and interdisciplinary risk-benefit assessment should be carried out. This includes factors that make anaesthesia more risky, such as a recent heart attack or severe untreated coronary artery disease, other severe functional cardiopulmonary limitations, treatment-resistant severe arterial hypertension, increased intracranial pressure, an extended and recent cerebral stroke, an intracerebral tumor with associated oedema, an acute glaucoma attack or vascular malformations with a known high risk of rupture. Advanced age [53], pregnancy [54], young age (children and adolescents) [55], inability to give consent [56,57] or cardiac pacemakers [58,59] do not constitute an increased risk.

Informed consent

As with all medical procedures, the patient or – if they are unable to consent – the patient's legal representative provide informed consent before undergoing the treatment. Under the strict limitations provided by article §1906a of the German Civil Code (BGB), ECT can also be performed against the will of the patient; existing case-control studies have shown similar good efficacy and positive retrospective evaluation of patients undergoing involuntary ECT [56,57,60].

Participating Scientific Associations

- German Society for Psychiatry and Psychotherapy, Psychosomatics and Neurology (DPPPN)
- Swiss Society for Psychiatry and Psychotherapy (SGPP)
- Swiss Society for Interventional Psychiatry (SGIP)
- Swiss Society for Anxiety and Depression (SGAD)
- Austrian Society for Psychiatry, Psychotherapy and Psychosomatics (ÖGPP)
- Italian Society of Psychiatry (SIP), regional Trentino-South Tyrol section
- (German) Working Group for Neuropsychopharmacology and Pharmacopsychiatry (AGNP)
- German Society of Biological Psychiatry (DGBP)
- German Society of Brain Stimulation in Psychiatry (DGHP)

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Commentary

During the last decades and through continuous clinical and scientific progress Electroconvulsive therapy (ECT) has developed into a modern medical intervention. Although psychotherapy and pharmacotherapy have strongly improved the treatment of mental illness, they sometimes have a limited effect in patients with very severe psychotic, depressive or catatonic symptoms. Quite often these can dramatically improve with ECT. Bearing in mind the persistence of the illness, the side effects of the treatment are rather benign. Thereby, the therapy increasingly has gained worldwide acceptance, especially with patients and their caregivers.

Considering these insights, various academic conferences have been held in recent years in Italy, the birthplace of ECT. Symposia regarding the therapy were regularly organized within the annual meeting of scientific communities (e.g. SIP, SINPF, SOPSI) and projects were implemented to translate ECT literature into Italian language (e.g., the book "La terapia elettroconvulsivante. Un manuale per medici invianti e operatori con 22 illustrazioni", or the brochure "ECT by 24 questions", translated by the Italian Psychiatric Society) as to promote and disseminate scientific knowledge about brain stimulation therapies, especially with ECT.

Disregarding these efforts, the clinical supply with ECT has significantly decreased in Italy. In 2020, we published the paper "Electroconvulsive Therapy in Italy-Current Dissemination of Treatment and Determining Factors of the Past" [1] demonstrating that the current number of ECT centers in Italy is very low in comparison to European and worldwide practice and that it has dramatically declined during the last 10 years. Furthermore, a north-south division in terms of geographical distribution was observed: ECT centers are located almost exclusively in the north. Finally, in contrast to other countries worldwide, ECT is still on the decline in Italy. Here, the care of patients with severe mental illness requires a reconsideration of ECT as an evidence-based and modern treatment option in present and for the future.

It is important to assess the history of ECT with today's standards and not to assess modern ECT in view of its history [1]. Not historical attributions, but modern standards of ECT should be considered in order to identify existing treatment potentials: "… it is to understand better the assumptions – and treatments – that we have inherited, and to gain a meaningful perspective on practice today" [2]. This sets a stage for the translation and publication of the new position paper on indications for ECT, an effort lead by the German psychiatric association (DGPPN), in collaboration with German-speaking psychiatric associations from Germany, Switzerland, Austria and Trentino Alto Adige. It complements a prior publication of the consortium of professional associations on the timely and appropriate use of ECT [3]. The recommendations of the present statement are based on the current state of knowledge about ECT and cover indications, safety and side effects, the mechanisms of action and the risk benefit aspects [4].

Translating and publishing the recent position paper on ECT from scientific psychiatric associations in Germany, Austria, Switzerland and Italy in *Evidence Based Psychiatric Care*, the open-access Journal of the Italian Psychiatric Association (SIP), is a further important step toward integrated, personalized evidenced-based medicine.

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Ester di Giacomo

Original article

The first systematic Italian screening for post-partum depression: results from the first 6 months of the Northern Italy "Regional Screening for Post Partum Depression" project and networking

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Summary

Objective. Post-partum depression involves 10-20% of pregnant women worldwide with serious consequences for mother and newborn if untreated. The incidence in the Italian population was not attested yet and this first systematic screening aimed at measuring it.

Methods. Pregnant women from the districts of Lecco, Monza and Vimercate (Lombardy) were screened at T1 (first trimester), T2 (delivery) and T3 (40 days post-partum) with the EPDS. Those EPDS-positive had a psychological examination, tested with the HAM-D and offered psychological follow-up in case of depression rating from low to moderate; if moderate to severe, they were referred for psychiatric evaluation.

Results. 4480 women gave birth during the index period and 4757 EPDS were completed. At T1, 75 women (8.6%) scored EPDS-positive, 167 (7.1%) at T2 and 78 (8.9%) at T3. At the HAM-D 23.5% had low/moderate depression, 5% moderate/severe depression and accepted a psychiatric follow-up.

Conclusions. The Italian incidence was lower compared to international data.

Key words: post-partum depression, Italy, epidemiology

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Conflict of interest
The authors declare that they have no conflict of interest nor that they have received compensation from third parties for the creation of this article.

Introduction

Post partum depression (PPD) is a serious mental health concern that involves 10-20% of pregnant women worldwide. Adverse outcomes in both mother and child, if untreated, include physical (e.g. Intra-utero growth restriction-IUGR, low birth weight [1] and psychological short and long-term effects [2,3,4,5]. Newborns might appear more irritable or less reactive to stimuli, while during their personal development they might experience internalizing and externalizing problems reaching psychiatric issues as depression, anxiety disorders and behavioral disturbance to personality disorders.

Despite the relevance of PPD both in terms of incidence and clinical adverse implications, screening programs for detecting PPD are not routinely planned within Obstetric Departments, even if their importance have been more and more demonstrated. The most common screening tool is the Edinburgh Post-

Natal Depression Scale (EPDS), a quick self-administered test rating symptoms in the last 7 days.
A systematic screening has never been performed in the Italian context and, as a consequence, a true incidence in the Italian population is still unknown. The Lombardy Region enhanced attention to women's mental health and in 2016 required each Health Trust a systematic evaluation about the burden of perinatal depression.

Methods

Sample

All the women who had access, from December 2017 to May 2018, to Midwife services or Obstetric Departments of the districts of Lecco, Monza and Vimercate (Region of Lombardy) during pregnancy or post partum were offered to take part to the "Regional Screening for Post Partum Depression".

Study design (Fig. 1)

This longitudinal study established three times for recruitment: during the first obstetric appointment in the first trimester of pregnancy (T1), during admission for delivery (T2) and at obstetric control after delivery, usually within 40 days after giving birth (T3).
Women were given the EPDS and two dichotomic questions about family (Q1) and personal (Q2) psychiatric history. Women with an EPDS score ≥ 12 (cut-off) were invited for a psychological examination. During their psychological appointment, women were clinically evaluated and the level of their depressive symptoms rated through the Hamilton Depression Rating Scale (HAM-D). If the HAM-D score confirmed the presence of depression at a low to moderate level, women were offered psychological treatment. In case of depression from moderate to severe, they were referred for psychiatric evaluation.

Exclusion criteria

The only criterion of exclusion was a lack of fluency in understanding Italian due to the self-administered design of the screening.

Ethics

Informed consent of the participants was obtained after the nature of the procedures had been fully explained. None of the participants received a compensation for their contribution and participation was on a voluntary basis. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The study was authorized and approved by the Regional Health System (RHS).

Test

Edinburgh Postnatal Depression Scale (EPDS) [6]: It consists of ten short statements with four possible responses. The mother chooses which one is closest to how she has been feeling during the past week. The cut-off score is 12 or higher.

Results

4480 women gave birth from December 2017 to May 2018 in the districts of Lecco, Monza and Vimercate. 4757 screening were globally completed at T1, T2 and T3 with an acceptance rate of 98.3%. At T1, 75 women (8.6%) scored positive at the EPDS, while at T2 and T3 167 (7.1%) and 78 (8.9%) women had an EPDS score ≥ 12 (Fig. 2).
399 women reported a positivity for Q1 (20 of them were

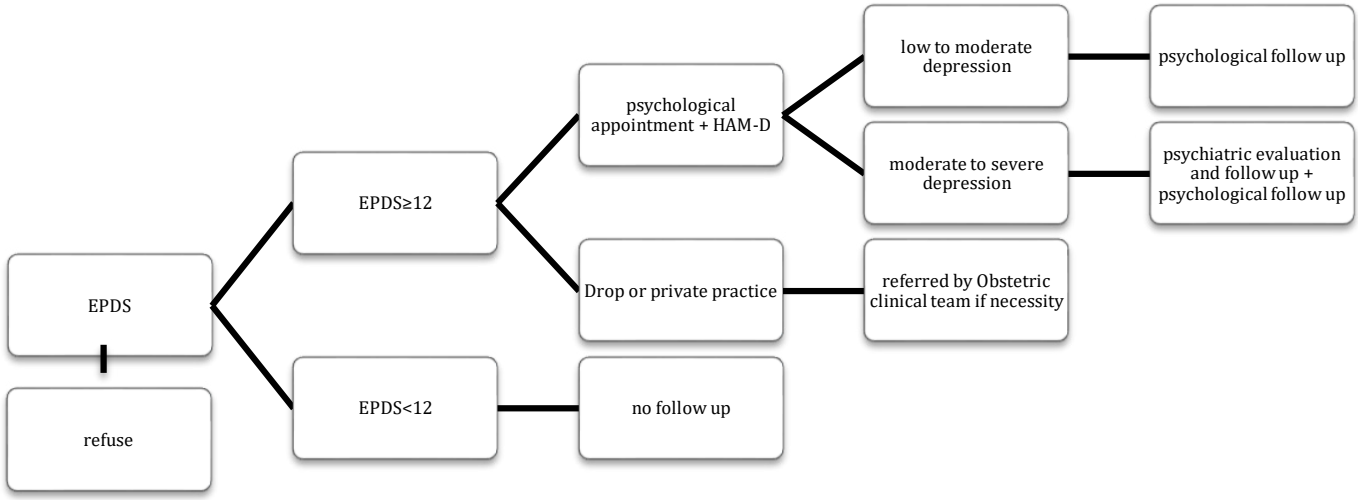

Figure 1.
Screening plan.

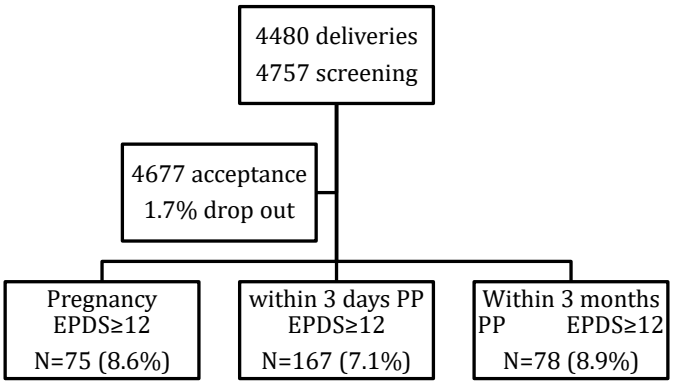

Figure 2.
Screening diagram.

EPDS^{+};p = .083) and 347 for Q2 (60 in EPDS^{+}; p < .0001), 161 scored positive to both (31 in EPDS^{+}; p < .0001).

In-depth evaluations and networking (Fig. 2)

23.5% of the women, evaluated with the HAM-D during the psychological follow-up, were classified as affected by low/moderate depression and all of them accepted a psychological follow up. Instead, 5% of the women, evaluated with the HAM-D during the psychological follow-up, were classified as affected by moderate/severe depression (5%), referred for psychiatric evaluation and accepted a psychiatric follow-up.
The screening is still ongoing and has involved 18176 screening evaluations at June 30th, 2019.

Discussion

This study documents the first systematic screening for post partum depression led in Italy on the general population and commissioned by the Regional Health System. Its historic importance is double since it is the first time it is possible to attest the real incidence of post partum depression in the Italian population and due to the directive of the Italian National Health System.
The region where it was led (Lombardy) is one of the biggest and most populated in Italy and it was selected as representative of the country.
The incidence detected in this sample is lower than expected from international data. Considering a global positivity at the EPDS, incidence was 8.2% compared to at least 10% documented in the Literature. Analyzing each time of recruitment, during pregnancy incidence was attested at 8.6%, immediately after giving birth at 7.1% and 8.9% within 40 days after delivery. 31% of women classified at risk of developing post partum depression accepted a follow up. After clinical in-depth evaluations 28% of them were diagnosed as affected by depressive disorders.
The amount of women who refused to have a psychological appointment even with a positivity to the EPDS might be detrimental for the demonstration of a punctual incidence. Otherwise, the aim of a screening is the identification of subjects at risk, who are subsequently offered an in-depth evaluation. From the point of view of the mere evaluation of this screening program, it had an excellent rate of adherence since drop outs were only 1.7%. Furthermore, focusing on clinical implications, 31% of women with a positivity to the screening tool were directly examined during follow up while those who refused follow up reported both treatment in private practice or an improvement in their mental well being, possibly implicating an active involvement in the problem.
Even if this last assumption is speculative, the aim of this project, according to the goal of a screening, implies public awareness and data justifies a cautious satisfaction.

Conclusion

This is the first systematic screening for post partum depression led in Italy. Its crucial importance highlights an increased attention to this relevant clinical problem and its implications for mothers and newborns. Furthermore, the incidence of this phenomenon has been attested for the first time in the Italian population and it shows to be lower compared to international data.

The Regional Screening Post Partum Depression (RSPPD) Network also includes: Lucia Accorsi, Chiara Arosio, Ivana Bassani, Francesca Bella, Emanuela Benaglia, Mariangela Beretta, Silvia Bertelli, Patrizia Biraghi, Elena Bosi, Michela Bracchi, Veronica Brembilla, Giulia Botta, Valentina Brivio, Luisella Calloni, Patrizia Calzi, Giulia Cappelletti, Sara Capodanno, Graziano Carniel, Giovanna Casarico, Olivia Casati, Ilaria Casiraghi, Elena Cattaneo, Maria Laura Cerasa, Francesca Cesana, Giulia Ciceri, Simona Ciervo, Aurora Cimieri, Elvia Colombo, Samantha Comandini, Greta Cosmai, Stefania De Gianni, Marianna De Rosa, Giovanna Di Lio, Liliana Di Nicolantonio, Marta Donati, Simona Episcopo, Federica Eynard, Angela Falcone, Giulia Fedele, Nazzarena Figliuzzi, Giovanna Franchi, Chiara Furlan, Valentina Galbusera, Cinzia Rosilde Galletti, M. Teresa Giambelli, Serena Giani, Piera Giussani, Teresa Gramegna, Giovanna Grasso, Chiarina Lanni, Giulia Li Sacchi, Barbara Lo Iacono, Anna Locatelli, Elena Locatelli, Elena Lo Monaco, Federica Malberti, Ersilia Mangifesta, Cecilia Mariani, Daniela Mattiolo, Giuseppina Mauri, Matilde Meneghini, Fulvia Merendi, Marina Meroni, Sara Montrasio, Silvia Morassut, Arianna Motta, Simonetta Motta, Antonio Nettuno, Elena Nova, Lucia Rosa Olivadoti, Katalin Palkovics, Lodovica Panzeri, Maria Panzeri, Viviana Paone, Sabrina Pelloia, Sara Perego, Sofia Perego, Anna Maria Perucchini, Francesca Pescatore, Rodolfo Pessina, Jessica Pezzotta, Valeria Placenti, Maria Teresa Pignari, Armando Pintucci, Consuelo Porro, Barbara Pucci, Stefania Puggioni, Angela Quinti, Gabriella Ramazzina, Emanuela Redaelli,

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Original article

Esketamine in treatment resistant depression: a study protocol for a retrospective, real-life, multicentric study

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Background

Major Depressive Disorder (MDD) is a common psychiatric disorder that impairs psychosocial functioning and limits the quality of life of those affected. Currently, mood disorders determine significant costs, amounting to 113.4 billion euros in Europe, with 37% of direct costs related to psychiatric treatments and 63% related to indirect social costs [1]. Furthermore, WHO ranked MDD as the third largest cause of global health expenditure on disease and predicted that it will be the first by 2030 [2].

MDD is a highly heterogeneous diagnostic entity that includes various and recurrent symptoms with clinical manifestations that could be supported by different pathophysiological mechanisms. Over the years, the clinical heterogeneity of depression has led to different attempts to define clinical subtypes of MDD to improve the diagnosis and treatment of this disorder. To date, however, we are still far from a correct categorization of the depressive universe in all its different clinical manifestations and from a correct subtyping that takes into account the different neurobiological mechanisms underlying MDD. Due to the clinical heterogeneity of depression, approximately 30-50% of patients do not respond to first-line therapies, experimenting treatment-resistant depression (TRD) [3], defined as the absence of a clinical response to two antidepressants of appropriate dose and duration (≥ 4-6 weeks) [4].

An open question concerns the substrates underlying this clinical heterogeneity and high rates of TRD. Conventional antidepressant treatments target the

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monoaminergic systems, which are thought to be the neurobiological substrates of depression. According to this hypothesis, depressive symptoms are associated with dysfunction of the dopamine, norepinephrine, and serotonin systems [5]. However, the absence of a clinical response to conventional antidepressant in a consistent part of MDD subjects suggests that a non-monoaminergic etiology may underlie TRD [6].

In light of this, several studies have focused on the role of glutamatergic neurotransmission in depressive disorders as a potential therapeutic target in TRD [7,8]. Glutamate plays a crucial role in synaptic transmission and neuronal plasticity, being involved in brain areas implicated in mood and affectivity [7]. Several neuroimaging studies have shown significant reductions in glutamate levels in unipolar depression in the anterior cingulate cortex and parietal white matter [9-11]. Furthermore, glutamatergic activity is reduced in the dorsolateral prefrontal cortical area (DLPFC) and in the dorsomedial and ventromedial anterolateral prefrontal areas in patients with TRD [12].

Besides, some studies have found normal or increased glutamate levels in patients who were in remission after electroconvulsive therapy [13,14], suggesting that glutamate levels can be rebalanced by treatments with proven antidepressant efficacy [15,16].

The relevance of glutamatergic activity in TRD is also supported by the antidepressant action of molecules with glutamatergic activity such as ketamine, an NMDA receptor antagonist [17], widely investigated by several studies [18,19]. Ketamine, despite its efficacy, remains a complex treatment due to the challenging management of the intravenous formulation and the significant risk of side effects [20].

Given the evidence supporting the glutamatergic hypothesis, a new therapeutic option for the treatment of TRD has recently been approved by the Italian Medicines Agency (AIFA): Esketamine nasal spray.

Esketamine (the S-enantiomer) shows a NMDA antagonism stronger than ketamine itself, [21] with lower side effects rates [22]. The antidepressant efficacy of esketamine has been demonstrated in several studies [23-25], with data indicating a remission rate greater than 50% in TRD [26]. A randomized clinical trial (RCT) showed significant improvement in depressive symptoms in patients treated with esketamine along with an oral antidepressant, lasting up to 52 weeks [26].

Esketamine also showed a favorable safety profile with few serious adverse events (less than 5%) in pivotal studies [22]. The most common adverse effects include dissociative symptoms (affecting between 11.1 and 31.4% of subjects in pivotal trials) [22], such as changes in body perception, depersonalization, and derealization [21].

Although previous findings show the good efficacy and tolerability of esketamine in TRD, real-world studies are needed to validate the results observed in RCTs in patients' samples from the general practice.

Furthermore, given the extreme clinical heterogeneity of both TRD and MDD, studies investigating clinical phenotypes, based on psychopathological and anamnestic data, more likely to respond to Esketamine are necessary. Finding valuable clinical markers of response to Esketamine would have a significant impact in clinical practice, reducing healthcare costs and limiting failed antidepressant trials.

Aims of the study

Considering previous evidences, the main aim of this study is:

- to evaluate efficacy of Esketamine nasal spray treatment in a clinical and non-experimental sample of TRD patients, estimating the reduction of depressive symptoms at one month (T1) and at three months (T2), highlighting its safety and tolerability.

Secondary aims of the study are:

- to investigate clinical TRD subphenotypes more responsive to Esketamine through anamnestic data and psychometric scales, used in the clinical practice of TRD management, aiming to identify clinical markers predictive of response to Esketamine;
- to evaluate differences in remission rates (MADRS score < 10) in different clinical profiles of patients with TRD.

Materials and methods

This will be an observational, retrospective and multicentric study conducted on a sample of patients with TRD treated with Esketamine nasal spray on the recommendation of a psychiatrist and in compliance with the indications provided by AIFA and the common clinical practice of TRD management.

Several centers will be involved in this study: the coordinating centers will be the "G. d'Annunzio" University of Chieti and the University of Brescia.

Other centers involved will be: Cattolica del Sacro Cuore "A. Gemelli" University Hospital of Rome, "A. Moro" University of Bari, Tor Vergata University of Rome, "Milano Statale" University, "Milano Bicocca" University, University of Siena, "Magna Graecia" University of Catanzaro, University of Pavia, University of Torino, "Villa Maria Pia" Clinic of Rome, "Von Siebenthal" Clinic of Rome, ASL Frosinone, ASL Napoli 1, ASL Sud Tirolo, ASL Messina, ASL Umbria 2.

In this retrospective study, psychometric scales and clinical information will be analyzed in patients with TRD who already performed treatment with Esketamine Nasal Spray.

Clinical and psychopathological parameters related to three different stages will be considered: baseline (T0), 1 month (T1) and three months (T2) from the treatment beginning.

Inclusion Criteria

- Patients over 18 years of age.
- Patients with a Major Depressive Episode, undergoing

at least two conventional antidepressant treatments in the absence of an adequate clinical response (TRD).
- Patients in treatment with an SSRI or SNRI.
- Patients for whom Esketamine nasal spray treatment has been considered appropriate, according to AIFA indications and common clinical practice of TRD management, regardless of the study.

Exclusion Criteria

- Comorbid organic pathologies (untreated arterial hypertension, previous cerebro-vascular disorders) which represent an absolute contraindication to Esketamine according to AIFA.

Anamnestic data

Anamnestic data will be considered concerning aspects related to affective temperament, any previous manic or hypomanic episodes, family history for mood disorders, concomitant use or substance abuse, number of previous depressive episodes, duration of the current depressive episode.

Psychometric scales

The scales considered at times T0, T1 and T2 will be as follows:
- **Montgomery Asberg Depression Rating Scale** (MADRS-10 items): to assess the severity of mood disorders, concentration, physical condition, sleep disorders found in depressive states [27];
- **Brief Psychiatric Rating Scale** (BPRS-24 items): for an assessment of the global psychopathological condiction [28];
- **Hamilton Depression Scale** (HAM-D-21 items): to assess the severity and pervasiveness of depression;
- **Beck Depression Inventory** (BDI-21 items): self-administered scale consisting of 21 items to evaluate the subjective perception of depressive symptoms;
- **Hamilton Anxiety Scale** (HAM-A-21 items): to assess the severity of the anxious symptoms.

Sample size calculation and Statistical Analysis

Sample size was calculated using the G*Power software and the ANOVA: repeated measures, within factors test.
The sample size calculation will be based on an expected response to Esketamine of 40%, in line with previous findings, considering a significance level of 0.05% and a power of 95%, and with the hypothesis of a premature dropout or a non-initiation of the treatment of 20% of the patients, considering the non-experimental sample. Thus, the estimated sample size will be n = 100.
Statistical analyses will be performed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). All tests will be two-tailed, with a statistical significance level set at $p < 0.05$.
Pearson's t-tests for continuous variables and $\chi 2$ tests for categorical variables will be performed. The comparison of psychometric data in the different stages (T0, T1 and T2) will be performed with a t-test for paired samples.
For the identification of predictors of efficacy, change in clinical rating scale scores (response/remission) between the different stages (T0, T1 and T2) will be considered as a dependent variable. Potential predictors (clinical and demographic characteristics, baseline scores and change in clinical measures) will then be included in a multiple regression analysis. Based on clinical and anamnestic data, possible stratification of the sample into different groups will be evaluated, and differences in response and remission between these groups will be assessed through t-test analysis for independent samples.

Ethical considerations

The study will be conducted in accordance with the ethical principles stated in the Helsinki Declaration (2013) [29]. The local ethics committee will examine all documentation to safeguard the rights and confidentiality of the subjects. The protocol and the documentation relating to this study and any revisions of these documents will be used only with the authorization of the local ethics committee.

Discussion

In recent years, new trends in psychiatry have focused on finding innovative and rapidly-acting tools to counteract TRD, considering the global economic and health burden of this disease, with large direct and indirect costs for those affected and their caregivers [30,31].
The rapid onset and the easy way of administration of Esketamine, together with a good safety profile, has determined its recent approval by FDA, EMA and AIFA as therapeutic tool for TRD. Several RCT have shown its antidepressant efficacy when administered together with an oral SSRI/SNRI [23-25], showing a symptoms' remission rate higher than 50% in TRD patients [26].
However, despite the availability of different experimental trial about Esketamine efficacy on TRD, there is a lack of studies conducted in a clinical and non-experimental setting.
In this observational, retrospective and multicentric study, we aim to evaluate the efficacy, safety, and tolerability of Esketamine in a clinical sample of TRD patients from different Italian Mental Health Services. Our goal is to provide a *real-world* experience of Esketamine to better understand its efficacy and safety profile, investigating both mild and serious adverse effects' rates. We will focus on possible risk of manic/hypomanic switches, intensity of dissociative symptoms, evaluating the drop-out rates in a clinical and non-experimental settings. Clinical setting will provide a *real-world* sample, possibly characterized by several differences from the experimental sample of esketamine RCT (with probably higher rates of co-occurrent disorders, substance abuse, longer illness duration and more heterogenous therapies administered).

The secondary aims of our study are in line with the urgent need of "tailored" therapies in the psychiatric field. Clinical markers predictor of response represents an important matter, in particular for TRD, a widespread disease with high economic and social burdens. Considering this, we will investigate any relationship between anamnestic data (e.g. time from disorder onset, episode duration, years of disease, number of episodes, affective temperaments, co-occurrent substance use, comorbidity with other psychiatric disorders) and clinical effectiveness of Esketamine. Besides, possible relationship between type of antidepressant molecules and add-on therapies (SSRI, SNRI, other antidepressants, mood stabilizers, antipsychotics) and clinical efficacy of Esketamine will be assessed.

Predicting esketamine efficacy and create data-driven TRD subtypes based on clinical features would have a significant impact in clinical practice, reducing costs in terms of healthcare expenditure and the average risk of failed trials.

Conclusions

This study will provide a real-world experience of esketamine use in the context of Italian mental health services, highlighting the external validity and clinical practice utility of this novel, rapidly acting tool for TRD. Investigating the use of esketamine in a real-world sample of patients may help to better clarify its clinical efficacy and safety profile, and help clinicians identify patient populations that are more likely to experience positive outcomes following esketamine administration, with significant implications for reducing costs and improving TRD treatments.

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Original article

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Regional Residential Centre for Eating Disorders "Mariconda": experience of a new frontier of care in the South of Italy

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Summary

Objectives. Eating Disorders (ED) represent one of the most common health problems in Western countries. This paper reports a descriptive analysis of the sample of ED patients admitted in residential rehabilitation at the Regional Residential Centre for ED "Mariconda" of Azienda Sanitaria (ASL) Salerno in the first 4 years of activity.

Methods. The sample includes patients admitted to residential care from December 2017 to December 2021. Admission at the Centre follows the criteria of the DSM-5 and the "National Guidelines for Nutritional Rehabilitation in Eating Disorders". Anthropometric parameters were collected for each subject at admission and discharge.

Results. Of the 105 inpatients, 10.5% was voluntary discharge in the first 8 days from admission; of the remaining 94, 5.4% were male, 94.6% female. 84% of the sample suffered from AN, 12.8% from BN, 3.2% from BED. The mean age of the sample is 19.24 ± 5.31 years, more than 66% of the entire sample was hospitalized between 2020 and 2021. The mean duration of hospitalization was 104.2 ± 70.3 days, with AN patients having the longest duration (108.5 ± 70) compared to the other categories. The mean BMI of the sample at admission was 16.533.4 kg/m^2; the mean BMI of the sample at discharge was 18.72.5. The sample originated about 70% from outside the ASL and 6% from outside the region. A positive correlation was found between BMI at discharge and length of stay ($r = 0.22$; $p = 0.032$).

Conclusions. The sample analyzed confirms the distribution of ED, especially AN, predominantly in females and adolescents/young adults; AN requires longer treatment, aimed at a better recovery of psycho-physical conditions. Over the last two years, the trend in the number diagnosis has been on the increase, due both to the SARS-CoV-2 pandemic, but also to the population's greater awareness of the disease, resulting in an earlier and more frequent diagnosis.

Key words: eating disorders, anorexia, rehabilitation, residential treatment

Introduction

The revision of the diagnostic criteria published in the new edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [1] set itself the goal of defining greater diagnostic continuity between adolescence and adulthood, adapting the criteria to the possibility of making the diagnosis also in childhood and adolescence, and uniting eating disorders with nutrition and

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eating disorders, which in DSM-IV [2] were included among the disorders that began in childhood and adolescence. The chapter is therefore defined as: 'Nutrition and Eating Disorders' and includes the following diagnoses: Pica, Rumination Disorder, Avoidant/Restrictive Eating Disorder, Anorexia Nervosa (AN), Bulimia Nervosa (BN), Binge-eating disorder (BED), Nutrition or Eating Disorder with other specification, Nutrition or Eating Disorder without specification. For Anorexia Nervosa the DSM-5 introduced two important changes in the diagnostic criteria: the first is the abolition of the DSM-IV criterion 'amenorrhea' because it cannot be applied to males, menopausal, premenopausal women and those taking estrogen and because some people exhibit all the other signs of Anorexia Nervosa but continue to menstruate. The second concerns the change of criterion A, which in DSM-IV required less than 85 per cent of what was expected (i.e., a BMI < 17.5) or the inability to reach the expected weight during growth, whereas in DSM-5 a significantly low weight below the minimum normal (i.e., BMI < 18.5) or, for children and adolescents, below the minimum expected weight (i.e., < 5th percentile) is required. In addition, the phrase "refusal to maintain body weight above or at the minimum normal weight for age and stature" was removed because it required intention on the part of the patient and could be difficult to assess objectively. In criterion C, the phrase "persistent behavior that interferes with weight gain, even in the presence of a significantly low weight" was added. Finally, criteria were introduced to assess the current level of severity based on BMI. For Bulimia Nervosa the DSM-5 retained the same diagnostic criteria as the DSM-IV except for criterion C (frequency and duration of binges). It is now required that binge eating and inappropriate compensatory behavior both occur on average at least once a week for three months, whereas in DSM-IV they had to occur at least twice a week for three months. Furthermore, as for Anorexia Nervosa, criteria were introduced to assess the current level of severity based on the number of episodes of compensatory conduct per week. Finally, the two subtypes (with and without elimination behavior) in the DSM-IV have been eliminated.

All Eating Disorders are more frequent in the female population than in the male population: in studies conducted on clinical populations, men account for 5-10% of all Anorexia Nervosa cases [3] and 10-15% of Bulimia Nervosa cases [3]. The incidence of Anorexia Nervosa is at least 8-9 new cases per 100,000 persons per year among women, while for men it is between 0.02 and 1.4 new cases. The incidence of Anorexia Nervosa is estimated to be at least 8 new cases per 100,000 persons per year among women, and between 0.02 and 1.4 new cases per 100,000 persons per year among men [3]. The incidence of Bulimia Nervosa is estimated to be at least 12 new cases per 100,000 persons per year among women and approximately 0.8 new cases per 100,000 persons per year among men [3]. In both Anorexia Nervosa and Bulimia Nervosa, the age group in which onset occurs most often is between 15 and 19 years. Some recent clinical annotations have reported an increase in early-onset cases [4]. This increase is partly explained by the lowering of the age of menarche observed in recent decades but could also be related to an earlier age at which adolescents are exposed to socio-cultural pressures to be thin, through media such as the Internet [5].

Rehabilitation in ED

Higher levels of care (HLC) – including inpatient hospitalization, residential treatment, partial hospitalization, and intensive outpatient treatment – are frequently utilized within routine care for eating disorders. Treatment approaches within HLC represent critically important alternatives for severe or treatment-refractory ED and aim to match illness severity with treatment dosage, while significantly reducing the overall cost of treatment [6].

Intensive/extensive inpatient/outpatient rehabilitation should be performed in a department specialized in the treatment of eating disorders that is able to provide the patient with a program that integrates nutritional, physical, psychological, and psychiatric rehabilitation.

Intensive rehabilitation represents a crucial node in the care network when: the level of severity and comorbidity is high; the impact on the patient's disability and quality of life is severe; the interventions to be implemented are numerous and it is appropriate, for both clinical and economic reasons, to concentrate them in a relatively short time according to a coordinated project; previous less intensive paths have not given the hoped-for results and the risk for the patient's state of health tends to increase [7]. Specifically, there are four situations that indicate the need for rehabilitation hospitalization: failure to respond to outpatient treatment conducted according to current guidelines; the presence of physical risk that makes outpatient treatment inappropriate; the presence of psychiatric risk that makes outpatient treatment inappropriate; the presence of psychosocial difficulties that make outpatient treatment inappropriate [8].

The Regional Network of Services for Eating Disorders in Campania

The Campania Region has shown an active interest in this issue setting up, since 2009, the Integrated Regional Network of Services for Eating Disorders. The purpose of this network is to set up an integrated regional network of services for the prevention, diagnosis, treatment and rehabilitation of Eating Disorders, to ensure that patients are taken into care at an early stage, to support team work and audits on individual cases, to encourage patients to remain in specific treatment and care facilities close to their own life context and family, to adopt unitary intervention strategies for adolescents, to pursue a rational use of resources, to prevent the onset of organic complications and the chronic nature of the disorders. The nodes of

this network are many: General Practitioners, freely chosen pediatricians, Prevention Departments, Health Districts, schools, sentinels on the territory deputed to the early detection of cases at risk for which it is necessary to provide an in-depth diagnostic investigation within a dedicated outpatient clinic (at least one in each ASL) of the Department of Mental Health competent for the territory. This first-level outpatient clinic, in addition to the in-depth diagnostic activity and the clinical-therapeutic management of cases that do not require intensive treatment, is the junction point towards the next level of care represented by day-hospital or ordinary in-patient treatment. Subsequently, the patient, if necessary, can be started on a therapeutic-rehabilitation pathway in public, semi-residential and residential facilities. The Regional Residential Centre for Eating Disorders "Mariconda" officially opens in December 2017. This paper offers a descriptive analysis of the sample of patients admitted in residential rehabilitation at the Regional Residential Centre for ED "Mariconda" of the Salerno ASL in the first 4 years of activity; another aim of this work is to demonstrate the correlation between anthropometric indices and length of hospitalization.

Materials and methods

Participants

All 105 subjects who were admitted between December 2017 and December 2021 at this Residential treatment program are included in these analyses. They came from Department of Salerno Mental Health and other Departments of Mental Health located in Campania, in the South of Italy.

All subjects included in this report were required to provide consent or assent for the use of data collected. Upon arrival at the facility, patients are required to complete a thorough intake that in includes a medical examination by a primary care physician and a nurse, as well as a meeting with a dietician. In addition to a medical examination, an extensive demographic and clinical assessment is required. The data collection process consisted of two data collection points noted as Admission and Discharge for each subject. The admission data collection procedures began on the day the subject was admitted to residential treatment with participants completing self-report questionnaires after informed consent was obtained. Body weight and height were determined by a calibrated scale and stadiometer. Data on body weight were extracted from the medical record in the same manner as the admission data collection point. Since the sample is heterogeneous, to provide more detailed information on the residents, the data are broken down by diagnosis (Anorexia Nervosa, Bulimia Nervosa, Binge Eating Disorder). Statistical differences by age and diagnosis are presented when appropriate.

Statistical analyses

Means are presented with standard deviations (SD). Comparisons of parametric independent samples were completed using analyses of variance (ANOVA).

Post-hoc Bonferroni corrections were made for multiple comparisons.

A significance level of.05 (after corrections) was used throughout.

To explore possible predictors of response, correlational analyses were performed using a variety of clinical variables to explore possible predictors of outcome. This included age, length of stay in the residential program and admission and discharge BMIs.

Correlations between variables were explored by means of Pearson's and Spearman's correlation tests.

Statistical significance level was set at $p \leq 0.05$ for all tests.

All analyses were carried out using SPSS 27 (SPSS Inc., Chicago, Illinois).

Results

Demographic data

Among the 105 subjects, 11 subjects (10.5%) refused to continue the Program within eight days from the admission. No significant difference was revealed between adult (63.6%) and adolescent (36.4%) $p > 0.01$ (Fig. 1).

Six subjects (5.7%) returned after discharge (for a second stay) after at least three months.

The demographic and clinical characteristics of the 94 study participants are shown in Table I by diagnosis. Of 94 patients with DCA as defined by DSM-V (American Psychiatric Association), all participated in the study, including 79 with AN, 12 with BN and 3 with BED (Tab. I).

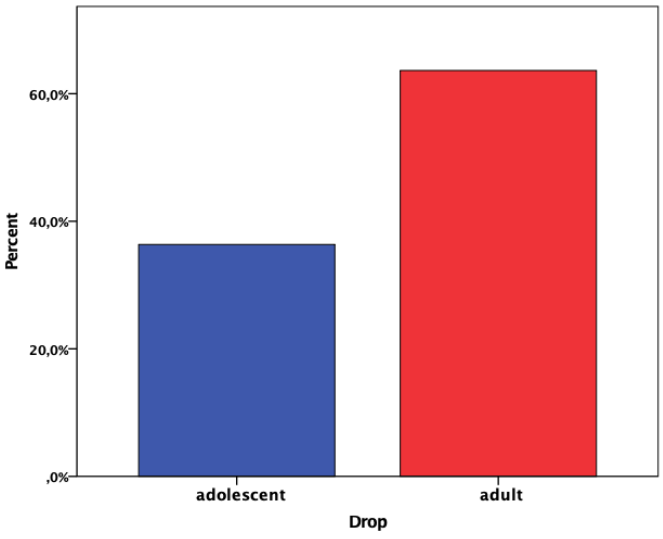

Figure 1.
Percentage of subjects that refused to continue the Program within eight days from the admission.

Table I. Demographic and clinical characteristics of residential treatment.

	Total sample (N = 94)	AN (N = 79)	BN (N = 12)	BED (N = 3)
Diagnosis at Admission %	-	84.0	12.8	32
Age (Mean ± SD)	19.24 ± 5.31	19.37 ± 5.61	18.5 ± 3.31	19.00 ± 4.36
Gender M/F (n)	5/89	5/74	0/12	0/3
Adolescent/adult (%)	47.9/52.1	48.1/51.9	41.7/58.3	66.7/33.3
Admission at residential treatment program (%)				
2018	11.7	10.1	16.7	33.3
2019	22.3	22.8	25.0	33.3
2020	30.9	30.4	33.3	33.3
2021	35.1	36.7	25.0	-
Length of stay (days, Mean ± SD)	104.20 ± 70.31	108.57 ± 70.01	75.92 ± 69.69	102.33 ± 80.93
Admit BMI (kg)	16.53±3.40	15.38± 1.66	22.17 ± 1.81	24.53 ± 8.43
Discharge BMI (kg)	18.77±2.50	18.710 ± 1.58	21.10 ± 2.39	22.46 ± 7.0

AN: Anorexia Nervosa; BN: Bulimia Nervosa; BED: Binge-eating disorder; BMI: Body mass index.

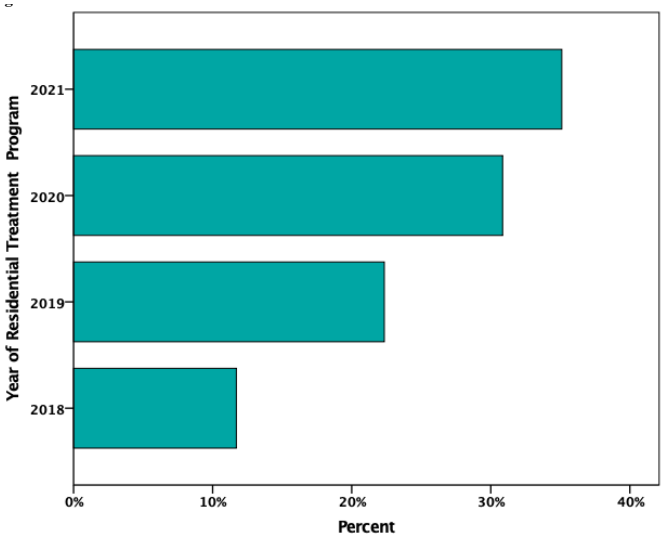

Figure 2.
Admission to rehabilitation treatment program.

The majority of patients was female (N = 94.7%) and included 45 adolescents (47.9%).
The age range of the participants with AN was 12 to 39 years, while that of the BN participants was 13 to 23 years. More than 66% of patients were admitted during the years 2020 and 2021 (Fig. 2).

Clinical characteristics

The majority of patients entering treatment was diagnosed with Anorexia Nervosa (AN), followed by Bulimia Nervosa (BN), and finally Binge Eating Disorder (BED).
The average age was 19.2 years old (SD = 5.3) and the average of admitted BMI was 16.53 (SD = 3.4), with Anorexia Nervosa having a statistically lower admitted

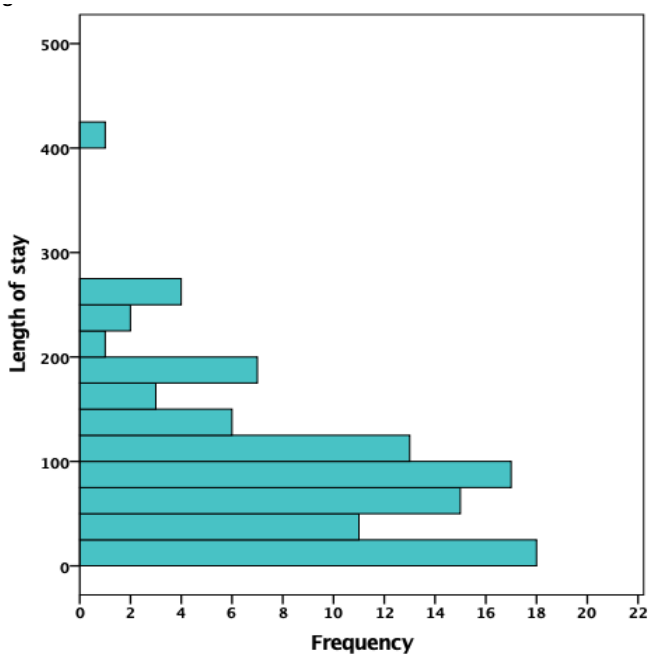

Figure 3.
Length of stay at Regional Residential Centre "Mariconda" of Azienda Sanitaria Locale di Salerno.

and discharge BMI than the comparison conditions $F_{(2, 91)} = 78.54$, $p < .000001$ and $F_{(2, 91)} = 28.74$, $p < .000001$.
Patients had a mean length of stay (LOS) of 104.20 ± 70.31 days (Fig. 3).
No between group differences were reported about age and length of stay ($p > 0.1$).

Correlation analysis

We examined the relationship between the age and the

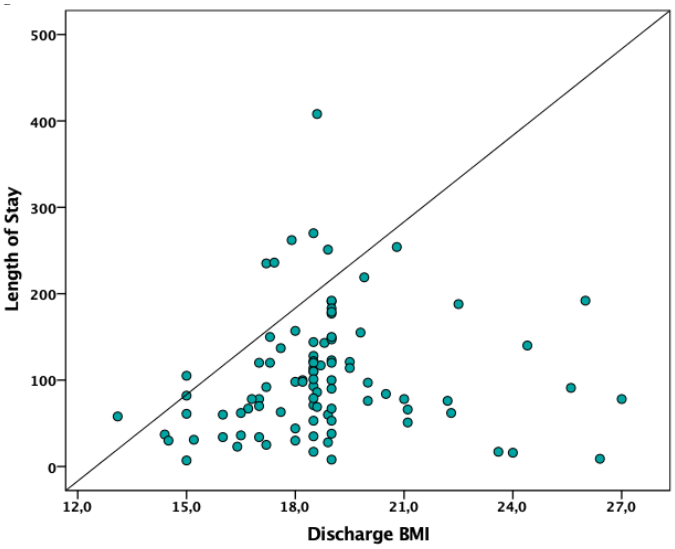

Figure 4.
Correlation between Discharge BMI and Length of stay.

length of stay in the residential setting and measures of Admitted and Discharge BMI. We observed no significant correlations between age and the length of stay and Admitted BMI.
A positive correlation between Discharge BMI and Length of stay ($r = 0.22$; $p = 0.032$; Fig. 4) were found.

Discussion

Anorexia and Bulimia Nervosa are the second leading cause of death among adolescent females, after traffic accidents. According to the latest literature Eating Disorders represent a growing public health problem in industrialized countries [9,10]; the age of onset is increasingly low, access to treatment is often critical and treatments require a good multidisciplinary organization. Treatment pathways are increasingly better structured and focused on the person in his or her complexity, rather than exclusively on the symptoms of the illness: more and more importance is given to the social, relational, communicative and environmental sphere of the person[11] and the treatment process increasingly takes on the meaning of a pathway of change, an experience of growth beyond the illness, in line with the recovery orientation that psychiatry has embraced in recent years [12]. The experience of illness, in fact, involves the person's entire life, devastating all areas and interrupting even their normal daily activities, yet proven interventions allow for the rehabilitation and remission of these aspects, and the earliness with which they are implemented is decisive. The data collected regarding the Regional Residential Centre "Mariconda" of Azienda Sanitaria Locale di Salerno from December 2017 to December 2021 show that 59% of patients suffering from Anorexia Nervosa, 23.2% from Bulimia Nervosa and 11.5% from Binge Eating Disorder were admitted to this Service. Also in the same period, 519 first visits were carried out, of which 31.8% required an assessment for the residential pathway, with 79% coming from outside the ASL; of those who required an assessment, 68% actually needed the residential pathway, with about 70% coming from outside the ASL.
In recent years, partly due to the SARS-CoV-2 pandemic, as evidenced by the most recent literature, the trend of services provided has been increasing [13]. Our results show that the outpatient setting is potentially ideal for the treatment of eating disorders, while the residential setting is only necessary in cases where there is a lack of response to outpatient treatment, the presence of psychosocial difficulties and a mild or moderate physical and/or psychiatric risk. The increase in the trend of services can certainly be attributed to an increase in the number of cases of Eating Disorders, but probably also to an increase in the number of diagnoses made, to a deeper and more widespread knowledge of this problem and to a greater awareness of the population on this subject, which are the results of the prevention, diagnosis, treatment and rehabilitation work carried out by the Regional Network for the Treatment of Eating Disorders.
Although our results are notable, there are some limitations to our study that warrant acknowledgment and discussion. The principal limitation is that it lacks a control or comparison group, another significant limitation of this study is the lack of a follow-up after the discharge.
Future research will be needed to focus on quantifying treatment program effectiveness in the residential treatment of individuals with eating disorders.

Conclusions

The sample analyzed confirms the distribution of ED, especially AN, predominantly in females and adolescents/young adults; AN requires longer treatment, aimed at a better recovery of psycho-physical conditions. In the last two years, also due to the SARS-CoV-2 pandemic, the trend in the number of services provided has been on the rise, attributable to an increase in the number of cases, better knowledge and greater awareness among the population with regard to the subjects, with a consequent increase in the number of diagnoses made.

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Letter to Editor

Società Italiana di Psichiatria

Letter to Editor

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Matteo Rocchetti

Dear Editors,
we are writing you regarding an interesting topic that is gaining resonance in the scientific community but is just beginning to be studied in Italy. Autoimmune encephalitis (AE) are inflammatory conditions of the brain often associated with neuronal synaptic antibodies (NSAbs) in the cerebrospinal fluid (CSF). Psychotic spectrum disorders (PSD) manifestations are common in AE, and in some cases represent the main or sole clinical feature, making this a relevant topic for psychiatrists. Indeed, up to 60% of patients with anti-NMDAR (the main ionotropic glutamate channel) encephalitis, the most common form of AE, present with PSD, and about one third are firstly evaluated in the psychiatric setting [1]. Red flags to help psychiatrists to identify AE in patients with PSD have been proposed [2], but never validated in clinical practice. In addition, some PSD patients without AE have NSAbs in serum, but not in CSF, with unclear clinical significance [3]. Since these NSAbs are pathogenic in-vitro, a blood brain barrier (BBB) impairment might allow them to cause chronic brain dysfunction without overt AE [4], but this has never been thoroughly assessed. To the best of our knowledge, the frequency of AE occurrence in PSD patients and the best strategy for their identification has never been investigated in Italy. Notwithstanding the expected low incidence of AE in the psychiatric setting, the identification of these patients is of the utmost importance, as the correct diagnosis might drastically change their management and prognosis.
Our research group has received a grant from the Ministry of Health (GR-2019-12369479) to specifically study this topic in our psychiatric services. Within the PHLAMES study, we aim to study the impact of a systematic diagnostic approach, that includes the evaluation of clinical red flags (Fig. 1) and the measurement of serum NSAbs to improve the diagnosis of AE in patients with acute and chronic PSD assessed in the psychiatric setting. Furthermore, we aim at investigating the meaning of serum NSAbs in patients with PSD

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Conflict of interest
The authors declare that they have no conflict of interest nor that they have received compensation from third parties for the creation of this article.

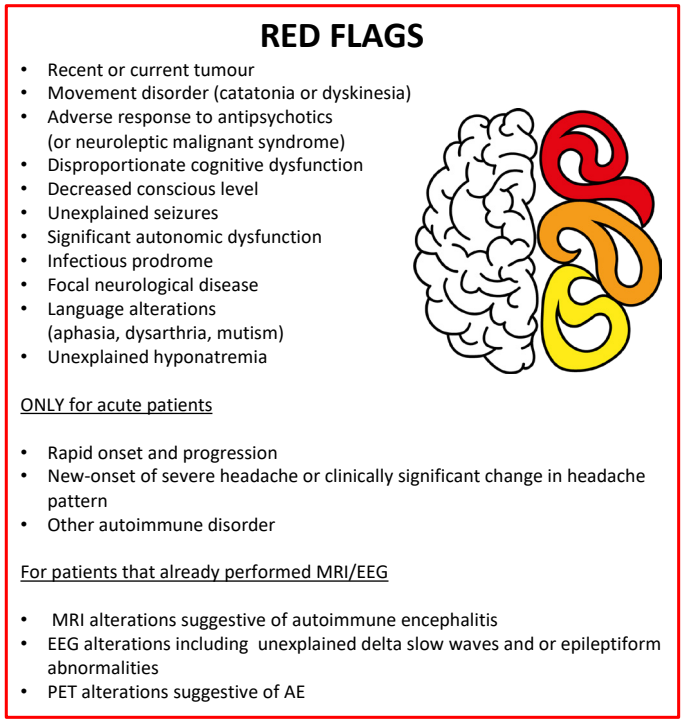

Figure 1.
Clinical red flags investigated in the PHLAMES study, adapted from Pollak, et al. [1].

without overt encephalitis, and to establish whether a BBB alteration might be one of the pathogenic mechanisms involved in PSD development in this subgroup. The first aim will have immediate and relevant clinical implications, providing a strategy to maximize the diagnostic accuracy for AE in the psychiatric setting, improve the outcome of the patients and rationalize costs. The second aim, although experimental, will provide insight into the role of NSAbs in chronic PSD patients that might have "mild forms" of encephalitis, and could pave the road for potentially efficacious immune treatments.

In conclusion, our study, that interweaves neurology and psychiatry, offers a unique opportunity to study the link between synaptic dysfunction and PSD from both a neuroimmunological and psychiatric perspective. We hope that this project will raise awareness of AE in the psychiatric community, as well as favor the collaboration between neurologists and psychiatrists.

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