

Cost-effectiveness of community versus hospital-based mental healthcare for severe mental illness in South-East Europe: evaluation of five randomised trials

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Abstract

Introduction

The RECOVER-E project supported the shift away from mental health care provided in institutional settings (treatment as usual, TAU) towards community-based mental healthcare by introducing multidisciplinary community mental health teams (CMHT) for people with schizophrenia, bipolar disorder, and severe depression across five sites in Bulgaria, Croatia, Montenegro, North Macedonia, and Romania. This paper presents the cost-effectiveness of CMHT compared to TAU.

Methods

Data from all five RECOVER-E trials (N = 931) was used to compute healthcare costs and societal costs which included additional patient and family costs, and costs stemming from productivity losses. Outcomes were incremental cost-effectiveness ratio's (ICER) for gaining a QALY and gaining a treatment responder (based on WHODAS 2.0).

Results

Compared to TAU, CMHT had small incremental effects favouring CMHT (QALY: M = 0.023, SD = 0.013; Response: M = 0.093, SD = 0.034). The incremental costs were higher in CMHT than in TAU as seen from both the societal and healthcare perspective (societal costs: M=€1,892, SD=€950; healthcare costs: M = 1,125, SD=€720). The ICER for gaining a QALY was €82,261 and €48,913 as seen from the societal and healthcare perspective, respectively. These ICERs were well above the willingness to pay threshold of €20,000 for gaining a QALY. A similar picture arose with treatment response as outcome.

Conclusion

Overall CMHT appeared to be more effective but also more costly, with the additional cost outweighing the benefits across countries, except in Bulgaria. Therefore, a recommendation for scaling up or sustaining CMHT must depend on arguments other than health-economic alone, such as medical ethical, equity and human rights considerations.

Trial registration

Bulgaria: NCT03922425, Croatia: NCT03862209, Macedonia: NCT03892473, Montenegro: NCT03837340, Romania NCT03884933.

INTRODUCTION

Mental disorders contribute 32.4% of all years lived with disability globally, which is expected to rise over the coming years [1, 2]. Mental disorders are responsible for high economic costs to both service users, their families and society as a whole via healthcare costs, costs incurred by the service users and their family and owing to productivity losses [3]. The need to improve mental healthcare to combat the rising

burden to both individuals and society as a whole has been recognised as a priority by the Lancet Psychiatry Commission [4]. As early as 2001, the World Health Organization (WHO) provided recommendations to improve mental health;[5]. one of the recommendations was provision of care in the community and to involve communities, families and service users in policies, programmes, and services. More than two decades later, at least two thirds of European countries have specific policies or plans for the development and implementation of community mental health services [6]. However, there remains a gap between population needs and actual service provision, especially in the low and middle-income countries in Europe [3]. Despite long-standing recommendations, there remain barriers to deinstitutionalisation, such as public-health priority setting and related funding, challenges to implementation, and a lack of trained personnel [7–9]. As a result, some mental health systems continue to rely on mental hospitals [10, 11].

Though prior research and policy documents have expressed the need for (economic) evaluations of mental health services [3, 4], such evaluations remain scarce, particularly in Southern and Eastern Europe. Such an evaluation enables decision-makers to weigh both the additional costs and the additional health outcomes in resource allocation decisions.

This paper presents the results of the economic evaluation of the introduction and implementation of a community based mental health service for people with severe and enduring mental ill health in Europe, in five sites in five countries (Bulgaria, Croatia, Montenegro, North Macedonia and Romania).. The economic evaluation's aim was to assess whether community-based mental healthcare was cost-effective compared to treatment as usual (TAU) in the five countries from a societal perspective looking at an 18-month time horizon. The economic evaluation was conducted both as a cost-effectiveness analysis (where treatment response, defined as improvement in global functioning, was the primary outcome) and as a cost-utility analysis (with quality adjusted life years (QALYs) gained was the main outcome).

METHODS

Study design

The health-economic evaluation was conducted alongside five hybrid effectiveness-implementation trials with assessments at baseline (t_0) and at 12 and 18 month follow-up (t_{12} and t_{18}). All five trials were pragmatic, non-blinded randomised clinical trials with service users randomised into two parallel groups: community-based mental healthcare versus treatment as usual (TAU) which was hospital-based in-patient or out-patient treatment. The selected sites were: Mental Health Centre Prof. N. Shipkoveski Ltd. (Sofia, Bulgaria), University Hospital Centre Zagreb (Zagreb, Croatia), University Clinic of Psychiatry, (Skopje, Macedonia), Psychiatric Hospital Dobrota (Kotor, Montenegro), and Siret Psychiatric Hospital (Suceava, Romania). This study is reported in agreement with the pertinent guidelines: the CONSORT statement for randomised trials and the Consolidated Health Economic Evaluation Reporting Standards

(CHEERS) statement for trial-based health-economic evaluation [12, 13]. A detailed description of the study's protocol is presented in Wijnen et al., 2020 [14].

Participants

Service users were recruited from the population being seen by psychiatrists at the sites participating in the study. The target population for inclusion in the study were consenting adults (ages 18–65 years) with severe mental illness defined as ICD-10 bipolar disorder, severe major depression, schizophrenia, schizophreniform, or schizoaffective disorder. Service users were excluded when under the age of 18 or when treatment was legally mandated.

Patient and public involvement

We carried out a thorough needs assessment at every site before beginning data collection to ensure the project aligned with local needs, policy priorities, and available resources. We also promoted public involvement by giving local research leads responsibility for aspects such as study design, recruitment, and clinical activities. Although service users were not directly involved in the research process at all five sites, a peer expert played a key role in developing and delivering training for service providers in the multidisciplinary community mental health teams, as well as training people with lived experience to become peer workers within the CMH teams.

Randomisation

Randomisation of consenting participants was carried out by an independent statistician in each of the five sites. Service users formed the unit of randomisation. Simple randomisation with a 1:1 allocation was applied using random.org for true random number generation. Randomisation status was not masked for clinicians and participants.

Intervention

The intervention consisted of a new community mental health service introduced in each site, a recovery-oriented multidisciplinary community mental health team CMHT(CMHTT). The CMHTT CMHT consisted of at least one psychiatrist, psychologist, nurse, social worker and a peer worker with lived experience of a severe mental disorder. The CMHT teams provided locally adapted but otherwise protocolized flexible assertive community treatment, with a focus on community outreach and home visits. In addition, CMHT teams were trained to work in a recovery-oriented way; that is, identifying and supporting service users' personal recovery goals, discussing choices and preferences for treatment and support, and focusing on strengths of the patient.

Control condition

The control condition consisted of routine mental healthcare in either inpatient or outpatient settings within the hospital, mainly offering pharmacological interventions (antidepressants, mood stabilisers, antipsychotics), sometimes also combined with psychological interventions.

Clinical outcomes

The EuroQoL with 5 dimensions and 3 levels (EQ-5D-3L) serves as the central outcome in the cost-utility analysis [15]. The EQ-5D-3L is a widely used generic quality of life instrument, with the (older) 3-level version more commonly used in Central and Eastern Europe. The EQ-5D-3L contains 5 dimensions (mobility, self-care, daily activities, pain/discomfort and depression/anxiety) to describe 3^5 health states. Next, utility values can be calculated for each of these health states. For this the valuation set elicited from the Slovenian population was used as a proxy, because valuation sets were not available for the participating countries [16]. The utility values give weight to the amount of time that a person spends in a certain health state, which helps to compute quality adjusted life years (QALYs) gains over the full 18-months period from t_0 to t_2 . QALYs were required to perform the cost-utility analysis.

The primary outcome for the cost-effectiveness analysis (CEA) was personal and social functioning as measured by the 36-item self-report version of the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) [17, 18]. The WHODAS 2.0 measures functional disability in accordance with the International Classification of Functioning (ICF) framework. The recommended scoring-algorithm of the WHODAS 2.0 is based on item-response theory and renders a scale from 0 to 100, with 0 meaning 'no disability' and 100 'severely disabled'. On this scale, treatment response is defined at individual level and occurs when a participant improves > 6 points from baseline (t_0) to last follow-up (t_{12}). The > 6 point improvement corresponds with a standardized mean change of $d \geq 0.33$ deemed to be the lower bound of a clinically relevant improvement [19]. WHODAS treatment response is the central outcome in the cost-effectiveness analysis (CEA).

Costs

Information on resource use pertinent to computing healthcare costs, patient and family out-of-pocket costs, and costs stemming from productivity losses were collected with the Trimbos and iMTA Cost questionnaire for Psychiatric illness (TiC-P) [20]. All costs were originally denoted in the national currency units of the participating countries at the 2019 price level and subsequently converted into Euro (€) using purchasing power parities (PPPs) as reported by the World Bank.

This paper presents costs from the healthcare perspective, but also from the more inclusive societal perspective encompassing (1) healthcare costs, (2) patient and family costs, and (3) costs stemming from productivity losses.

Statistical analysis

Power calculations showed that the randomised trials in each of the five sites would be well powered with $n = 90$ in each condition, in $N = 180$ in total [14]. This would suffice to detect a standardised effect of $d \geq 0.33$ (regarded as a clinically relevant improvement) on the WHODAS as statistically significant. Here it should be noted that the RECOVER-E trials were not powered for health-economic evaluation, which is a statistical hypothesis testing approach was not applied. Instead, inferences about cost-effectiveness will be based on probabilistic medical decision-making, more specifically on the cost-effectiveness acceptability curve (see below).

For each of the five sites the cumulative costs over the time interval between t_0 and t_{18} of 18 months were computed with the area under the curve (AUC) method, where costs are linearly interpolated between measurement points. The AUC method was also used to compute cumulative QALY gains over the full 18 months. The health-economic evaluation was conducted as a cost-effectiveness analysis (CEA) with costs (in € for the reference year 2019) related to WHODAS treatment response and a cost-utility analysis (CUA) with QALY gains as outcome. For both the CEA and the CUA the healthcare perspective and the societal perspective were considered.

To simultaneously evaluate both costs and outcomes, seemingly unrelated regression equations (SURE) models were used. The SURE models were baseline-adjusted with baseline WHODAS, EQ-5D utility, and cost as covariates. Because costs are usually non-normally distributed the SURE models were bootstrapped (2,500 times). For intention to treat (ITT) analysis, missing data was imputed using predictive mean matching nested in nonparametric bootstraps of SURE models of costs and effects, as recommended by Brandt and colleagues [21]. The imputed values were based on baseline variables that were predictive of clinical outcomes and cost; and predictive of dropout. This was done to enhance the precision of the imputed observations and to adjust for possibly selective dropout [22]. Relevant predictor variables were identified by means of regression analyses with costs, outcomes and missingness at both (t_{12} and t_{18}) follow-up measurements as the dependent variables, and condition, age, employment status, history, diagnosis, gender, and baseline score of the corresponding outcome variable as predictors. Given that we found imbalances in costs and utilities between both conditions at baseline, we adjusted the SURE models for baseline costs and utilities as recommended in Van Asselt et al. 2009 [23]. Costs and QALYs that were generated after the 12-months follow-up were discounted by 3.5% [24].

Subsequently, 2,500 Incremental cost-effectiveness ratios (ICERs) were computed, by dividing the between-condition difference in costs by the difference in effects. Next, the scatter of 2,500 bootstrapped ICERs was plotted on the ICER plane. In addition, the acceptability curve depicts the likelihood that one finds CMHT acceptable relative to TAU given varying willingness-to-pay (WTP) thresholds for gaining one additional QALY or one additional treatment responder. For the countries in which the study was conducted, no established WTP thresholds are currently available. However, the WHO Choosing Interventions that are Cost-Effective (WHO-CHOICE) project recommends a WTP

threshold of three times the national annual gross domestic product (GDP) per capita [25]. This would result in WTP threshold ranging from €13,500 (Macedonia) to €33,500 (Croatia) per QALY gained. For the joint analysis of all five countries, we have set the WTP threshold at €20,000 for gaining a QALY (i.e. the midrange of the calculates thresholds).

As set out in the protocol paper, a series of pre-planned sensitivity analyses were performed. First, in absence of country-specific tariffs, an analysis was performed in which West-European EQ-5D-3L tariffs were used instead of Slovenian tariffs [26]. Second, the EQ-5D visual analogue scale (VAS) was used to calculate country-specific QALYs. Lastly, winsorizing was used to reduce the impact of outliers in the cost data by replacing the top 10% highest costs by more modest costs corresponding with the 90th percentile [27]. The analyses were conducted in statistical software package R (version 4.1.2) and Stata (version 17.0).

Finally, we conducted an extra (post hoc) sensitivity analysis because COVID-19 incidence peaks may have had a disruptive impact on mental healthcare delivery in both the CMHT and TAU conditions during the t_1 , t_{12} , and t_{18} data collection. Using WHO data on confirmed COVID-19 case peaks in Eastern Mediterranean countries (<https://covid19.who.int>), we deduced that healthcare delivery was likely disrupted during four periods: March-April 2020, July-August 2020, November 2020-April 2021, and August 2021-February 2022. Given that these COVID-19 peaks coincided with a decrease in healthcare delivery volume and changes in the delivery method, they likely affected the effectiveness of both the TAU and CMHT interventions. To account for the confounding effect of the COVID-19 peaks, we included COVID-19 peak indicator which was assigned a value of 1 if a participant’s assessment occurred during one of these COVID-19 peaks or in the month following such a peak. This indicator was then added as a covariate in the SURE model to adjust for the possible confounding effect of the COVID-19 peaks in TAU and CMHT.

RESULTS

Recruitment

Participant recruitment commenced and was completed respectively between December 24th, 2018, and May 5th 2020 (Zagreb, Croatia), February 25th 2019 and December 12th 2019 (Kotor, Montenegro), April 1st 2019 and January 1st 2020 (Siret, Romania), June 21st 2019 and February 27th 2020 (Skopje, North Macedonia), October 23rd 2019 and March 9th 2020 (Sofia, Bulgaria).

Figure 1 depicts the flow of participants through the aggregated trials, showing numbers of health service users screened for inclusion, eligible and consenting, providing baseline data and randomised, participating in the t_{12} and t_{18} follow-ups, and included for the intention-to-treat analysis.

Sample at baseline

Table 1 shows the characteristics of the sample by condition at baseline.

Table 1
Baseline characteristics of the sample by condition

Demographics	Community mental health (N = 464)	Treatment as usual (N = 467)	Both conditions (N = 931)
· Age, mean (Sd)	47·3 (12·3)	47·8 (12·9)	47·5 (12·6)
· Female gender, N (%)	253 (54·5%)	230 (49·3%)	483 (51·9%)
· Has a partner, N (%)	44 (9·5%)	41 (8·8%)	85 (9·1%)
· Employed, N (%)	106 (22·8%)	95 (20·3%)	201 (21·6%)
· Above average income, N (%)	23 (5·0%)	13 (2·8%)	36 (3·9%)
<i>Education</i>			
· Primary, N (%)	98 (21·2%)	108 (23·2%)	206 (22·2%)
· Secondary, N (%)	208 (44·9%)	199 (42·8%)	407 (43·9)
· Lower vocational, N (%)	49 (10·6%)	65 (14·0%)	114 (12·3%)
· Higher vocational and academic, N (%)	108 (23·3%)	93 (20·0%)	201 (21·7%)
<i>ICD-10 diagnosis and history</i>			
· Schizophrenia, N (%)	224 (48·3%)	212 (45·4%)	436 (46·8%)
· Bipolar, N (%)	53 (11·4%)	59 (12·6%)	112 (12·0%)
· Major depression, N (%)	99 (21·3%)	92 (19·7%)	191 (20·5%)
· Treatment history > 5 years, N (%)	328 (70·7%)	331 (70·9%)	659 (70·8%)
<i>Costs, in 2019 €</i>			
· Healthcare, Mean (Sd)	817 (1285)	500 (920)	658 (1128)
· Patient and Family, Mean (Sd)	737 (1009)	693 (928)	715 (969)
· Productivity, Mean (Sd)	238 (902)	164 (716)	201 (815)
· Societal, Mean (Sd)	1791 (2128)	1357 (1600)	1573 (1893)
<i>Health</i>			
· WHODAS disability, Mean (SD)	34·42 (19·41)	35·78 (18·38)	35·10 (18·90)
· EQ-5D-3L utility, Mean (SD)	0·668 (0·236)	0·664 (0·234)	0·666 (0·235)

The mean age of participants at baseline was 47.5 years, with 51.9% of them being female, and 9.1% indicating to have a partner. Most of the participants (78.4%) were unemployed and only 3.9% reported to have an above average income. A large majority (70.8%) of the participants had a treatment history longer than 5 years, with schizophrenia being the most prevalent condition (46.8%), followed by depression (20.5%), and bipolar disorder (12.0%). Baseline demographics were similar between both groups except for gender (i.e. higher proportion of females in the TAU condition).

Despite randomisation, differences between the groups can be observed across baseline costs, with higher baseline costs in CMHT as compared to TAU (€817 versus €500 in healthcare costs, and €1791 versus €1357 in societal costs). The health-economic evaluation accounted for these baseline imbalances.

At baseline, the mean WHODAS score was 35.1 (SD: 18.9) and mean utility value was 0.66 (SD: 0.235) with no clinically relevant differences between both groups.

Loss to follow-up

At t_{12} , the wave non-response was $n = 88$ (19.0%) in CMHT and $n = 97$ (20.8%) in TAU. At the t_{18} follow-up, the total cumulative dropout was $n = 83$ (17.9%) in CMHT and $n = 95$ (20.3%) in TAU, as some of those not participating at t_{12} did participate in t_{18} .

In the 6-months interval between t_{12} and t_{18} , four participants died by suicide (three in the TAU condition and one in CMHT, all deaths were not associated with the study). These participants were included in the intention-to-treat analyses with their WHODAS score set at 100 ('fully disabled') and their EQ-5D-3L quality of life score set at 0 ('death') at t_{18} .

Cumulative costs and effects

Table 2 presents the cumulative costs and outcomes over 18-months follow up for both conditions. Cumulative societal costs were €27,465 (95%CI = €25,594; €29,345) for CMHT and €21,750 (95%CI = €20,175; €23,358) for TAU. The higher societal costs in CMHT were mainly caused by higher healthcare costs in the CMHT condition (€12,117 vs €8,480) and higher patient and family costs (€13,205 vs €11,399). The CMHT condition resulted in larger QALY gains compared to TAU (1.042 vs 1.014) and higher WHODAS mean scores (33.25 vs. 27.96).

Incremental cost-effectiveness ratios

According to the combined data from all five trials, CMHT compared to CAU was associated with mean incremental costs of $M = €1,892$ (SD = €950) and $M = €1,125$ (SD = €720) from the societal and healthcare perspective, respectively. CMHT was further associated with an incremental QALY gain of 0.023 (SD = 0.013). This resulted in an ICER of €82,261 per QALY gained (societal perspective) and €48,913 per QALY gained (healthcare perspective). From the acceptability curve, the probability of CMHT being cost-effective was low with a probability of < 5% at a willingness to pay threshold of €20,000 per QALY gained (see Table 3 and Fig. 2).

Table 2
Cumulative costs (in 2019 €) and outcomes by condition over 18-months follow up

	Community mental healthcare (N = 464)			Treatment as usual (N = 467)		
	Mean	95%CI		Mean	95%CI	
Healthcare	€12,117	€10,797	€13,494	€8,480	€7,417	€9,646
Patient & family	€13,205	€12,114	€14,344	€11,399	€10,394	€12,476
Productivity	€2,143	€1,496	€2,834	€1,872	€1,228	€2,561
Societal	€27,465	€25,594	€29,345	€21,750	€20,175	€23,358
QALY	1·042	1·013	1·071	1·014	0·982	1·044
WHODAS	33·25	31·03	35·44	27·96	26·02	29·96
QALYs: Quality-adjusted life years; CI: confidence interval based on 2,500 bootstrap simulations						

The mean incremental WHODAS treatment response rate was $M = 0.093$ ($SD = 0.034$) in favour of the CMHT group, resulting in an ICER of €20,344 per responder (societal perspective) and €12,097 per responder (healthcare perspective). Please note that, although there is no willingness to pay threshold for 'one additional responder' the willingness to pay is likely lower as being a responder does not constate being in perfect health (i.e. as a QALY would imply).

Table 3

Base-case and sensitivity analyses based on 2,500 bootstrap replications of the imputed data of all five trials combined

CUA	Incremental costs	Incremental effects	Mean bstrp ICER/ICUR	Distribution on cost-effectiveness plane, %			
	€ (SD)	QALY (SD)	ICUR	NE	NW	SW	SE
Main analysis	€1,892 (€950)	0·023 (0·013)	€82,261 per QALY gained	94	4	0	2
Healthcare perspective	€1,125 (€720)	0·023 (0·013)	€48,913 per QALY gained	91	3	0	5
Sensitivity analysis using W European tariffs	€1,892 (€950)	0·027 (0·012)	€70,074 per QALY gained	96	1	0	3
Sensitivity analysis using VAS	€1,892 (€950)	0·046 (0·014)	€41,130 per QALY gained	97	0	0	3
Sensitivity analysis winsorizing costs	€2,007 (€744)	0·023 (0·013)	€87,261 per QALY gained	96	4	0	0
CEA	€ (SD)	Resp. rate (SD)	ICER	NE	NW	SW	SE
Main analysis	€1,892 (€950)	0·093 (0·034)	€20,344 per responder	97	0	0	3
Healthcare perspective	€1,125 (€720)	0·093 (0·034)	€12,097 per responder	94	0	0	6
Sensitivity analysis winsorizing costs	€2,007 (€744)	0·093 (0·034)	€21,581 per responder	100	0	0	0

Sensitivity analyses

Results of the sensitivity analyses are presented in Table 3. Using European tariffs instead of Slovenia tariffs to value the EQ-5D, use the VAS included in the EQ-5D to calculate QALYs, winsorizing cost data (i.e. replacing the top 10% highest costs by more modest costs corresponding with the 90th percentile), or adding a COVID dummy to account for possible effects of COVID peaks all resulted in similar or lower costs per QALY/responder. However, costs per QALY estimates remained above the acceptable willingness to pay threshold.

Country-specific results

Figure 3 depicts how the ICERs are distributed on the ICER plane for each of the five participating countries and shows the between-country variability.

Footnote: The solid dot represents the point estimate of the ICER for each of the countries. The ellipses represent the 95% confidence ellipse around each of the country-specific ICERs. The light grey dots represent the 2,500 bootstrap replications of the ICERs of the merged sample. The dotted straight line represents the ICER in the merged population.

For each site, country-specific analyses were performed. A detailed overview of country-specific results can be found in online supplementary file 1.

Bulgaria

In Bulgaria, CMHT was associated with lower incremental costs and better incremental effects (both in terms of responder rate as well as QALY gains) from both the societal and healthcare perspective. This resulted in dominant ICERs for both cost per responders and cost per QALY gained (see Online supplementary file 1; table S1). A large proportion (range 0.77–0.90) of the bootstrap-simulated ICERs were lying in the South-East quadrant, indicating that CMHT was both more effective and less costly than TAU, hence dominant (see Online supplementary file 1; figures S1 & S2).

Croatia

In Croatia, the CMHT group demonstrated higher incremental costs and marginally higher incremental effects (in terms responder rate) and marginally lower effects in terms of QALYs from both a societal and a healthcare perspective. This resulted in CMHT being inferior in terms of costs per QALY and an ICER of €1,920 per responder (see Online supplementary file 1; table S2). A large portion of the bootstrap-simulated ICERs were lying in the North-West, South-West, and South-East quadrant of the CE-plane, indicating that the intervention performs relatively similar in terms of costs and effects when compared to the CAU group (see Online supplementary file 1; figures S3 & S4).

Montenegro

In Montenegro, the CMHT group demonstrated higher incremental costs and marginally higher incremental effects (both in terms of responder rate as well as QALYs) from both a societal and a healthcare perspective. The small difference in effects resulted in relatively high ICERs for both cost costs per QALY gained and costs per responder (see Online supplementary file 1; table S3). A large portion of the bootstrap-simulated ICERs were lying in the North-West and North-East quadrant of the CE-plane, indicating that the intervention performs relatively similar in terms of effects when compared to the CAU group but likely results in increased costs (see Online supplementary file 1; figures S5 & S6).

North-Macedonia

In North-Macedonia, the CMHT group demonstrated higher incremental costs and higher incremental QALYs from both a societal and a healthcare perspective. Looking at the responder rate, the CMHT group demonstrated a marginally lower rate. The small difference in effects resulted in inferior ICERs for cost per responders (Online supplementary file 1; see table S5). Looking at the cost per QALY gained, ICERs rose above any acceptable willingness to pay threshold. A large portion of the bootstrap-simulated

ICERs were lying in the North-West quadrant of the CE-plane, indicating that the intervention performs relatively similar in terms of effects when compared to the CAU group but likely results in increased costs (Online supplementary file 1; see figures S9 & S10).

Romania

In Romania, the CMHT group demonstrated higher incremental costs and marginally higher incremental QALYs with marginally lower response rates from both a societal and a healthcare perspective. The small difference in effects resulted in inferior ICERs for cost per responders and relatively high ICERs for the cost per QALY gained (see Online supplementary file 1; table S4). A large portion of the bootstrap-simulated ICERs were lying in the North-West quadrant and North-East quadrant of the CE-plane, indicating that the intervention performs relatively similar in terms of effects when compared to the CAU group but likely results in increased costs (see Online supplementary file 1; figures S7 & S8).

DISCUSSION

Main findings

This study aimed to assess whether community-based recovery-oriented care delivered by multidisciplinary community mental health (CMHT) teams was cost-effective compared to treatment as usual (TAU) in five Southern and Eastern European countries, as seen from both the healthcare and societal perspective, over a 18-month time horizon

Across the 5 trials in the five countries, results indicated that the new CMHT compared to TAU produced relatively comparable health outcomes for higher costs, with Bulgaria as a possible exception given that CMHT appeared to be superior in producing better health outcomes for lower incremental costs than TAU (i.e. CMHT dominating CAU). When the effect difference across conditions is close to zero, the calculation of ICERs result in substantially high ratios given that would amount to division by zero. This is relevant for Croatia, Montenegro, North-Macedonia and Romania. For these countries, it may be easier to conclude that similar health gains are being produced for higher costs with the implication that the willingness to pay for the higher costs can only be motivated by other considerations than cost-effectiveness alone. For example, one may still prefer the more expensive interventions because it is better accepted by service users and deemed more appropriate by clinicians, or because CMH provides other benefits, such as alignment with human rights, restoration of relationships with one's community, contribution to community organisations and work.

Overall, CMHT was associated with higher incremental costs and marginally higher effects to TAU in terms of QALY gains and response rates. In fact, costs per QALY were relatively high and above acceptable willingness to pay thresholds (i.e. ICER of €82,261 per QALY gained (societal perspective) and €48,913 per QALY gained (healthcare perspective). Consequently, there was a low likelihood of being cost-effective at a willingness to pay threshold of €20,000 per QALY gained.

Findings in context

In spite of many reform efforts in the past, a balance of community and hospital mental health services has not yet been achieved in all parts of Southern and Eastern Europe [11]. There is a paucity of evidence on the cost-effectiveness of CMHT in Southern and Eastern European countries [28]. A study by Zavrashvili et al. (2010) reported the results of the implementation of assertive community care with the aim to engage socially isolated service users in Tbilisi (Georgia) and concluded that community care was less costly than usual treatment and seems to be effective in improving clinical and social outcomes [29]. Moreover, Winkler et al. (2018) demonstrated economic evidence for deinstitutionalisation by showing that discharge to community care was cost-effective compared with care in psychiatric hospitals in the Czech Republic [30].

Limitations

This study has several limitations. First, as indicated, COVID and subsequent lockdowns disrupted healthcare delivery in the participating countries and compromised the quality of care since 2020. However, the sensitivity analyses indicated that COVID-19 had very little effect on the cost and effect estimates as obtained in the base-case analysis. Despite the disruption caused by COVID-19 since 2020 the five sites have been successful in recruiting the required number of participants into the randomised trials, collected their data at baseline and the 12-month and 18-months follow-ups with little loss to follow-up. Yet, COVID-19 and subsequent lockdowns severely disrupted healthcare delivery in the participating countries and may also have compromised the quality of care. To illustrate, in Croatia the number of days of inpatient hospitalisations and the number of day care hospitalisations were reduced by 27% and 63% respectively during COVID in the year 2020 as compared to the year 2019 before COVID. Fewer hospitalisations and shorter hospital stays may have reduced the costs of hospital-based TAU and thus biased the economic evaluation in favour of TAU.

Second, in the absence of country-specific EQ-5D tariffs, we had to rely on the Slovenian tariff [26], which may have introduced some bias in the QALY estimations. Sensitivity analyses using both the West-European tariffs as well as VAS score demonstrated similar but slightly higher QALY estimates.

Third, in lieu of national standard cost prices in each of the participating countries, unit cost prices for health services (e.g. a visit at the GP's, a contact with a psychiatrist, a day in an hospital) were obtained from national health insurance funds. These tariffs may not reflect the full economic cost price of resource use. However, it was expected that these biases occur to the same degree in the CMHT condition as in the TAU condition, thus cancelling each other out when computing cost differences across the CMHT and TAU conditions.

Lastly and most importantly, health-economic evaluations have inherent limitations when used to inform decision-making in healthcare, where many other considerations beyond costs and effects have to play a prominent role, like medical-ethics, human rights, equity, the acceptability and appropriateness of the

new intervention as perceived by healthcare users and healthcare professionals. The latter was also confirmed in an earlier study of our consortium [31].

Conclusion

As indicated, the results should be interpreted with caution in the light of the study's limitations and in the wider context in which the data for the health-economic evaluation has been generated. Results indicated that CMHT produced slightly better mental health outcomes than hospital-based care, albeit for higher per-patient costs in Croatia, Montenegro, North Macedonia and Romania, but not Bulgaria where health effects were better and costs of community mental healthcare lower than those of TAU. This resulted in ICERs often (but not always) exceeding acceptable willingness-to-pay threshold signalling that the costs of CMHT are not acceptable as seen from a strict health-economic perspective. Establishing, implementing, and sustaining CMH services in SEE countries requires investments and initially are likely to be more expensive than care as usual or, at best, no more costly than hospital-based care. However, reallocating resources away from psychiatric hospitals and providing sufficient funding are fundamental to establishing community mental health care and may lead to improved cost-effectiveness on the long run [32]. Hence, cost effectiveness analyses need to be repeated after a significantly longer period of time to see if over time, with normalisation of a new model of care, costs can be balanced out. By implication, more consideration to cost-effectiveness should be embedded in the planning and implementation stage before rollout of CMHT, or else the decision to scale up CMHT must be motivated by arguments other than cost-effectiveness such as medical-ethical, equity and human rights considerations [9]. It is therefore important to communicate to decision makers that they should not expect community services to necessarily be cheaper, but they should expect them to produce benefits to individuals and societies that justify the costs [32].

Declarations

Declaration of Interest

None declared.

Ethics approval

Ethical approval from a local institutional review board has been acquired in each implementation site: - Sofia, Bulgaria: Commission of Ethics at the National Center of Public Health and Analyses. Ethics approval nr: 25.1.2019. - Zagreb, Croatia: University Hospital Center Zagreb Ethical Committee. Ethics approval nr: 18.7.2018. - Skopje, North Macedonia: Ethical Committee for Research on Human Subjects, Medical Faculty, SS Cyril and Methodius University Skopje, Ethics approval nr: 21.5.2018. - Kotor, Montenegro: Specialized Psychiatric Hospital Dobrota Kotor Ethics Committee. Ethics approval nr:

28.9.2018. - Siret, Romania: Consiliul de Etica Spitalul de Psihiatrica Cronici Siret. Ethics approval nr: 21.11.2018.

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Author Contribution

Designing and coordinating the project: IP and LSZ. Co-ordination health economic evaluation: AIU, BW, and FS. Data management CR, MW. Data curation and analysis CR, BW, FS. Drafting the manuscript: FS, BW, LSZ, and AIU. Critical appraisal of the manuscript: all authors. All authors have read and approved the manuscript.

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Data Availability

The data underlying this study are not publicly available due to privacy and data protection regulations. Individual-level patient data cannot be shared. Aggregate data that support the findings of this study may be made available from the authors upon reasonable request.

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Figures

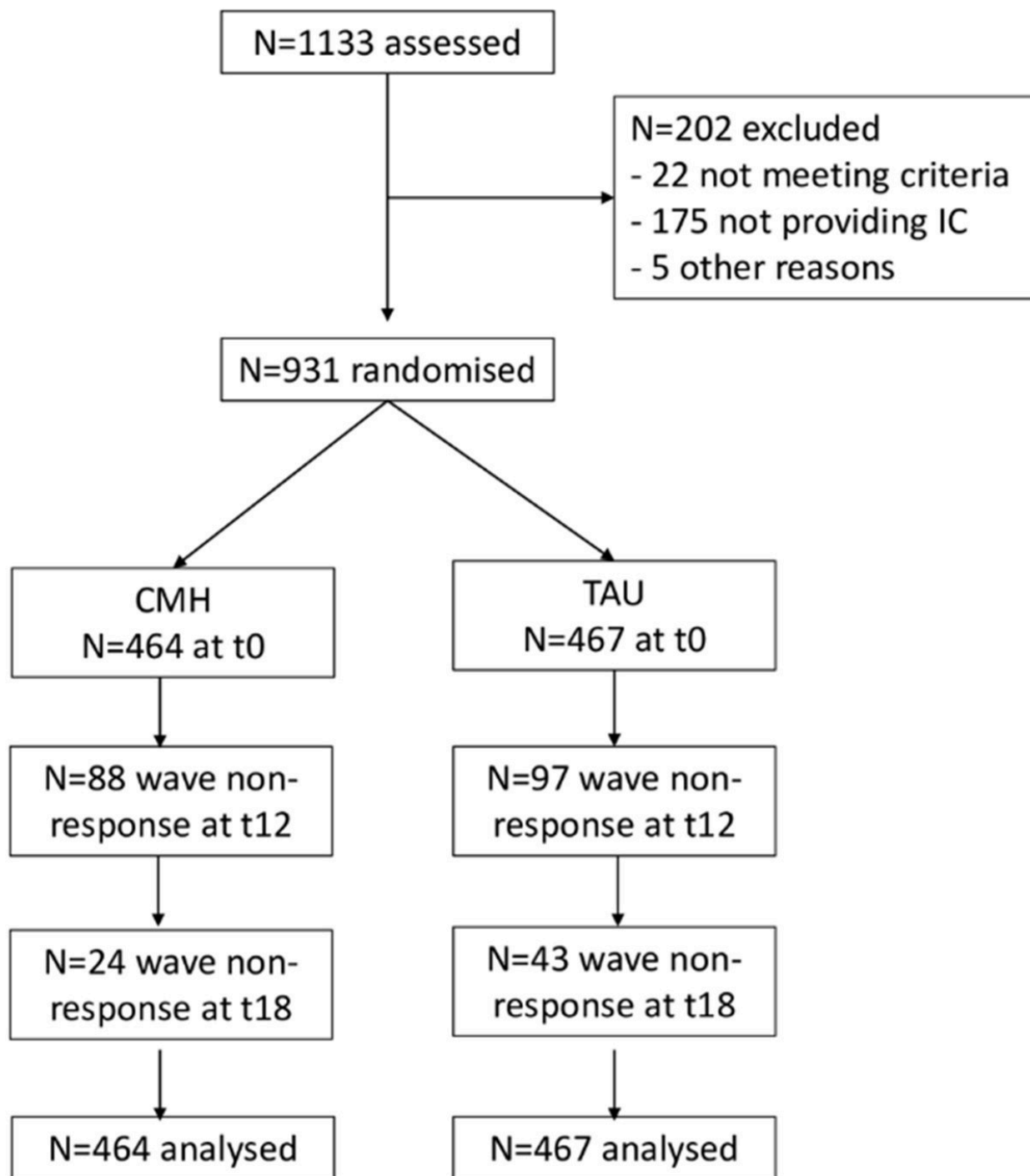


Figure 1

CONSORT flow chart

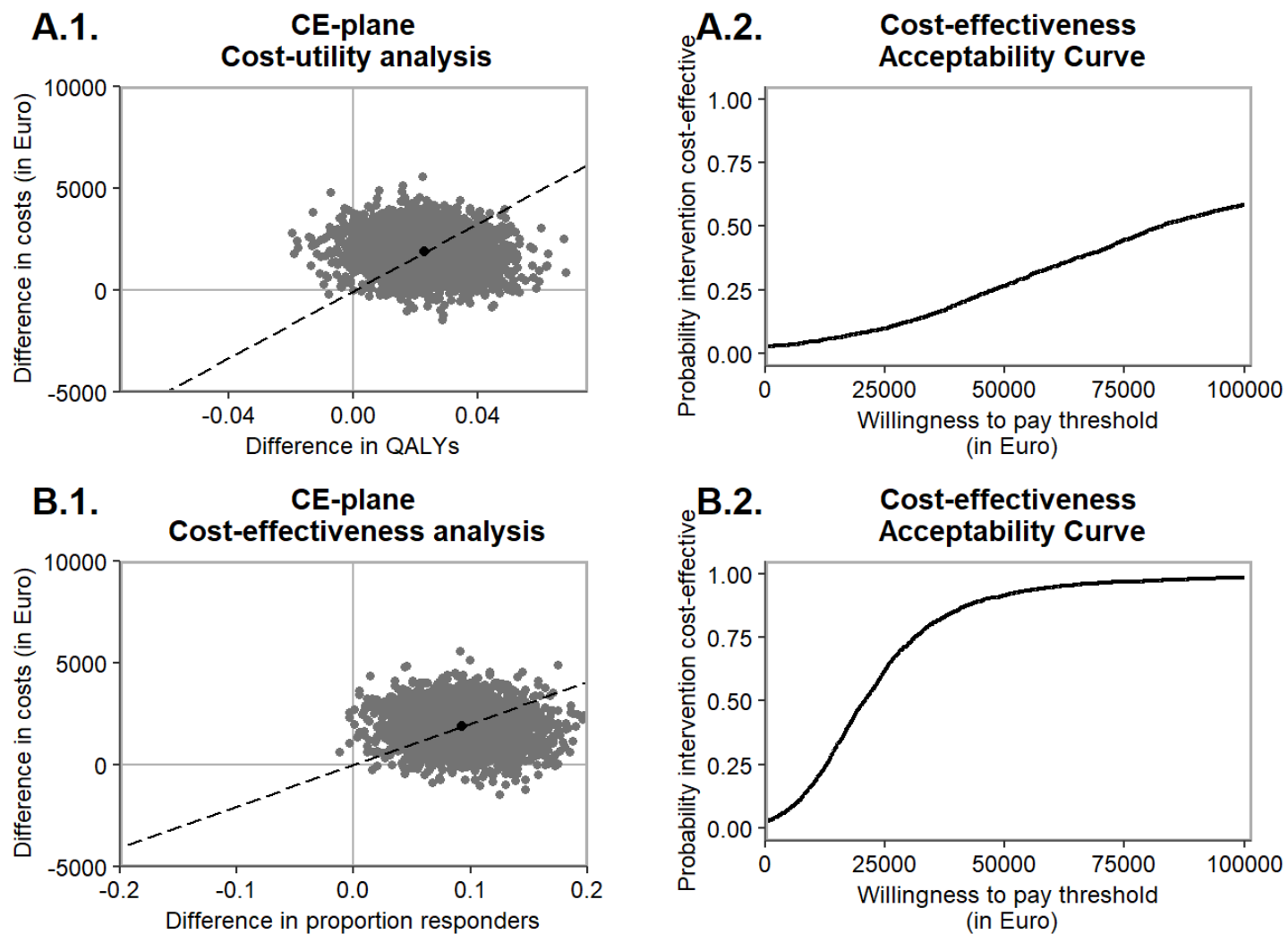


Figure 2

Incremental costs per QALY (top) and costs per responder (bottom): ICER plane (left) and acceptability curves (right)

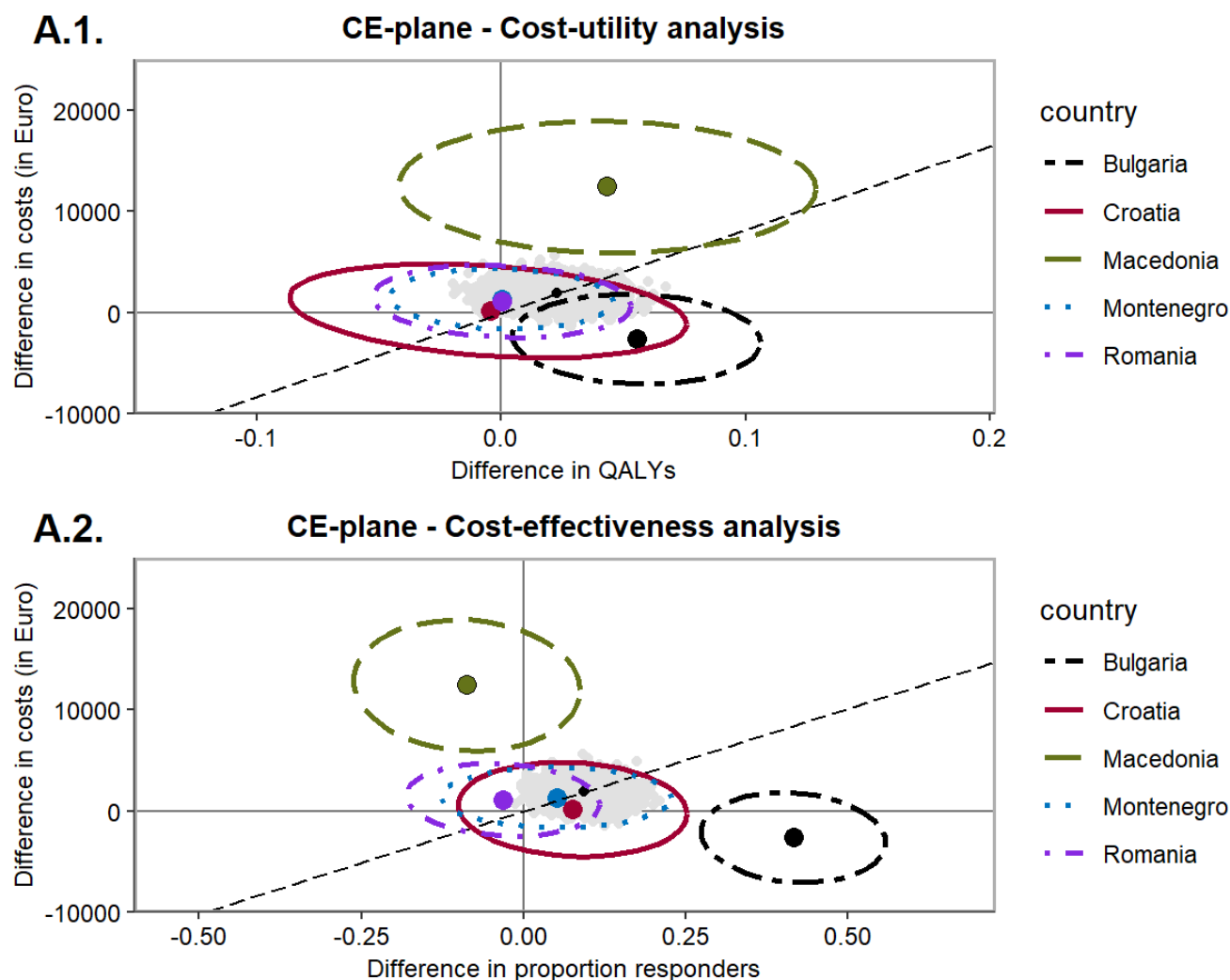


Figure 3

Distribution of the ICERs by country

Footnote: The solid dot represents the point estimate of the ICER for each of the countries. The ellipses represent the 95% confidence ellipse around each of the country-specific ICERs. The light grey dots represent the 2,500 bootstrap replications of the ICERs of the merged sample. The dotted straight line represents the ICER in the merged population.

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