Cost-effectiveness of WHO Problem Management Plus for adults impaired by psychological distress in a post-conflict setting of Pakistan

Journal:	*BJPsych*
Manuscript ID	BJPsych-19-0817.R3
Manuscript Type:	Paper
Date Submitted by the Author:	10-Jun-2020
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Keywords:	Cost-effectiveness, lay health workers, psychological interventions, humanitarian settings, Problem Management Plus
Publishing Category:	Mental Health Services
Abstract:	Background With the development of evidence-based interventions for treatment of priority mental health conditions in humanitarian settings, it is important to establish the cost-effectiveness of such interventions to enable their scale-up. Aims To evaluate the cost-effectiveness of Problem Management Plus (PM+) intervention, compared to Enhanced Usual Care (EUC) for common mental disorders in primary healthcare in Peshawar, Pakistan. Methods We randomly allocated 346 participants to either PM+ (n=172) or EUC (n=174). Cost-effectiveness analysis was performed as incremental costs (measured in Pakistani Rupees) [PKR] per unit change in anxiety and depression scores measured using Hospital Anxiety and Depression Scale (HADS) at 3 months' post-intervention. Results The total cost of delivering PM+ per participant was estimated at PKR 16,967 (US $ 163.14) using an international master trainer/supervisor and PKR 3,645 (US$35.04; US$ 7 per session) employing a national trainer/supervisor. The mean cost per unit score improvement in anxiety and depression symptoms on HADS was PKR 2957 (95% CI: 2262, 4029) [US$ 28] with international trainer/supervision and PKR 588 (95%

	CI: 434, 820) or US$ 6 with local trainer. The mean Incremental Cost-Effectiveness Ratio (ICER) to successfully treat a case of depression (PHQ-9 ≥ 10) using an international supervisor was PKR 53,770 (95% CI: 39,394, 77,399) [US$ 517] versus a local supervisor PKR 10,705 (95% CI: 7731, 15,627) [US$ 102.93]. Conclusions The PM+ was more effective but also more costly than EUC in reducing symptoms of anxiety, depression and improving functioning in adults impaired by psychological distress in a post-conflict setting of Pakistan.

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Word count (except abstract): 3497

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Funding

This work was supported by Enhanced Learning and Research for Humanitarian Assistance's (Elhra's) Research for Health in Humanitarian Crises (R2HC) initiative funded by the UK Department for International Development and the Wellcome Trust.

Role of the Funder/Sponsor

The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Acknowledgements

We thank the project staff at the Department of Psychiatry, Lady Reading Hospital, Peshawar, and Human Development Research Foundation (HDRF), Islamabad, Pakistan, for their contributions, the primary health care staff and physicians for their support in the conduct of the study, and the participants and their families for their voluntary participation. We would like to specially thank Dr Victoria Baranov (Senior Lecturer in Economics, the University of Melbourne) for sharing her insights in revising the manuscript for re-submission.

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Competing interests

All authors have declared no conflicts of interest.

ABSTRACT

Background

With the development of evidence-based interventions for treatment of priority mental health conditions in humanitarian settings, it is important to establish the cost-effectiveness of such interventions to enable their scale-up.

Aims

To evaluate the cost-effectiveness of Problem Management Plus (PM+) intervention, compared to Enhanced Usual Care (EUC) for common mental disorders in primary healthcare in Peshawar, Pakistan.

Methods

We randomly allocated 346 participants to either PM+ (n=172) or EUC (n=174). Effectiveness was measured using Hospital Anxiety and Depression Scale (HADS) at 3 months' post-intervention. Cost-effectiveness analysis was performed as incremental costs (measured in Pakistani Rupees [PKR] per unit change in anxiety, depression and functioning scores.

Results

The total cost of delivering PM+ per participant was estimated at PKR 16,967 (US $ 163.14) using an international master trainer and supervisor, and PKR 3,645 (US$35.04; US$ 7 per session) employing a national trainer. The mean cost per unit score improvement in anxiety and depression symptoms on HADS was PKR 2957 (95% CI: 2262, 4029) [US$ 28] with international trainer/supervision and PKR 588 (95% CI: 434, 820) or US$ 6 with local trainer/supervisor. The mean Incremental Cost-Effectiveness Ratio (ICER) to successfully treat a case of depression (PHQ-9 ≥ 10) using an international supervisor was PKR 53,770 (95% CI: 39,394, 77,399) [US$ 517] versus a local supervisor PKR 10,705 (95% CI: 7731, 15,627) [US$ 102.93].

Conclusions

The PM+ was more effective but also more costly than EUC in reducing symptoms of anxiety, depression and improving functioning in adults impaired by psychological distress in a post-conflict setting of Pakistan.

Key words: Cost-effectiveness, lay health workers, Low and Middle Income Countries (LMIC), humanitarian settings, Problem Management Plus, Common Mental Disorders (CMDs)

Trial Registration anzctr.org.au Identifier: ACTRN12614001235695

Mental health problems cause a significant burden of disease in Low and Middle Income Countries (LMICs), yet the documented 'mental health treatment gap' is up to 90% [1-3]. The need for mental health services is much greater in populations affected by humanitarian crises. More than 135 million people are in need of humanitarian assistance due to ongoing humanitarian crises and conflicts globally [4]. A systematic review and meta-analysis of mental health outcomes in population affected by conflict and displacements showed that mood and anxiety disorders were common, with rates of 17.3% for depression and 15.4% for posttraumatic stress disorder [5]. Epidemiological studies from areas affected by humanitarian crises in Pakistan found high rates of psychological distress in these populations. One study reported rates as high as 38% to 65% for psychological distress in women [6, 7]. Majority of people have no access to mental health services in such settings [6]. Over the past decade, significant progress has been made in terms of availability of evidence based mental health intervention packages for populations affected by humanitarian crises [8]. However, sustainability and scalability of such psychological interventions remains a challenge in populations affected by humanitarian crises in low resource settings globally [9].

We developed and tested a brief, multicomponent behavioural intervention, Problem Management Plus (PM+) delivered by lay health workers for Common Mental Disorders (CMDs) in conflict affected settings. The intervention was effective for treating the symptoms of CMDs in a post-conflict setting of Pakistan. Trial protocol and results of pilot and definitive clinical trials have been published [10-12]. In the present study, we conduct an economic evaluation alongside the randomized controlled trial to assess the cost-effectiveness of this intervention in order to inform policy and implementation in routine clinical practice.

Method

Study site and participants

Participants included 346 primary care attendees with high level of psychological distress (score above 2 on General Health Questionnaire [GHQ-12]) [13] and functional impairment (score above 16 on World Health Organization Disability Assessment Schedule 2.0 [WHODAS 2.0]) [14]. The participants were individually randomized in 1:1 ratio to either intervention arm i.e. PM+ (n=172) along with Enhanced Usual Care (EUC)) or the Control arm consisting of Enhanced Usual Care (EUC) only (n=174). The study was approved locally by the Institutional Review and Ethics Board of the

Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, and by the WHO Ethical Review Committee. Written informed consent was obtained from all study participants.

The Intervention

Participants in the intervention arm received a brief multicomponent intervention called Problem Management Plus (PM+) [15]. The intervention is trans-diagnostic as it applies the same underlying principles across mental disorders, without tailoring the protocol to specific diagnoses [16]. PM+ is based on well-established principles of problem solving and behavioural techniques. It is designed to be used for adults experiencing common mental health problems (e.g. anxiety, stress, depression and grief) only. It is not suitable for the treatment of severe mental health problems (including psychosis or risk for suicide). Both an individual and group version of the intervention exists. The current study involves the individual version.

PM+ consists of 5 weekly face-to-face sessions of 90 minutes each, delivered by trained lay health workers. The intervention is composed of four core strategies i.e. stress management, managing problems, get going, keep doing (behavioural activation), strengthening social support, introduced sequentially in the intervention sessions. In the last session, all the strategies are reviewed with a particular emphasis on using these strategies for self-management in the future and to prevent relapse.

Training and supervision followed a cascade model. An international master trainer trained local trainers in a 6-day training workshop. Training consisted of intervention delivery, training and supervision skills. Local trainers cascaded the training to lay health workers (with 12-16 year of education) in an 8-day training. Lay health workers were provided weekly supervision by local trainers/supervisors (hereafter local supervisor) who were in turn, supervised monthly by the international master trainer/supervisor (hereafter international supervisor) via video conference for 2 to 3 hours. The intervention is available in Urdu and English on the WHO website [17]. Further details of intervention are described elsewhere [15].

Enhanced care as usual

The participants in both intervention arm and control arm received Enhanced Usual Care (EUC). The treatment was enhanced as the Primary Health Care (PHC) physicians in the participating primary health care centres received a 5-day training in the management of Common Mental Disorders (CMDs)

in primary health care settings. The training was reinforced through a one-day refresher training for the primary health care physicians. The study participants in both arms were able to seek other health care services from their PHC physicians.

Data Collection

A. Health outcomes

The outcomes were measured at baseline and 3 months' post-intervention. The cost-effectiveness analysis was performed as incremental costs per unit change in anxiety, depression and functioning scores. The primary outcome was change in symptoms of anxiety and depression measured with the Hospital Anxiety and Depression Scale (HADS) [18, 19]. Severity of symptoms was measured using the -HADS-Anxiety (anxiety; 7 items; possible score range, 0-21) and Depression (depression; 7 items; possible score range, 0-21). Higher scores indicate more anxiety and/or depression. Secondary outcomes were functional impairment and presence of depressive disorders. WHODAS-12 was used to assess functional impairment. Polytomous scoring algorithm of WHODAS-12 was used to transform the functional impairment scores on a scale of 1-100[14]. Presence of depressive disorder was measured using a 9-item Patient Health Questionnaire (PHQ-9) [20]. Other secondary outcome measure included PCL-5 [21], results of which are attached as a web appendix.

B. Health resource use profiling

The data on health resource use was collected using the Client Services Receipt Inventory (CSRI) [22], which records the clients' contact with out-patient services (i.e. mental health specialist, general physician, traditional healer, community health workers etc.), inpatient (hospital admissions) services and out of pocket costs associated with travel, medications and tests/investigations during the preceding recall period. A section on seeking religious help and retreats was added to adapt the tool for use in local population. Study participants self-reported their health-care utilization, medication use and out-of-pocket expenditures on CSRI [22] at baseline and 3-months' post-intervention.

C. Cost measurement and analysis

Economic analysis was conducted primarily from a health system perspective, consisting of a) costs incurred over the trial period in the delivery of the intervention itself, b) use of other healthcare and

related services by study participants, including religious help and retreats, and c) patient and family costs (such as number of days with reduced working hours, informal caregiving time by relatives or friends as well as travel costs and time spent travelling to or waiting for consultations). No discounting of costs was applied since the study was performed within one year.

Intervention costs: These included costs for the intervention adaptation workshops, translations of intervention manual and training materials; printing of adapted training manuals, staff recruitment, training and supervision. Supervision costs included time spent by master trainer, supervisors, transport costs for fieldwork supervision, and costs of all other resources used.

To estimate the cost of intervention delivery, we evaluated unit cost per minute of health care providers' time including the international master trainer/supervisor, local supervisors, lay health workers and physicians. The unit cost per minute was multiplied with the total estimated time spent by each health care provider to the participants to calculate the total cost of intervention delivery. We calculated the cost of intervention delivery with the international master trainer/supervisor and modelled the cost for a local supervisor as a potentially more sustainable way to support task-shifting in low resource settings. Costs of the intervention were calculated by multiplying the total contact time (number of minutes) a participant had in the intervention arm with a lay health worker by the per-minute cost of the lay health workers' time and the costs spent on travelling by lay health workers (unit cost calculations are provided as web appendix).

Calculation of these intervention costs as well as contacts with a range of formal health care providers was facilitated by the use of a simplified costing template for unit cost calculations reported in health economic evaluation of mental health services [23]. Unit cost templates accounted for the costs of salaries of staff employed in the provision of intervention delivery (including master trainer, supervisors, lay health workers and PHC staff), facility operating costs where the service was provided, overhead costs relating to the provision of service (personnel, finance etc.) and the capital costs of the facility where the intervention was provided (land, buildings etc.). Sources of data for these variables included public health system financial records and project's financial records. All costs were calculated in Pakistani rupees (PKR) and are reported in Pakistani Rupees and United States Dollars for

the year 2016, when the study was implemented ([1]Exchange rate 1 USD= PKR 104). No adjustment was made for Purchasing Power Parity (PPP) since the focus of interest was on the actual resource costs incurred in the study country (rather than a comparison to other countries, whereby differences in the relative price of goods and services would need to be taken into account).

Statistical Analysis

The mean and standard deviation for the total cost was calculated using generalized linear regression model with Gamma distribution after adjustment for baseline total cost. The group difference and its 95% CI was also calculated [24]. The Incremental Cost-effectiveness Ratio (ICER) was calculated as the additional costs of the intervention divided by the change in HADS-A, HADS- D, HADS Total, PHQ, and WHODAS related to the intervention. The confidence intervals for ICER was estimated by non-parametric bootstrapping. The bootstrap technique sampled with replacement from the original observed paired of costs and effects, maintaining the correlation structure between costs and benefits, to create a new dataset with 1000 observations. For each bootstrap resample, an estimate of differential total mean costs, expected mean effectiveness was calculated [25]. The 95% CIs for the differential estimates were derived from the calculated 2.5th and 97.5th percentiles. We plotted cost-effectiveness acceptability curves [26] to evaluate the probability of PM+ intervention being cost-effective at increasing monetary values representing willingness-to-pay thresholds for PM+ intervention from policy makers' perspective [27]. For the effectiveness data, we used linear mixed models to study treatment effects as indicated in our main trial report [12] which allowed the number of observations to vary at random between subjects and effectively handles missing data [28].. 14% cost data was missing for medicines, complementary medicines, seeking retreats and religious help and for outpatient services at the end point. Summary stats for each specific cost were presented without imputation but the total cost were calculated assuming missing data as 0 in a conservative way [25].

Results

As reported in the clinical effectiveness evaluation [12], mean combined depression and anxiety symptom scores on HADS were significantly lower at 3-months post-intervention (AMD, −5.75; 95%

[1] Global Economic Data, Indicators, Charts, & Forecasts: CEIC https://www.ceicdata.com/en

CI, −7.21 to −4.29). Similarly, functional impairment significantly improved (AMD, −4.17; 95% CI, −5.84 to −2.51) on WHODAS-12 in the intervention arm compared to EUC arm. At baseline depression rate was 94.2% and 89.4% in intervention and EUC arms respectively. at the end of 3-months follow up period, the intervention arm had significantly lower rates of depression (26.9%) compared to EUC arm (58.9%) (risk difference, −31.98; 95% CI: −41.03 to −22.94).

Costs

No significant difference in the cost of other health-care services accessed by study participants was observed between treatment and control groups, with the exception of religious help and retreats. The mental health condition of the majority of trial participants did not result in reduction in their or their family members or friends' usual work/activities (Table 1). Table 2 presents summary statistics and cost results from the mixed-model analysis.

With an international master trainer/supervisor total cost of delivering PM+ intervention per participant was PKR 16,967 (US $ 163.14). Total intervention arm costs (PM+ costs plus cost of services accessed by intervention arm) was PKR17,473 (SD, 912) or US$ 168. The cost of EUC (treatment as usual plus cost of services accessed by control arm participant) was PKR 848 (SD, 1734) or US $ 8.15 (See Table 2).

Substituting the cost of international master trainer/supervisor with national trainer would substantially decrease intervention costs. Total cost of delivering PM+ intervention, involving a national master trainer/supervisor, was estimated to be PKR 3,645 (US $ 35.04). This would be PKR 729 (US $ 7.00) per session. Total costs of delivering the intervention (with a national trainer/supervisor) plus EUC in the intervention arm would be PKR 4151 (SD, 912) or US$ 40.

Cost-effectiveness

Incremental cost-effectiveness ratios (ICERs) indicate that the intervention was both more effective and costlier than EUC for all the health outcomes studied (Table 3). Analysis was conducted to evaluate the cost-effectiveness of PM+ intervention under two scenarios; 1) PM+ delivery by lay health workers

supervised by international master trainer/supervisor (as observed in the trial) and 2) PM+ delivery by lay health workers supervised by local supervisor. The second scenario will be the case for scale-up of the intervention package in real world setting. The additional costs associated with the intervention led to a relative improvement in outcomes, e.g. the mean cost per unit score improvement in anxiety and depression on HADS was PKR 2957 (95% CI: 2262, 4029) or US$ 28 with an international trainer/supervisor. This would be PKR 588 (95% CI: 434, 820) or US$ 6 with a national trainer/supervisor; with an international supervisor, each 1-point improvement on WHODAS costed PKR 4097 (95% CI: 2978, 6046) or US$ 40 and with a national supervisor it was estimated to be PKR 815 (95% CI: 576, 1225) or US$ 8. We plotted 1,000 resampled estimates of costs and outcomes on a cost-effectiveness plane for the primary and secondary outcomes. The results show that all the resampled estimates fall in the upper-right quadrant, i.e. PM+ intervention is 'more effective but costlier' in all of the resampled estimates.

The mean ICER to successfully treat a case of depression (PHQ-9 cut-off 10 or above) using an international supervisor was PKR 53,770 (95% CI: 39,394, 77,399) [US$ 517] versus a local supervisor PKR 10,705 (95% CI: 7731, 15,627) [US$ 102.93]. ICERs for other outcome measures are compared in Table 3.

The cost-effectiveness acceptability curves of PM+ intervention on the outcomes of HADS (anxiety & depression) and WHODAS-12 with an international specialist supervisor are provided in Figures 1a and 2a. The intervention has more than 90% probability of being cost-effective as compared to EUC above a willingness-to-pay threshold of PKR 7000 (US$ 67) for a one-point improvement in depression and anxiety (HADS Total) (Figure 1a) and PKR 6000 (US$ 57) for a one-point improvement in functioning (WHODAS) using international supervisors (Figure 2a). These thresholds would be reduced by 80% using local supervisors (Figure 1b & 2b).

Discussion

Our results show that PM+ intervention is more effective and more costly than EUC in reducing symptoms of anxiety and depression. Although there is inevitable uncertainty around point estimates, our analysis has shown that even at very modest levels of willingness to pay for a one-point improvement in symptoms or functioning outcomes there is at least a 90% probability of this

intervention being a cost-effective use of resources compared to enhanced usual care. We concluded that the value is 'modest' because that amount is equivalent to, for example, less than 10% of the minimum monthly wage in Pakistan in 2017 [29]. These findings are consistent with evidence from LMICs on the cost-effectiveness of task-shifting approach to deliver psychological interventions compared with EUC delivered by primary health care physicians, for the treatment of common mental disorders [30, 31]. With the current model of training and supervision from international master trainer/supervisor, the intervention was 5 times more costly for treating one person with depression, compared to modelled costs of training and supervision from local trainers. This emphasizes the need for building the capacity for local mental health workforce [32].

The resources, capacity and infrastructure for mental health services research including health economic evaluation alongside randomized controlled trials is limited in humanitarian settings of LMICs [33]. This is one of the very few studies to evaluate the cost-effectiveness of a psychological intervention in a humanitarian setting. There are only a few published studies on the cost-effectiveness of task-shifting interventions in global mental health. Araya et al (2006) evaluated the incremental cost-effectiveness of a stepped-care multicomponent program for the treatment of depressed women in primary care in Chile. The stepped-care program was more effective and costlier than usual care (an extra US$ 0.75 per depression-free day) [34]. Buttorff et al (2012) conducted an economic evaluation of a task-shifting intervention for the treatment of depressive and anxiety disorders in primary-care settings in India. They concluded that the use of lay heath workers for treatment of CMDs in the public primary-care facilities was not only cost-effective but also cost-saving. The mean health system cost per case recovered at the end of follow-up was US$ 128 (95% CI: 105 to 157) in the intervention arm and US$ 149 (95% CI: 131 to 169) in the control arm [30]. Other similar studies of lay-health counsellor delivered psychological interventions from India [31] have replicated the findings of cost-effectiveness of task-shifting interventions for treating depression and alcohol problems in primary care settings. Sikandar et al., (2019) evaluated the cost-effectiveness of a peer-volunteer delivered CBT based intervention for post-natal depression versus EUC in community settings of rural Pakistan. The intervention was costlier as compared to EUC but was effective in improving the severity of post-natal depression (costs per unit improvement in PHQ-9 score of US $15·50 (9·59 to 21·61) for the whole study period. The intervention had a 98% probability of being cost-effective over a willingness-to-pay

threshold of US$ 60 per unit of improvement on PHQ-9 score compared to EUC [35]. Although it is difficult to compare the results of cost-effectiveness evaluations across studies due to differences in analytical approaches, treatment conditions and different outcome measures, the results of these studies demonstrate cost-effectiveness of brief psychological intervention using a task-shifting approach.

During humanitarian crises, health systems tend to be overwhelmed, human resources are overstretched and access to specialists for referral and support is limited. It is therefore, important to determine how interventions with proven efficacy can be scaled-up in a cost effective way [36]. Our study and evidence from the literature supports the effectiveness of implementation strategies such as task-shifting and trans-diagnostic approaches to bridge the treatment gap for mental health problems in low resource settings. With the increased availability of evidence-based psychological intervention packages, further health economic evaluations are needed to inform the resource needs to scale-up evidence-based care for mental health.

Limitations

A limitation of the cost-effectiveness approach used in our study is that the results are limited to direct health care costs and health-related outcomes of PM+ intervention, and does not extend to the wider economic or social value of investing in mental health, which may be quite significant in a humanitarian context. The future health economic evaluations in global mental health will benefit by integrating the opportunity and time cost of lay health workers and non-specialists. The added value that results from such task-sharing implementation strategies in terms of empowerment, opportunities and career growth for non-specialist health work force as well as increase in treatment coverage for priority mental health conditions will also need to be accounted for in future studies. We did not make any adjustment for purchasing power parity since the focus of this study was on the actual resource costs incurred in the study country. However, for the purpose of international comparison, the PPP adjusted total intervention costs of PM+ were I$ 546 per participant. Estimated costs of delivering PM+ using a national master trainer in Pakistan would be I$ 114 per participant. Another limitation of our study is that we estimated costs per point reduction in symptoms of anxiety and depression and cost per case recovered from depression which limits the ability to compare results with other interventional studies on the basis of cost-utility measures (QALYs). Future studies may use change in health outcomes that are easily interpretable and meaningful enough for policy makers to make decision and should also

collect data on population-based health state preference scores that would enable the calculation of Quality Adjusted Life Years (QALYs).

Conclusions

The literature on cost effectiveness of interventions for treating common mental disorders in LMICs, especially in humanitarian context is limited to only few studies. Present study provides the evidence on cost-effectiveness of a task-shifting intervention using a trans-diagnostic approach. We found that the intervention was effective but more costly for treating one person with depression when training and supervision to lay health workers was provided by an international master trainer. We conclude that PM+ may be a cost-effective intervention by using the training and supervision provided by the local health workers in primary health care settings. With the increased availability of evidence-based psychological intervention packages, further health economic evaluations are needed to inform the resource needed to scale-up evidence-based care for mental health.

Table 1: *Health services utilization (including religious help and retreats, inpatient services and reduced usual work/activities due to health condition) across two arms at baseline and during past 3-months

			Baseline			Endpoint		
		Group	**N (%)**	**Mean number of visits (SD)**	**Mean Duration in Mins (SD)**	**N (%)**	**Mean number of visits (SD)**	**Mean Duration in Mins (SD**
Outpatient services	Traditional healer	PM+	40 (12.0)	4.03 (3.83)	26 (28.04)	9 (3.0)	3.38 (3.15)	6.54 (16.75)
		TAU	50 (15.1)	3.47 (2.50)	25.13 (25.17)	19 (6.3)	2.26 (0.80)	5.00 (9.71)
	Mental health professional	PM+	91 (29.4)	4.36 (4.73)	15.82 (13.08)	80 (26.9)	3.61 (1.87)	16.73 (9.39)
		TAU	76 (24.5)	3.09 (2.38)	17.21(15.28)	98 (33.0)	3.08 (1.49)	17.48 (9.98)
	Medical doctor	PM+	57 (18.4)	2.98 (2.20)	17.93(24.58)	39 (13.1)	2.17 (1.72)	11.79 (7.23)
		TAU	54 (17.5)	3.56 (4.23)	23.29(29.42)	37 (12.5)	1.94 (1.01)	16.67 (12.50)
	Community health worker	PM+	56 (16.9)	4.90 (5.72)	---	25 (8.2)	4.0 (2.58)	---
		TAU	54 (16.3)	3.87 (4.33)	---	25 (8.2)	2.54 (1.53)	---
	Any Others services	PM+	11 (3.4)	2.56 (2.87)	---	6 (2.0)	1.20 (0.44)	---
		TAU	8 (2.5)	1.38 (0.91)	---	3 (1.0)	2.0 (1.73)	---
Religious help and retreats		PM+	37 (11)	6.86 (11.90)	---	7 (2.4)	3.71 (5.02)	---
		TAU	45 (13.4)	3.33 (4.84)	---	14 (4.8)	3.15 (2.99)	---
Inpatient services		PM+	8 (2.3)	3.29 (2.43) *	---	7 (2.3)	7.20 (12.75) *	---
		TAU	13 (3.8)	3.91 (4.10) *	---	8 (2.6)	2.5 (0.53) *	---
Reduced usual work/activities due to health condition (oneself/family		PM+	6 (1.8)	21.33 (15.01) **	---	0 (0.0)	---	---

member)	TAU	1 (0.3)	--	---	1 (0.3)	---	---

* **Night stays in hospital-** In case of inpatient services only

** Mean number of days of reduced usual work/activities due to health condition (oneself/family member)

Table 2: Cost of health services (outpatient, inpatient care, drugs and complimentary medicines and religious retreats) by trial arm in PKR (1 USD = 104 PKR; 2016)

		Descriptive statistics n; mean* (SD)*					
Cost of Services	Time point	Intervention (N=172)		EUC (N=174)		Difference in LS mean (95%CI)	p-value
		N	Mean (SD)	N	Mean (SD)		
Out-patient care	Pre-Treatment	106	2641 (14946)	95	727 (1161)		
	Follow-Up	73	485 (651)	72	667 (1033)	-182 (-465,101)	0.206
	Change since baseline	49	743(2751)	41	305(984)	437(-462,1281)	0.336
In-patient care	Pre-Treatment	170	135 (929)	172	273 (1545)		
	Follow-Up	142	49 (344)	155	171 (1056)	-122 (-304,61)	0.191
	Change since baseline	140	114(866)	153	108(1953)	6(-337,349)	0.971
Drugs/medications	Pre-Treatment	158	736 (1364)	159	725 (1232)		
	Follow-Up	132	277 (650)	149	228 (461)	50 (-82,181)	0.458
	Change since baseline	124	378(1314)	136	496(1341)	-118(-442,207)	0.477
Complimentary medicines	Pre-Treatment	168	124 (624)	167	110 (945)		
	Follow-Up	139	10 (88.14)	156	3 (40)	7 (-9,22)	0.393
	Change since baseline	136	55(456)	150	115(998)	-60(-244,123)	0.518
Religious Retreats	Pre-Treatment	167	390 (2208)	165	674 (3773)		
	Follow-Up	136	4 (43)	154	131 (655)	-127 (-238,-17)	0.024
	Change since baseline	131	432(2451)	145	626(4080)	-193(-983,596)	0.638
Total cost of all services	Pre-Treatment	172	3145 (14302)	174	2445 (6053)		
	Follow-Up	145	601 (694)	159	848 (1734)	-247 (-568,73)	0.130
	Change since baseline	145	2746 (15491)	159	1714 (6632)	1032(-1709,3774)	0.444
Total cost of intervention with international specialist supervisor[2]		172	17473 (912)	159	848 (1734)	16625 (16329,16922)	<.0001
Total cost of intervention with local specialist supervisor[3]		172	4151 (912)	159	848 (1734)	3303 (3007,3600)	<.0001

Table 2 shows costs of other services accessed by the participants. The data was collected using CSRI at baseline and 3 months' post-intervention follow-up assessment.

[2] Intervention costs plus cost of services. The cost of intervention with international supervisor is PKR 16,967
[3] Intervention costs plus cost of services. The cost of intervention with local supervisor is PKR 3,645

Table 3: Incremental Cost Effectiveness Ratios (ICERs) for PM+ intervention in PKR (1 USD = 104 PKR; 2016)

	International specialist supervisor		Local specialist supervisor	
Endpoint	Mean ICER	95% CI	Mean ICER	95% CI
HADS Anxiety	6172.99	[4575.49,8787.73]	1228.91	[882.86,1796.12]
HADS Depression	5704.27	[4384.51, 7651.85]	1135.81	[849.23,1561.68]
HADS Total	2957.45	[2261.64, 4029.00]	588.82	[434.01,820.27]
WHO DAS	4096.51	[2978.13, 6045.66]	815.89	[575.80,1225.10]
Depression caseness	53769.91	[39393.57, 77398.62]	10705.35	[7730.95,15627]

Note: (1) The cost was estimated after adjusting several baseline variables (baseline total cost, age, gender, occupation, marital status). (2) We used non-parametric bootstrapping to estimate confidence intervals with1000 resamples.

Abbreviations.; HADS = Hospital Anxiety and Depression Scales (subscale score range: 0-21; higher scores indicate elevated anxiety or depression, respectively); WHODAS = WHO Disability Assessment Schedule (total score range: 0-48; higher scores indicate more severe impairment); Depression caseness defined as (PHQ-9 cut-off 10 or above), PHQ = Patient Health Questionnaire

Figure 1a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

Figure 1b: Cost-effectiveness acceptability curve for PM+ - with local trainer (in PKR) (1 USD = 104 PKR; 2016)

Figure 2a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

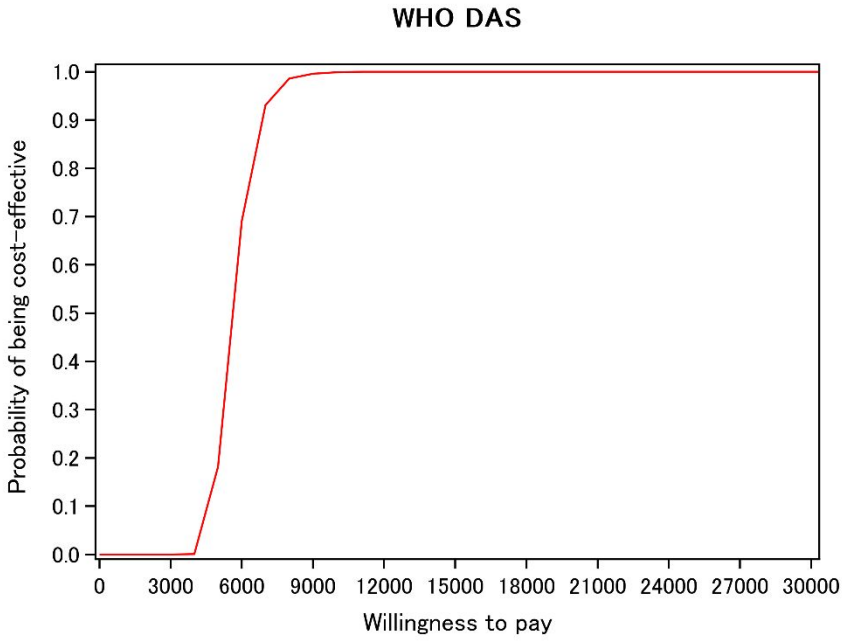
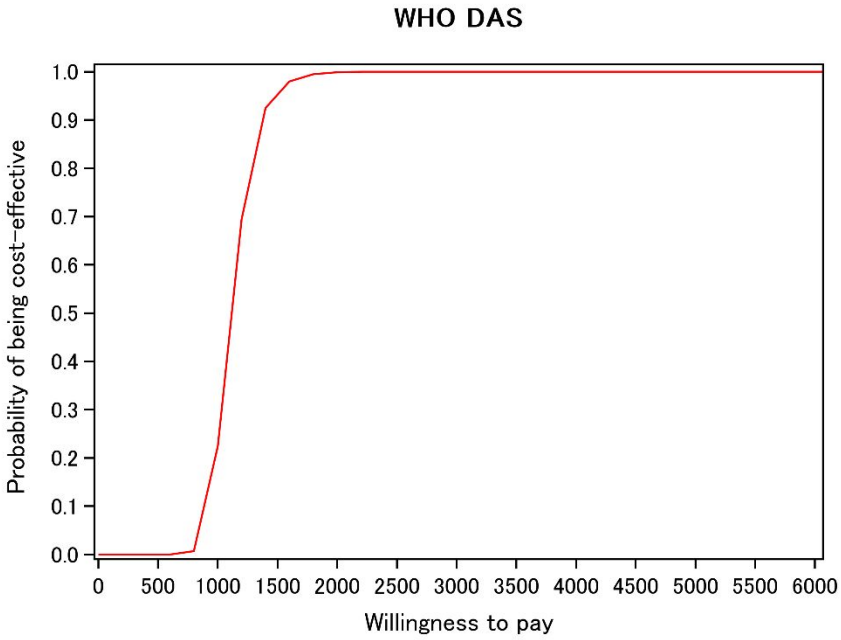


Figure 2b: Cost-effectiveness acceptability curve for PM+ with local supervisor (in PKR) (1 USD = 104 PKR; 2016)



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Cost-effectiveness of WHO Problem Management Plus for adults impaired by psychological distress in a post-conflict setting of Pakistan

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Word count (except abstract): 34973224

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Funding

This work was supported by Enhanced Learning and Research for Humanitarian Assistance's (Elhra's) Research for Health in Humanitarian Crises (R2HC) initiative funded by the UK Department for International Development and the Wellcome Trust.

Role of the Funder/Sponsor

The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Acknowledgements

We thank the project staff at the Department of Psychiatry, Lady Reading Hospital, Peshawar, and Human Development Research Foundation (HDRF), Islamabad, Pakistan, for their contributions, the primary health care staff and physicians for their support in the conduct of the study, and the participants and their families for their voluntary participation. We would like to specially thank Dr Victoria Baranov (Senior Lecturer in Economics, the University of Melbourne) for sharing her insights in revising the manuscript for re-submission.

Disclaimer

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Competing interests

All authors have declared no conflicts of interest.

ABSTRACT

Background

With the development of evidence-based interventions for treatment of priority mental health conditions in humanitarian settings, it is important to establish the cost-effectiveness of such interventions to enable their scale-up.

Aims

To evaluate the cost-effectiveness of Problem Management Plus (PM+) intervention, compared to Enhanced Usual Care (EUC) for common mental disorders in primary healthcare in Peshawar, Pakistan.

Methods

We randomly allocated 346 participants to either PM+ (n=172) or EUC (n=174). Effectiveness was measured using Hospital Anxiety and Depression Scale (HADS) at 3 months' post-intervention. Cost-effectiveness analysis was performed as incremental costs (measured in Pakistani Rupees [PKR] per unit change in anxiety, depression and functioning scores.

Results

The total cost of delivering PM+ per participant was estimated at PKR 16,967 (US $ 163.14) using an international master trainer and supervisor, and PKR 3,645 (US$35.04; US$ 7 per session) employing a national trainer. The mean cost per unit score improvement in anxiety and depression symptoms on HADS was PKR 2957 (95% CI: 2262, 4029) [US$ 28] with international trainer/supervision and PKR 588 (95% CI: 434, 820) or US$ 6 with local trainer/supervisor. The mean Incremental Cost-Effectiveness Ratio (ICER) to successfully treat a case of depression (PHQ-9 ≥ 10) using an international supervisor was PKR 53,770 (95% CI: 39,394, 77,399) [US$ 517] versus a local supervisor PKR 10,705 (95% CI: 7731, 15,627) [US$ 102.93].

Conclusions

The PM+ was more effective but also more costly than EUC in reducing symptoms of anxiety, depression and improving functioning in adults impaired by psychological distress in a post-conflict setting of Pakistan.

Key words: Cost-effectiveness, lay health workers, Low and Middle Income Countries (LMIC), humanitarian settings, Problem Management Plus, Common Mental Disorders (CMDs)

Trial Registration anzctr.org.au Identifier: ACTRN12614001235695

Mental health problems cause a significant burden of disease in Low and Middle Income Countries (LMICs), yet the documented 'mental health treatment gap' is up to 90% [1-3]. The need for mental health services is much greater in populations affected by humanitarian crises. More than 135 million people are in need of humanitarian assistance due to ongoing humanitarian crises and conflicts globally [4]. A systematic review and meta-analysis of mental health outcomes in population affected by conflict and displacements showed that mood and anxiety disorders were common, with rates of 17.3% for depression and 15.4% for posttraumatic stress disorder [5]. Epidemiological studies from areas affected by humanitarian crises in Pakistan found high rates of psychological distress in these populations. One study reported rates as high as 38% to 65% for psychological distress in women [6, 7]. Majority of people have no access to mental health services in such settings [6]. Over the past decade, significant progress has been made in terms of availability of evidence based mental health intervention packages for populations affected by humanitarian crises [8]. However, sustainability and scalability of such psychological interventions remains a challenge in populations affected by humanitarian crises in low resource settings globally [9].

We developed and tested a brief, multicomponent behavioural intervention, Problem Management Plus (PM+) delivered by lay health workers for Common Mental Disorders (CMDs) in conflict affected settings. The intervention was effective for treating the symptoms of CMDs in a post-conflict setting of Pakistan. Trial protocol and results of pilot and definitive clinical trials have been published [10-12]. In the present study, we conduct an economic evaluation alongside the randomized controlled trial to assess the cost-effectiveness of this intervention in order to inform policy and implementation in routine clinical practice.

Method

Study site and participants

Participants included 346 primary care attendees with high level of psychological distress (score above 2 on General Health Questionnaire [GHQ-12]) [13] and functional impairment (score above 16 on World Health Organization Disability Assessment Schedule 2.0 [WHODAS 2.0]) [14]. The participants were individually randomized in 1:1 ratio to either intervention arm i.e. PM+ (n=172) along with Enhanced Usual Care (EUC)) or the Control arm consisting of Enhanced Usual Care (EUC) only (n=174). The study was approved locally by the Institutional Review and Ethics Board of the

Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, and by the WHO Ethical Review Committee. Written informed consent was obtained from all study participants.

The Intervention

Participants in the intervention arm received a brief multicomponent intervention called Problem Management Plus (PM+) [15]. The intervention is trans-diagnostic as it applies the same underlying principles across mental disorders, without tailoring the protocol to specific diagnoses [16]. PM+ is based on well-established principles of problem solving and behavioural techniques. It is designed to be used for adults experiencing common mental health problems (e.g. anxiety, stress, depression and grief) only. It is not suitable for the treatment of severe mental health problems (including psychosis or risk for suicide). Both an individual and group version of the intervention exists. The current study involves the individual version.

PM+ consists of 5 weekly face-to-face sessions of 90 minutes each, delivered by trained lay health workers. The intervention is composed of four core strategies i.e. stress management, managing problems, get going, keep doing (behavioural activation), strengthening social support, introduced sequentially in the intervention sessions. In the last session, all the strategies are reviewed with a particular emphasis on using these strategies for self-management in the future and to prevent relapse.

Training and supervision followed a cascade model. An international master trainer trained local trainers in a 6-day training workshop. Training consisted of intervention delivery, training and supervision skills. Local trainers cascaded the training to lay health workers (with 12-16 year of education) in an 8-day training. Lay health workers were provided weekly supervision by local trainers/supervisors (hereafter local supervisor) who were in turn, supervised monthly by the international master trainer/supervisor (hereafter international supervisor) via video conference for 2 to 3 hours. The intervention is available in Urdu and English on the WHO website [17]. Further details of intervention are described elsewhere [15].

Enhanced care as usual

The participants in both intervention arm and control arm received Enhanced Usual Care (EUC). The treatment was enhanced as the Primary Health Care (PHC) physicians in the participating primary health care centres received a 5-day training in the management of Common Mental Disorders (CMDs)

in primary health care settings. The training was reinforced through a one-day refresher training for the primary health care physicians. The study participants in both arms were able to seek other health care services from their PHC physicians.

Data Collection

A. Health outcomes

The outcomes were measured at baseline and 3 months' post-intervention. The cost-effectiveness analysis was performed as incremental costs per unit change in anxiety, depression and functioning scores. The primary outcome was change in symptoms of anxiety and depression measured with the Hospital Anxiety and Depression Scale (HADS) [18, 19]. Severity of symptoms was measured using the -HADS-Anxiety (anxiety; 7 items; possible score range, 0-21) and Depression (depression; 7 items; possible score range, 0-21). Higher scores indicate more anxiety and/or depression. Secondary outcomes were functional impairment and presence of depressive disorders. WHODAS-12 was used to assess functional impairment. Polytomous scoring algorithm of WHODAS-12 was used to transform the functional impairment scores on a scale of 1-100[14]. Presence of depressive disorder was measured using a 9-item Patient Health Questionnaire (PHQ-9) [20]. Other secondary outcome measure included PCL-5 [21], results of which are attached as a web appendix.

B. Health resource use profiling

The data on health resource use was collected using the Client Services Receipt Inventory (CSRI) [22], which records the clients' contact with out-patient services (i.e. mental health specialist, general physician, traditional healer, community health workers etc.), inpatient (hospital admissions) services and out of pocket costs associated with travel, medications and tests/investigations during the preceding recall period. A section on seeking religious help and retreats was added to adapt the tool for use in local population. Study participants self-reported their health-care utilization, medication use and out-of-pocket expenditures on CSRI [22] at baseline and 3-months' post-intervention.

C. Cost measurement and analysis

Economic analysis was conducted primarily from a health system perspective, consisting of a) costs incurred over the trial period in the delivery of the intervention itself, b) use of other healthcare and

related services by study participants, including religious help and retreats, and c) patient and family costs (such as number of days with reduced working hours, informal caregiving time by relatives or friends as well as travel costs and time spent travelling to or waiting for consultations). No discounting of costs was applied since the study was performed within one year.

Intervention costs: These included costs for the intervention adaptation workshops, translations of intervention manual and training materials; printing of adapted training manuals, staff recruitment, training and supervision. Supervision costs included time spent by master trainer, supervisors, transport costs for fieldwork supervision, and costs of all other resources used.

To estimate the cost of intervention delivery, we evaluated unit cost per minute of health care providers' time including the international master trainer/supervisor, local supervisors, lay health workers and physicians. The unit cost per minute was multiplied with the total estimated time spent by each health care provider to the participants to calculate the total cost of intervention delivery. We calculated the cost of intervention delivery with the international master trainer/supervisor and modelled the cost for a local supervisor as a potentially more sustainable way to support task-shifting in low resource settings. Costs of the intervention were calculated by multiplying the total contact time (number of minutes) a participant had in the intervention arm with a lay health worker by the per-minute cost of the lay health workers' time and the costs spent on travelling by lay health workers (unit cost calculations are provided as web appendix).

Calculation of these intervention costs as well as contacts with a range of formal health care providers was facilitated by the use of a simplified costing template for unit cost calculations reported in health economic evaluation of mental health services [23]. Unit cost templates accounted for the costs of salaries of staff employed in the provision of intervention delivery (including master trainer, supervisors, lay health workers and PHC staff), facility operating costs where the service was provided, overhead costs relating to the provision of service (personnel, finance etc.) and the capital costs of the facility where the intervention was provided (land, buildings etc.). Sources of data for these variables included public health system financial records and project's financial records. All costs were calculated in Pakistani rupees (PKR) and are reported in Pakistani Rupees and United States Dollars for

the year 2016, when the study was implemented ([1]Exchange rate 1 USD= PKR 104). No adjustment was made for Purchasing Power Parity (PPP) since the focus of interest was on the actual resource costs incurred in the study country (rather than a comparison to other countries, whereby differences in the relative price of goods and services would need to be taken into account).

Statistical Analysis

The mean and standard deviation for the total cost was calculated using generalized linear regression model with Gamma distribution after adjustment for baseline total cost. The group difference and its 95% CI was also calculated [24]. The Incremental Cost-effectiveness Ratio (ICER) was calculated as the additional costs of the intervention divided by the change in HADS-A, HADS- D, HADS Total, PHQ, and WHODAS related to the intervention. The confidence intervals for ICER was estimated by non-parametric bootstrapping. The bootstrap technique sampled with replacement from the original observed paired of costs and effects, maintaining the correlation structure between costs and benefits, to create a new dataset with 1000 observations. For each bootstrap resample, an estimate of differential total mean costs, expected mean effectiveness was calculated [25]. The 95% CIs for the differential estimates were derived from the calculated 2.5th and 97.5th percentiles. We plotted cost-effectiveness acceptability curves [26] to evaluate the probability of PM+ intervention being cost-effective at increasing monetary values representing willingness-to-pay thresholds for PM+ intervention from policy makers' perspective [27]. For the effectiveness data, we used linear mixed models to study treatment effects as indicated in our main trial report [12] which allowed the number of observations to vary at random between subjects and effectively handles missing data [28]. ~~the post hoc sensitivity analysis using multiple imputation was performed to assess the robustness of treatment effect to the missing values~~. 14% cost data was missing for medicines, complementary medicines, seeking retreats and religious help and for outpatient services at the end point. Summary stats for each specific cost were presented without imputation but the total cost were calculated assuming missing data as 0 in a conservative way [25].

Results

[1] Global Economic Data, Indicators, Charts, & Forecasts: CEIC https://www.ceicdata.com/en

As reported in the clinical effectiveness evaluation [12], mean combined depression and anxiety symptom scores on HADS were significantly lower at 3-months post-intervention (AMD, −5.75; 95% CI, −7.21 to −4.29). Similarly, functional impairment significantly improved (AMD, −4.17; 95% CI, −5.84 to −2.51) on WHODAS-12 in the intervention arm compared to EUC arm. At baseline depression rate was 94.2% and 89.4% in intervention and EUC arms respectively. at the end of 3-months follow up period, the intervention arm had significantly lower rates of depression (26.9%) compared to EUC arm (58.9%) (risk difference, −31.98; 95% CI: −41.03 to −22.94).

Costs

No significant difference in the cost of other health-care services accessed by study participants was observed between treatment and control groups, with the exception of religious help and retreats. The mental health condition of the majority of trial participants did not result in reduction in their or their family members or friends' usual work/activities (Table 1). Table 2 presents summary statistics and cost results from the mixed-model analysis.

With an international master trainer/supervisor total cost of delivering PM+ intervention per participant was PKR 16,967 (US $ 163.14). Total intervention arm costs (PM+ costs plus cost of services accessed by intervention arm) was PKR17,473 (SD, 912) or US$ 168. The cost of EUC (treatment as usual plus cost of services accessed by control arm participant) was PKR 848 (SD, 1734) or US $ 8.15 (See Table 2).

Substituting the cost of international master trainer/supervisor with national trainer would substantially decrease intervention costs. Total cost of delivering PM+ intervention, involving a national master trainer/supervisor, was estimated to be PKR 3,645 (US $ 35.04). This would be PKR 729 (US $ 7.00) per session. Total costs of delivering the intervention (with a national trainer/supervisor) plus EUC in the intervention arm would be PKR 4151 (SD, 912) or US$ 40.

Cost-effectiveness

Incremental cost-effectiveness ratios (ICERs) indicate that the intervention was both more effective and costlier than EUC for all the health outcomes studied (Table 3). Analysis was conducted to evaluate the cost-effectiveness of PM+ intervention under two scenarios; 1) PM+ delivery by lay health workers supervised by international master trainer/supervisor (as observed in the trial) and 2) PM+ delivery by lay health workers supervised by local supervisor. The second scenario will be the case for scale-up of the intervention package in real world setting. The additional costs associated with the intervention led to a relative improvement in outcomes, e.g. the mean cost per unit score improvement in anxiety and depression on HADS was PKR 2957 (95% CI: 2262, 4029) or US$ 28 with an international trainer/supervisor. This would be PKR 588 (95% CI: 434, 820) or US$ 6 with a national trainer/supervisor; with an international supervisor, each 1-point improvement on WHODAS costed PKR 4097 (95% CI: 2978, 6046) or US$ 40 and with a national supervisor it was estimated to be PKR 815 (95% CI: 576, 1225) or US$ 8. We plotted 1,000 resampled estimates of costs and outcomes on a cost-effectiveness plane for the primary and secondary outcomes. The results show that all the resampled estimates fall in the upper-right quadrant, i.e. PM+ intervention is 'more effective but costlier' in all of the resampled estimates.

The mean ICER to successfully treat a case of depression (PHQ-9 cut-off 10 or above) using an international supervisor was PKR 53,770 (95% CI: 39,394, 77,399) [US$ 517] versus a local supervisor PKR 10,705 (95% CI: 7731, 15,627) [US$ 102.93]. ICERs for other outcome measures are compared in Table 3.

The cost-effectiveness acceptability curves of PM+ intervention on the outcomes of HADS (anxiety & depression) and WHODAS-12 with an international specialist supervisor are provided in Figures 1a and 2a. The intervention has more than 90% probability of being cost-effective as compared to EUC above a willingness-to-pay threshold of PKR 7000 (US$ 67) for a one-point improvement in depression and anxiety (HADS Total) (Figure 1a) and PKR 6000 (US$ 57) for a one-point improvement in functioning (WHODAS) using international supervisors (Figure 2a). These thresholds would be reduced by 80% using local supervisors (Figure 1b & 2b).

Discussion

Our results show that PM+ intervention is more effective and more costly than EUC in reducing symptoms of anxiety and depression. Although there is inevitable uncertainty around point estimates, our analysis has shown that even at very modest levels of willingness to pay for a one-point improvement in symptoms or functioning outcomes there is at least a 90% probability of this intervention being a cost-effective use of resources compared to enhanced usual care. We concluded that the value is 'modest' because that amount is equivalent to, for example, less than 10% of the minimum monthly wage in Pakistan in 2017 [29]. These findings are consistent with evidence from LMICs on the cost-effectiveness of task-shifting approach to deliver psychological interventions compared with EUC delivered by primary health care physicians, for the treatment of common mental disorders [30, 31]. With the current model of training and supervision from international master trainer/supervisor, the intervention was 5 times more costly for treating one person with depression, compared to modelled costs of training and supervision from local trainers. This emphasizes the need for building the capacity for local mental health workforce [32].

The resources, capacity and infrastructure for mental health services research including health economic evaluation alongside randomized controlled trials is limited in humanitarian settings of LMICs [33]. This is one of the very few studies to evaluate the cost-effectiveness of a psychological intervention in a humanitarian setting. There are only a few published studies on the cost-effectiveness of task-shifting interventions in global mental health. Araya et al (2006) evaluated the incremental cost-effectiveness of a stepped-care multicomponent program for the treatment of depressed women in primary care in Chile. The stepped-care program was more effective and costlier than usual care (an extra US$ 0.75 per depression-free day) [34]. Buttorff et al (2012) conducted an economic evaluation of a task-shifting intervention for the treatment of depressive and anxiety disorders in primary-care settings in India. They concluded that the use of lay heath workers for treatment of CMDs in the public primary-care facilities was not only cost-effective but also cost-saving. The mean health system cost per case recovered at the end of follow-up was US$ 128 (95% CI: 105 to 157) in the intervention arm and US$ 149 (95% CI: 131 to 169) in the control arm [30]. Other similar studies of lay-health counsellor delivered psychological interventions from India [31] have replicated the findings of cost-effectiveness of task-shifting interventions for treating depression and alcohol problems in primary care settings. Sikandar et al., (2019) evaluated the cost-effectiveness of a peer-volunteer delivered CBT based

intervention for post-natal depression versus EUC in community settings of rural Pakistan. The intervention was costlier as compared to EUC but was effective in improving the severity of post-natal depression (costs per unit improvement in PHQ-9 score of US $15·50 (9·59 to 21·61) for the whole study period. The intervention had a 98% probability of being cost-effective over a willingness-to-pay threshold of US$ 60 per unit of improvement on PHQ-9 score compared to EUC [35]. Although it is difficult to compare the results of cost-effectiveness evaluations across studies due to differences in analytical approaches, treatment conditions and different outcome measures, the results of these studies demonstrate cost-effectiveness of brief psychological intervention using a task-shifting approach.

During humanitarian crises, health systems tend to be overwhelmed, human resources are overstretched and access to specialists for referral and support is limited. It is therefore, important to determine how interventions with proven efficacy can be scaled-up in a cost effective way [36]. Our study and evidence from the literature supports the effectiveness of implementation strategies such as task-shifting and trans-diagnostic approaches to bridge the treatment gap for mental health problems in low resource settings. With the increased availability of evidence-based psychological intervention packages, further health economic evaluations are needed to inform the resource needs to scale-up evidence-based care for mental health.

Limitations

A limitation of the cost-effectiveness approach used in our study is that the results are limited to direct health care costs and health-related outcomes of PM+ intervention, and does not extend to the wider economic or social value of investing in mental health, which may be quite significant in a humanitarian context. The future health economic evaluations in global mental health will benefit by integrating the opportunity and time cost of lay health workers and non-specialists. The added value that results from such task-sharing implementation strategies in terms of empowerment, opportunities and career growth for non-specialist health work force as well as increase in treatment coverage for priority mental health conditions will also need to be accounted for in future studies. We did not make any adjustment for purchasing power parity since the focus of this study was on the actual resource costs incurred in the study country. However, for the purpose of international comparison, the PPP adjusted total intervention costs of PM+ were I$ 546 per participant. Estimated costs of delivering PM+ using a national master trainer in Pakistan would be I$ 114 per participant. Another limitation of our study is

that we estimated costs per point reduction in symptoms of anxiety and depression and cost per case recovered from depression which limits the ability to compare results with other interventional studies on the basis of cost-utility measures (QALYs). Future studies may use change in health outcomes that are easily interpretable and meaningful enough for policy makers to make decision and should also collect data on population-based health state preference scores that would enable the calculation of Quality Adjusted Life Years (QALYs).

Conclusions

The literature on cost effectiveness of interventions for treating common mental disorders in LMICs, especially in humanitarian context is limited to only few studies. Present study provides the evidence on cost-effectiveness of a task-shifting intervention using a trans-diagnostic approach. We found that the intervention was effective but more costly for treating one person with depression when training and supervision to lay health workers was provided by an international master trainer. We conclude that PM+ may be a cost-effective intervention by using the training and supervision provided by the local health workers in primary health care settings. With the increased availability of evidence-based psychological intervention packages, further health economic evaluations are needed to inform the resource needed to scale-up evidence-based care for mental health.

Table 1: *Health services utilization (including religious help and retreats, inpatient services and reduced usual work/activities due to health condition) across two arms at baseline and during past 3-months

			Baseline			Endpoint		
		Group	**N (%)**	**Mean number of visits (SD)**	**Mean Duration in Mins (SD)**	**N (%)**	**Mean number of visits (SD)**	**Mean Duration in Mins (SD**
Outpatient services	Traditional healer	PM+	40 (12.0)	4.03 (3.83)	26 (28.04)	9 (3.0)	3.38 (3.15)	6.54 (16.75)
		TAU	50 (15.1)	3.47 (2.50)	25.13 (25.17)	19 (6.3)	2.26 (0.80)	5.00 (9.71)
	Mental health professional	PM+	91 (29.4)	4.36 (4.73)	15.82 (13.08)	80 (26.9)	3.61 (1.87)	16.73 (9.39)
		TAU	76 (24.5)	3.09 (2.38)	17.21(15.28)	98 (33.0)	3.08 (1.49)	17.48 (9.98)
	Medical doctor	PM+	57 (18.4)	2.98 (2.20)	17.93(24.58)	39 (13.1)	2.17 (1.72)	11.79 (7.23)
		TAU	54 (17.5)	3.56 (4.23)	23.29(29.42)	37 (12.5)	1.94 (1.01)	16.67 (12.50)
	Community health worker	PM+	56 (16.9)	4.90 (5.72)	---	25 (8.2)	4.0 (2.58)	---
		TAU	54 (16.3)	3.87 (4.33)	---	25 (8.2)	2.54 (1.53)	---
	Any Others services	PM+	11 (3.4)	2.56 (2.87)	---	6 (2.0)	1.20 (0.44)	---
		TAU	8 (2.5)	1.38 (0.91)	---	3 (1.0)	2.0 (1.73)	---
Religious help and retreats		PM+	37 (11)	6.86 (11.90)	---	7 (2.4)	3.71 (5.02)	---
		TAU	45 (13.4)	3.33 (4.84)	---	14 (4.8)	3.15 (2.99)	---
Inpatient services		PM+	8 (2.3)	3.29 (2.43) *	---	7 (2.3)	7.20 (12.75) *	---
		TAU	13 (3.8)	3.91 (4.10) *	---	8 (2.6)	2.5 (0.53) *	---
Reduced usual work/activities due to health condition (oneself/family		PM+	6 (1.8)	21.33 (15.01) **	---	0 (0.0)	---	---

member)	TAU	1 (0.3)	--	---	1 (0.3)	---	---

* **Night stays in hospital-** In case of inpatient services only

** Mean number of days of reduced usual work/activities due to health condition (oneself/family member)

Table 2: Cost of health services (outpatient, inpatient care, drugs and complimentary medicines and religious retreats) by trial arm in PKR (1 USD = 104 PKR; 2016)

		Descriptive statistics n; mean* (SD)*					
Cost of Services	Time point	Intervention (N=172)		EUC (N=174)		Difference in LS mean (95%CI)	p-value
		N	Mean (SD)	N	Mean (SD)		
Out-patient care	Pre-Treatment	106	2641 (14946)	95	727 (1161)		
	Follow-Up	73	485 (651)	72	667 (1033)	-182 (-465,101)	0.206
	Change since baseline	49	743(2751)	41	305(984)	437(-462,1281)	0.336
In-patient care	Pre-Treatment	170	135 (929)	172	273 (1545)		
	Follow-Up	142	49 (344)	155	171 (1056)	-122 (-304,61)	0.191
	Change since baseline	140	114(866)	153	108(1953)	6(-337,349)	0.971
Drugs/medications	Pre-Treatment	158	736 (1364)	159	725 (1232)		
	Follow-Up	132	277 (650)	149	228 (461)	50 (-82,181)	0.458
	Change since baseline	124	378(1314)	136	496(1341)	-118(-442,207)	0.477
Complimentary medicines	Pre-Treatment	168	124 (624)	167	110 (945)		
	Follow-Up	139	10 (88.14)	156	3 (40)	7 (-9,22)	0.393
	Change since baseline	136	55(456)	150	115(998)	-60(-244,123)	0.518
Religious Retreats	Pre-Treatment	167	390 (2208)	165	674 (3773)		
	Follow-Up	136	4 (43)	154	131 (655)	-127 (-238,-17)	0.024
	Change since baseline	131	432(2451)	145	626(4080)	-193(-983,596)	0.638
Total cost of all services	Pre-Treatment	172	3145 (14302)	174	2445 (6053)		
	Follow-Up	145	601 (694)	159	848 (1734)	-247 (-568,73)	0.130
	Change since baseline	145	2746 (15491)	159	1714 (6632)	1032(-1709,3774)	0.444
Total cost of intervention with international specialist supervisor[2]		172	17473 (912)	159	848 (1734)	16625 (16329,16922)	<.0001
Total cost of intervention with local specialist supervisor[3]		172	4151 (912)	159	848 (1734)	3303 (3007,3600)	<.0001

Table 2 shows costs of other services accessed by the participants. The data was collected using CSRI at baseline and 3 months' post-intervention follow-up assessment.

[2] Intervention costs plus cost of services. The cost of intervention with international supervisor is PKR 16,967
[3] Intervention costs plus cost of services. The cost of intervention with local supervisor is PKR 3,645

Table 3: Incremental Cost Effectiveness Ratios (ICERs) for PM+ intervention in PKR (1 USD = 104 PKR; 2016)

	International specialist supervisor		Local specialist supervisor	
Endpoint	Mean ICER	95% CI	Mean ICER	95% CI
HADS Anxiety	6172.99	[4575.49,8787.73]	1228.91	[882.86,1796.12]
HADS Depression	5704.27	[4384.51, 7651.85]	1135.81	[849.23,1561.68]
HADS Total	2957.45	[2261.64, 4029.00]	588.82	[434.01,820.27]
WHO DAS	4096.51	[2978.13, 6045.66]	815.89	[575.80,1225.10]
Depression caseness	53769.91	[39393.57, 77398.62]	10705.35	[7730.95,15627]

Note: (1) The cost was estimated after adjusting several baseline variables (baseline total cost, age, gender, occupation, marital status). (2) We used non-parametric bootstrapping to estimate confidence intervals with1000 resamples.

Abbreviations.; HADS = Hospital Anxiety and Depression Scales (subscale score range: 0-21; higher scores indicate elevated anxiety or depression, respectively); WHODAS = WHO Disability Assessment Schedule (total score range: 0-48; higher scores indicate more severe impairment); Depression caseness defined as (PHQ-9 cut-off 10 or above), PHQ = Patient Health Questionnaire

Figure 1a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

Figure 1b: Cost-effectiveness acceptability curve for PM+ - with local trainer (in PKR) (1 USD = 104 PKR; 2016)

Figure 2a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

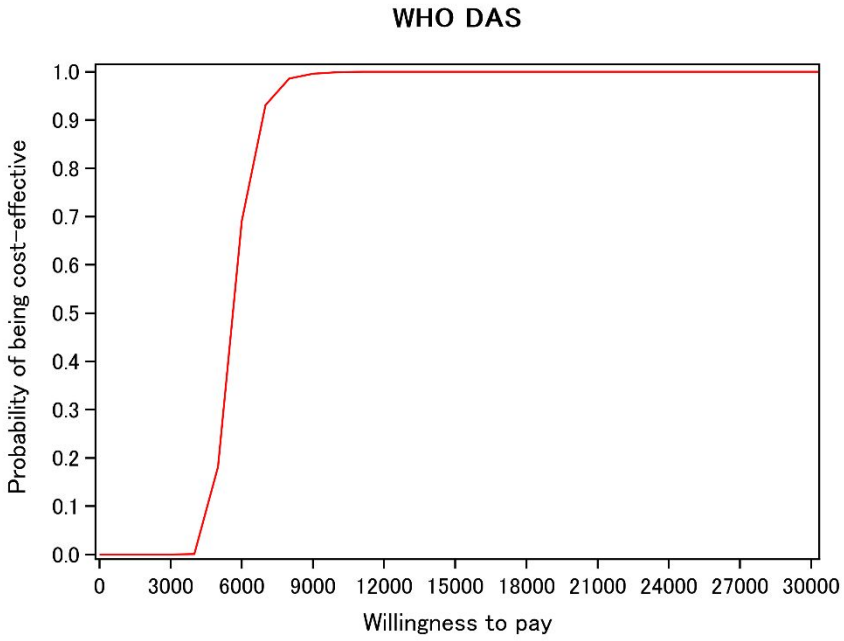
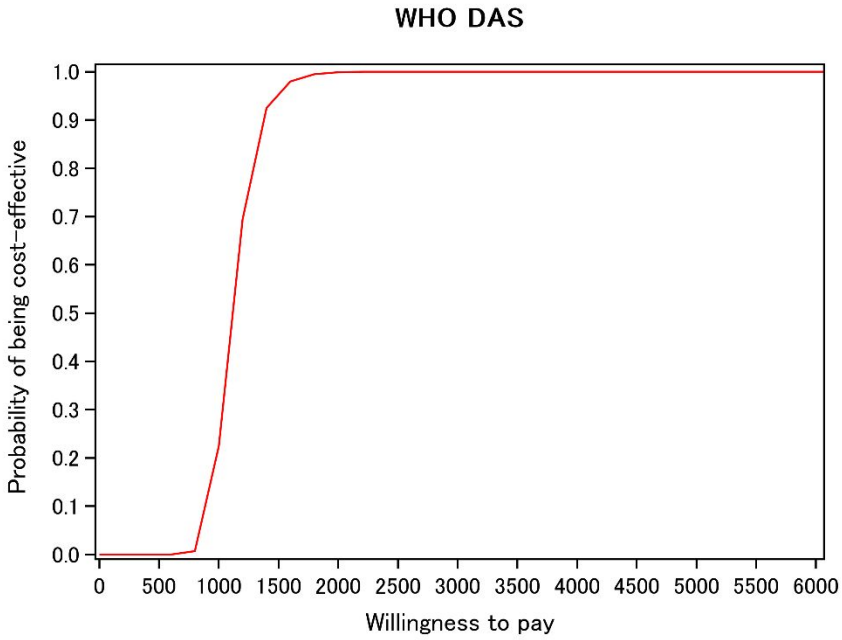


Figure 2b: Cost-effectiveness acceptability curve for PM+ with local supervisor (in PKR) (1 USD = 104 PKR; 2016)



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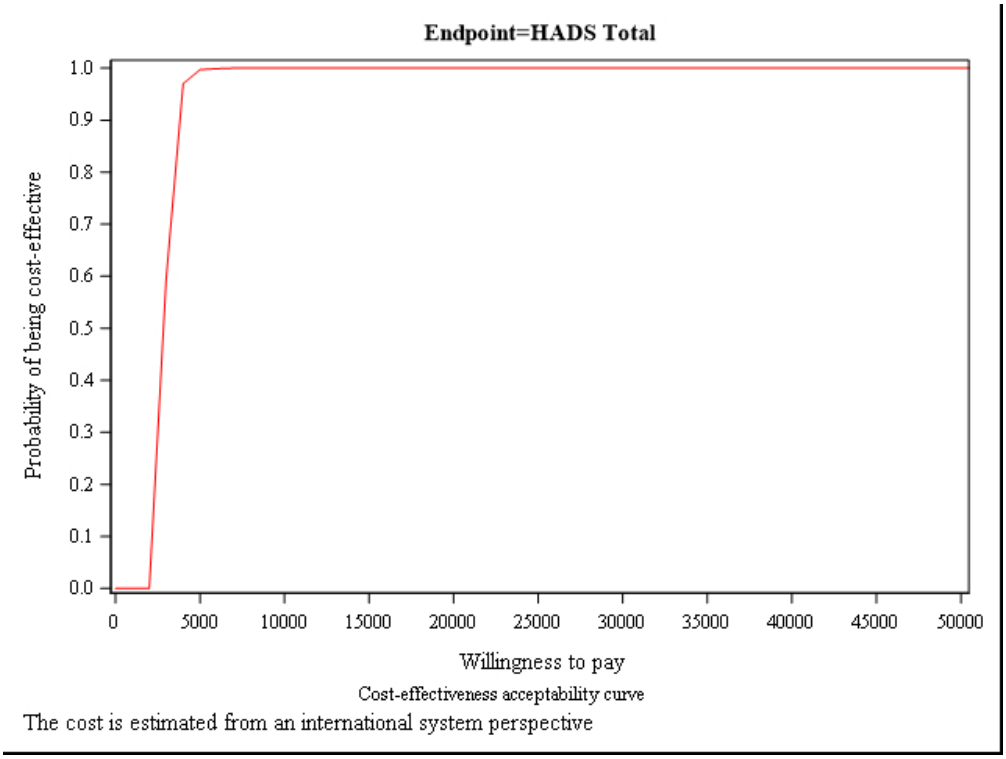

Figure 1a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

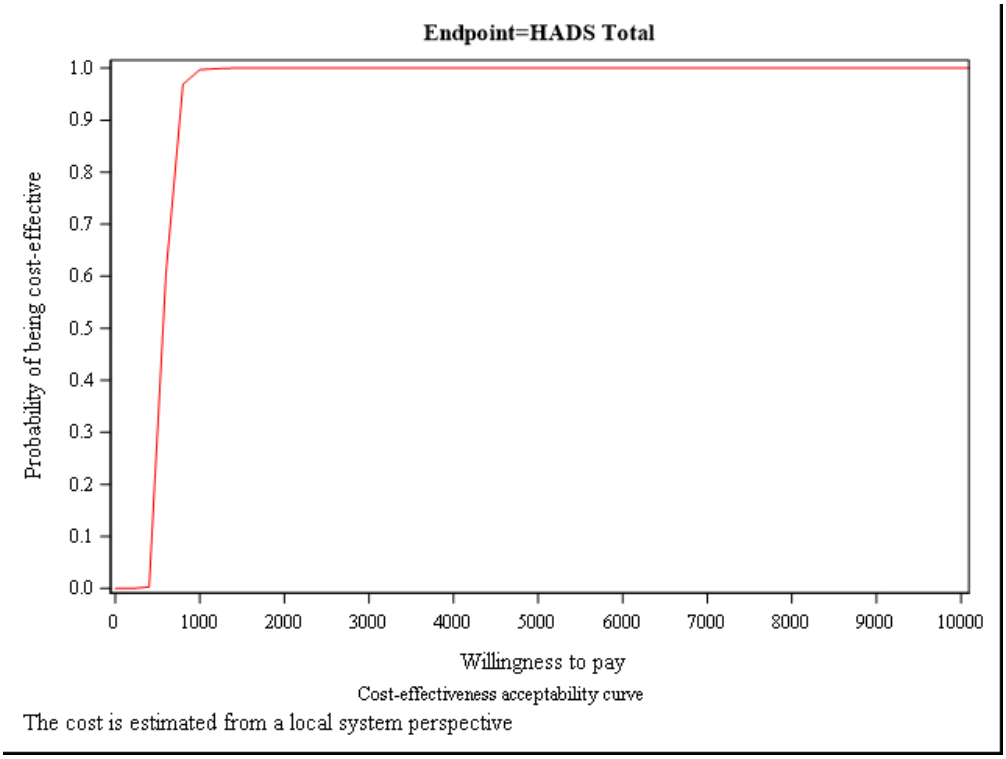

Figure 1b: Cost-effectiveness acceptability curve for PM+ - with local trainer (in PKR) (1 USD = 104 PKR; 2016)

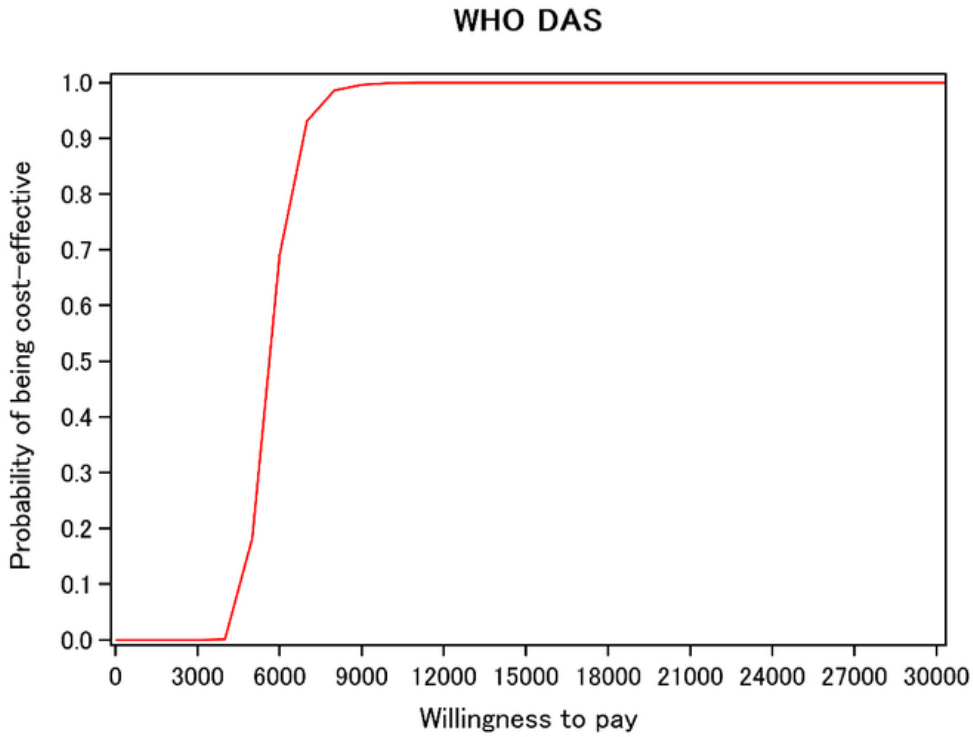

Figure 2a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

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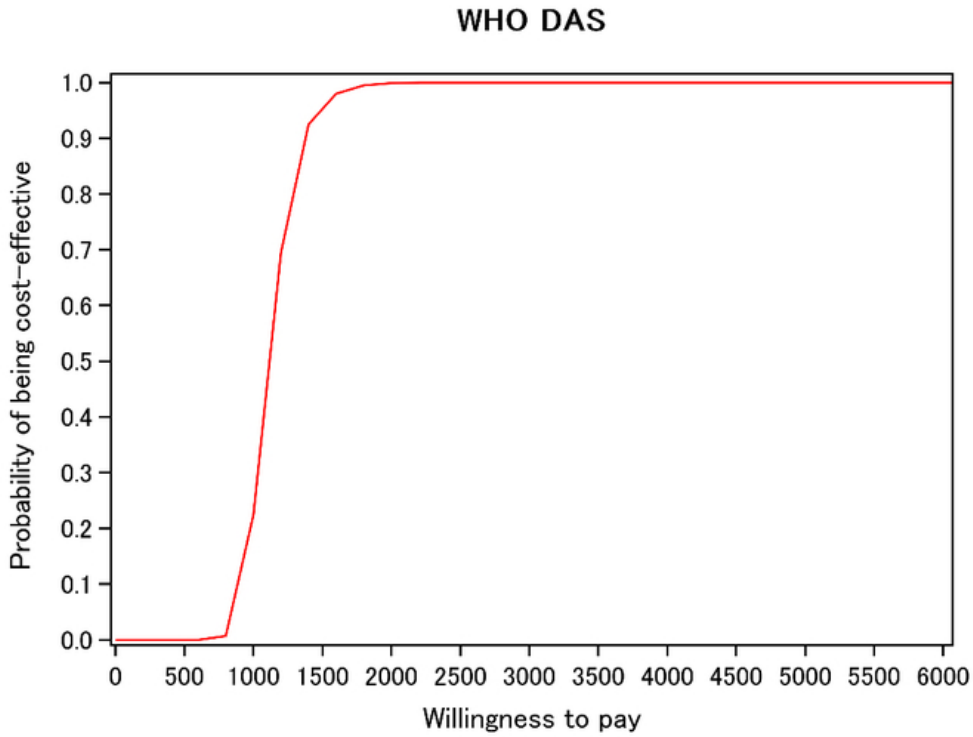

Figure 2b: Cost-effectiveness acceptability curve for PM+ with local supervisor (in PKR) (1 USD = 104 PKR; 2016)

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