

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

Journal:	<i>BJPsych</i>
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:	<p>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.</p> <p>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.</p> <p>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.</p> <p>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%</p>

	<p>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 \geq 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].</p> <p>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.</p>

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

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21

22 **Word count (except abstract): 3497**

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30 responsibility for the integrity of the data and the accuracy of the data analysis.

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40 Ommeren.

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42 **Funding**

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

46 **Role of the Funder/Sponsor**

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

50 **Acknowledgements**

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

57 **Disclaimer**

58 MvO and DC are staff members of the World Health Organization. The authors alone are responsible
59 for the views expressed in this publication and they do not necessarily represent the decisions, policy
60 or views of the World Health Organization.

61 **Competing interests**

62 All authors have declared no conflicts of interest.

63

64

For Peer Review

65 ABSTRACT**66 Background**

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

70

71 Aims

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

75

76 Methods

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

81

82 Results

83 The total cost of delivering PM+ per participant was estimated at PKR 16,967 (US \$ 163.14) using an
84 international master trainer and supervisor, and PKR 3,645 (US\$35.04; US\$ 7 per session) employing
85 a national trainer. The mean cost per unit score improvement in anxiety and depression symptoms on
86 HADS was PKR 2957 (95% CI: 2262, 4029) [US\$ 28] with international trainer/supervision and PKR
87 588 (95% CI: 434, 820) or US\$ 6 with local trainer/supervisor. The mean Incremental Cost-
88 Effectiveness Ratio (ICER) to successfully treat a case of depression (PHQ-9 \geq 10) using an
89 international supervisor was PKR 53,770 (95% CI: 39,394, 77,399) [US\$ 517] versus a local supervisor
90 PKR 10,705 (95% CI: 7731, 15,627) [US\$ 102.93].

91 Conclusions

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

95

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

98 **Trial Registration** anzctr.org.au Identifier: ACTRN12614001235695

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103 Mental health problems cause a significant burden of disease in Low and Middle Income Countries
104 (LMICs), yet the documented ‘mental health treatment gap’ is up to 90% [1-3]. The need for mental
105 health services is much greater in populations affected by humanitarian crises. More than 135 million
106 people are in need of humanitarian assistance due to ongoing humanitarian crises and conflicts globally
107 [4]. A systematic review and meta-analysis of mental health outcomes in population affected by conflict
108 and displacements showed that mood and anxiety disorders were common, with rates of 17.3% for
109 depression and 15.4% for posttraumatic stress disorder [5]. Epidemiological studies from areas affected
110 by humanitarian crises in Pakistan found high rates of psychological distress in these populations. One
111 study reported rates as high as 38% to 65% for psychological distress in women [6, 7]. Majority of
112 people have no access to mental health services in such settings [6]. Over the past decade, significant
113 progress has been made in terms of availability of evidence based mental health intervention packages
114 for populations affected by humanitarian crises [8]. However, sustainability and scalability of such
115 psychological interventions remains a challenge in populations affected by humanitarian crises in low
116 resource settings globally [9].

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

124 **Method**

125 **Study site and participants**

126 Participants included 346 primary care attendees with high level of psychological distress (score above
127 2 on General Health Questionnaire [GHQ-12]) [13] and functional impairment (score above 16 on
128 World Health Organization Disability Assessment Schedule 2.0 [WHODAS 2.0]) [14]. The participants
129 were individually randomized in 1:1 ratio to either intervention arm i.e. PM+ (n=172) along with
130 Enhanced Usual Care (EUC)) or the Control arm consisting of Enhanced Usual Care (EUC) only
131 (n=174). The study was approved locally by the Institutional Review and Ethics Board of the

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

134 **The Intervention**

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

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

148

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

157 **Enhanced care as usual**

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

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

164 **Data Collection**

165 **A. Health outcomes**

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

177

178 **B. Health resource use profiling**

179 The data on health resource use was collected using the Client Services Receipt Inventory (CSRI)
180 [22], which records the clients' contact with out-patient services (i.e. mental health specialist, general
181 physician, traditional healer, community health workers etc.), inpatient (hospital admissions) services
182 and out of pocket costs associated with travel, medications and tests/investigations during the preceding
183 recall period. A section on seeking religious help and retreats was added to adapt the tool for use in
184 local population. Study participants self-reported their health-care utilization, medication use and out-
185 of-pocket expenditures on CSRI [22] at baseline and 3-months' post-intervention.

186

187 **C. Cost measurement and analysis**

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

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

194

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

199

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

210

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

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

224

225 **Statistical Analysis**

226 The mean and standard deviation for the total cost was calculated using generalized linear regression
227 model with Gamma distribution after adjustment for baseline total cost. The group difference and its
228 95% CI was also calculated [24]. The Incremental Cost-effectiveness Ratio (ICER) was calculated as
229 the additional costs of the intervention divided by the change in HADS-A, HADS- D, HADS Total,
230 PHQ, and WHODAS related to the intervention. The confidence intervals for ICER was estimated by
231 non-parametric bootstrapping. The bootstrap technique sampled with replacement from the original
232 observed paired of costs and effects, maintaining the correlation structure between costs and benefits,
233 to create a new dataset with 1000 observations. For each bootstrap resample, an estimate of differential
234 total mean costs, expected mean effectiveness was calculated [25]. The 95% CIs for the differential
235 estimates were derived from the calculated 2.5th and 97.5th percentiles. We plotted cost-effectiveness
236 acceptability curves [26] to evaluate the probability of PM+ intervention being cost-effective at
237 increasing monetary values representing willingness-to-pay thresholds for PM+ intervention from
238 policy makers' perspective [27]. For the effectiveness data, we used linear mixed models to study
239 treatment effects as indicated in our main trial report [12] which allowed the number of observations
240 to vary at random between subjects and effectively handles missing data [28]. 14% cost data was
241 missing for medicines, complementary medicines, seeking retreats and religious help and for outpatient
242 services at the end point. Summary stats for each specific cost were presented without imputation but
243 the total cost were calculated assuming missing data as 0 in a conservative way [25].

244

245 **Results**

246 As reported in the clinical effectiveness evaluation [12], mean combined depression and anxiety
247 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>

248 CI, -7.21 to -4.29). Similarly, functional impairment significantly improved (AMD, -4.17 ; 95% CI,
249 -5.84 to -2.51) on WHODAS-12 in the intervention arm compared to EUC arm. At baseline depression
250 rate was 94.2% and 89.4% in intervention and EUC arms respectively. at the end of 3-months follow
251 up period, the intervention arm had significantly lower rates of depression (26.9%) compared to EUC
252 arm (58.9%) (risk difference, -31.98 ; 95% CI: -41.03 to -22.94).

253

254

255 **Costs**

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

261

262 With an international master trainer/supervisor total cost of delivering PM+ intervention per participant
263 was PKR 16,967 (US \$ 163.14). Total intervention arm costs (PM+ costs plus cost of services accessed
264 by intervention arm) was PKR17,473 (SD, 912) or US\$ 168. The cost of EUC (treatment as usual plus
265 cost of services accessed by control arm participant) was PKR 848 (SD, 1734) or US \$ 8.15 (See Table
266 2).

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

272

273 **Cost-effectiveness**

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

277 supervised by international master trainer/supervisor (as observed in the trial) and 2) PM+ delivery by
278 lay health workers supervised by local supervisor. The second scenario will be the case for scale-up of
279 the intervention package in real world setting. The additional costs associated with the intervention led
280 to a relative improvement in outcomes, e.g. the mean cost per unit score improvement in anxiety and
281 depression on HADS was PKR 2957 (95% CI: 2262, 4029) or US\$ 28 with an international
282 trainer/supervisor. This would be PKR 588 (95% CI: 434, 820) or US\$ 6 with a national
283 trainer/supervisor; with an international supervisor, each 1-point improvement on WHODAS costed
284 PKR 4097 (95% CI: 2978, 6046) or US\$ 40 and with a national supervisor it was estimated to be PKR
285 815 (95% CI: 576, 1225) or US\$ 8. We plotted 1,000 resampled estimates of costs and outcomes on a
286 cost-effectiveness plane for the primary and secondary outcomes. The results show that all the
287 resampled estimates fall in the upper-right quadrant, i.e. PM+ intervention is 'more effective but
288 costlier' in all of the resampled estimates.

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

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

300 **Discussion**

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

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

314 The resources, capacity and infrastructure for mental health services research including health
315 economic evaluation alongside randomized controlled trials is limited in humanitarian settings of
316 LMICs [33]. This is one of the very few studies to evaluate the cost-effectiveness of a psychological
317 intervention in a humanitarian setting. There are only a few published studies on the cost-effectiveness
318 of task-shifting interventions in global mental health. Araya et al (2006) evaluated the incremental cost-
319 effectiveness of a stepped-care multicomponent program for the treatment of depressed women in
320 primary care in Chile. The stepped-care program was more effective and costlier than usual care (an
321 extra US\$ 0.75 per depression-free day) [34]. Buttorff et al (2012) conducted an economic evaluation
322 of a task-shifting intervention for the treatment of depressive and anxiety disorders in primary-care
323 settings in India. They concluded that the use of lay health workers for treatment of CMDs in the public
324 primary-care facilities was not only cost-effective but also cost-saving. The mean health system cost
325 per case recovered at the end of follow-up was US\$ 128 (95% CI: 105 to 157) in the intervention arm
326 and US\$ 149 (95% CI: 131 to 169) in the control arm [30]. Other similar studies of lay-health counsellor
327 delivered psychological interventions from India [31] have replicated the findings of cost-effectiveness
328 of task-shifting interventions for treating depression and alcohol problems in primary care settings.
329 Sikandar et al., (2019) evaluated the cost-effectiveness of a peer-volunteer delivered CBT based
330 intervention for post-natal depression versus EUC in community settings of rural Pakistan. The
331 intervention was costlier as compared to EUC but was effective in improving the severity of post-natal
332 depression (costs per unit improvement in PHQ-9 score of US \$15.50 (9.59 to 21.61) for the whole
333 study period. The intervention had a 98% probability of being cost-effective over a willingness-to-pay

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

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

346 **Limitations**

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

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

365 **Conclusions**

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

375

376

377

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

		Group	Baseline			Endpoint			
			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)	---	---
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* **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)

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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)

Endpoint	International specialist supervisor		Local specialist supervisor	
	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 with 1000 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)

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

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

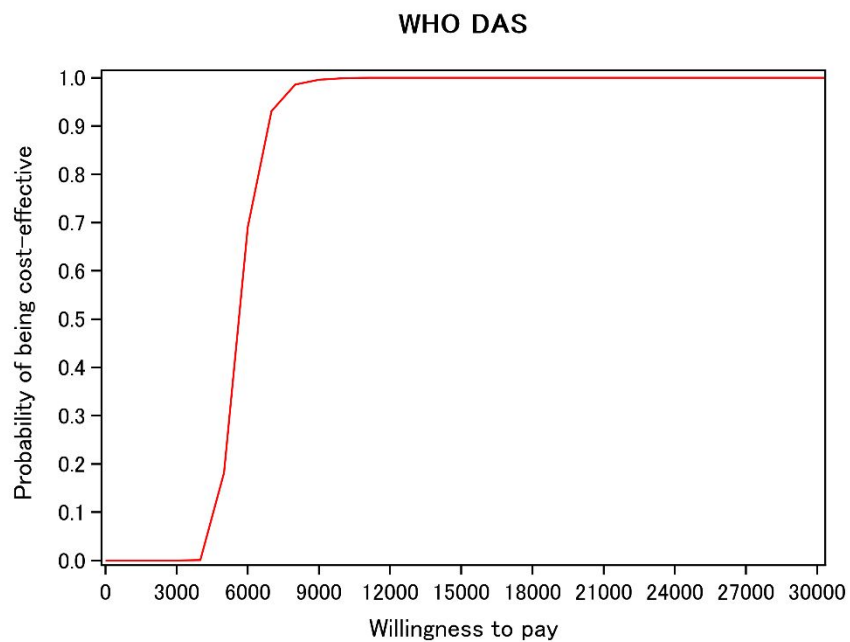
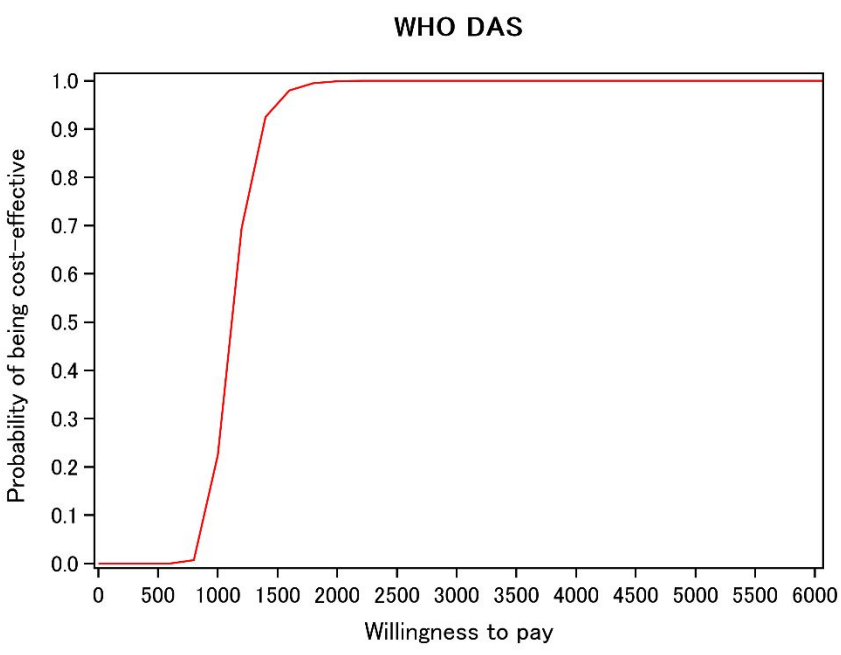


Figure 2b: Cost-effectiveness acceptability curve for PM+ with local supervisor (in PKR) (1 USD = 104 PKR; 2016)



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

3

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22 **Word count (except abstract): 34973224**

23

24

25

26

27

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40 Ommeren.

41 **Study supervision:** Hamdani, Rahman, Farooq, van Ommeren.

42 **Funding**

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

46 **Role of the Funder/Sponsor**

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

50 **Acknowledgements**

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

57 **Disclaimer**

58 MvO and DC are staff members of the World Health Organization. The authors alone are responsible
59 for the views expressed in this publication and they do not necessarily represent the decisions, policy
60 or views of the World Health Organization.

61 **Competing interests**

62 All authors have declared no conflicts of interest.

63

64

For Peer Review

65 **ABSTRACT**

66 **Background**

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

70

71 **Aims**

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

75

76 **Methods**

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

81

82 **Results**

83 The total cost of delivering PM+ per participant was estimated at PKR 16,967 (US \$ 163.14) using an
84 international master trainer and supervisor, and PKR 3,645 (US\$35.04; US\$ 7 per session) employing
85 a national trainer. The mean cost per unit score improvement in anxiety and depression symptoms on
86 HADS was PKR 2957 (95% CI: 2262, 4029) [US\$ 28] with international trainer/supervision and PKR
87 588 (95% CI: 434, 820) or US\$ 6 with local trainer/supervisor. The mean Incremental Cost-
88 Effectiveness Ratio (ICER) to successfully treat a case of depression (PHQ-9 \geq 10) using an
89 international supervisor was PKR 53,770 (95% CI: 39,394, 77,399) [US\$ 517] versus a local supervisor
90 PKR 10,705 (95% CI: 7731, 15,627) [US\$ 102.93].

91 **Conclusions**

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

95

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

98 **Trial Registration** anzctr.org.au Identifier: ACTRN12614001235695

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102

103 Mental health problems cause a significant burden of disease in Low and Middle Income Countries
104 (LMICs), yet the documented ‘mental health treatment gap’ is up to 90% [1-3]. The need for mental
105 health services is much greater in populations affected by humanitarian crises. More than 135 million
106 people are in need of humanitarian assistance due to ongoing humanitarian crises and conflicts globally
107 [4]. A systematic review and meta-analysis of mental health outcomes in population affected by conflict
108 and displacements showed that mood and anxiety disorders were common, with rates of 17.3% for
109 depression and 15.4% for posttraumatic stress disorder [5]. Epidemiological studies from areas affected
110 by humanitarian crises in Pakistan found high rates of psychological distress in these populations. One
111 study reported rates as high as 38% to 65% for psychological distress in women [6, 7]. Majority of
112 people have no access to mental health services in such settings [6]. Over the past decade, significant
113 progress has been made in terms of availability of evidence based mental health intervention packages
114 for populations affected by humanitarian crises [8]. However, sustainability and scalability of such
115 psychological interventions remains a challenge in populations affected by humanitarian crises in low
116 resource settings globally [9].

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

124 **Method**

125 **Study site and participants**

126 Participants included 346 primary care attendees with high level of psychological distress (score above
127 2 on General Health Questionnaire [GHQ-12]) [13] and functional impairment (score above 16 on
128 World Health Organization Disability Assessment Schedule 2.0 [WHODAS 2.0]) [14]. The participants
129 were individually randomized in 1:1 ratio to either intervention arm i.e. PM+ (n=172) along with
130 Enhanced Usual Care (EUC)) or the Control arm consisting of Enhanced Usual Care (EUC) only
131 (n=174). The study was approved locally by the Institutional Review and Ethics Board of the

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

134 **The Intervention**

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

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

148

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

157 **Enhanced care as usual**

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

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

164 **Data Collection**

165 **A. Health outcomes**

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

177

178 **B. Health resource use profiling**

179 The data on health resource use was collected using the Client Services Receipt Inventory (CSRI)
180 [22], which records the clients' contact with out-patient services (i.e. mental health specialist, general
181 physician, traditional healer, community health workers etc.), inpatient (hospital admissions) services
182 and out of pocket costs associated with travel, medications and tests/investigations during the preceding
183 recall period. A section on seeking religious help and retreats was added to adapt the tool for use in
184 local population. Study participants self-reported their health-care utilization, medication use and out-
185 of-pocket expenditures on CSRI [22] at baseline and 3-months' post-intervention.

186

187 **C. Cost measurement and analysis**

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

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

194

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

199

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

210

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

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

224

225 **Statistical Analysis**

226 The mean and standard deviation for the total cost was calculated using generalized linear regression
227 model with Gamma distribution after adjustment for baseline total cost. The group difference and its
228 95% CI was also calculated [24]. The Incremental Cost-effectiveness Ratio (ICER) was calculated as
229 the additional costs of the intervention divided by the change in HADS-A, HADS- D, HADS Total,
230 PHQ, and WHODAS related to the intervention. The confidence intervals for ICER was estimated by
231 non-parametric bootstrapping. The bootstrap technique sampled with replacement from the original
232 observed paired of costs and effects, maintaining the correlation structure between costs and benefits,
233 to create a new dataset with 1000 observations. For each bootstrap resample, an estimate of differential
234 total mean costs, expected mean effectiveness was calculated [25]. The 95% CIs for the differential
235 estimates were derived from the calculated 2.5th and 97.5th percentiles. We plotted cost-effectiveness
236 acceptability curves [26] to evaluate the probability of PM+ intervention being cost-effective at
237 increasing monetary values representing willingness-to-pay thresholds for PM+ intervention from
238 policy makers' perspective [27]. For the effectiveness data, we used linear mixed models to study
239 treatment effects as indicated in our main trial report [12] which allowed the number of observations
240 to vary at random between subjects and effectively handles missing data [28].the post hoc sensitivity
241 analysis using multiple imputation was performed to assess the robustness of treatment effect to the
242 missing values. 14% cost data was missing for medicines, complementary medicines, seeking retreats
243 and religious help and for outpatient services at the end point. Summary stats for each specific cost
244 were presented without imputation but the total cost were calculated assuming missing data as 0 in a
245 conservative way [25].

246

247 **Results**

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

248 As reported in the clinical effectiveness evaluation [12], mean combined depression and anxiety
249 symptom scores on HADS were significantly lower at 3-months post-intervention (AMD, -5.75 ; 95%
250 CI, -7.21 to -4.29). Similarly, functional impairment significantly improved (AMD, -4.17 ; 95% CI,
251 -5.84 to -2.51) on WHODAS-12 in the intervention arm compared to EUC arm. At baseline depression
252 rate was 94.2% and 89.4% in intervention and EUC arms respectively. at the end of 3-months follow
253 up period, the intervention arm had significantly lower rates of depression (26.9%) compared to EUC
254 arm (58.9%) (risk difference, -31.98 ; 95% CI: -41.03 to -22.94).

255

256

257 **Costs**

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

263

264 With an international master trainer/supervisor total cost of delivering PM+ intervention per participant
265 was PKR 16,967 (US \$ 163.14). Total intervention arm costs (PM+ costs plus cost of services accessed
266 by intervention arm) was PKR17,473 (SD, 912) or US\$ 168. The cost of EUC (treatment as usual plus
267 cost of services accessed by control arm participant) was PKR 848 (SD, 1734) or US \$ 8.15 (See Table
268 2).

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

274

275 **Cost-effectiveness**

276 Incremental cost-effectiveness ratios (ICERs) indicate that the intervention was both more effective
277 and costlier than EUC for all the health outcomes studied (Table 3). Analysis was conducted to evaluate
278 the cost-effectiveness of PM+ intervention under two scenarios; 1) PM+ delivery by lay health workers
279 supervised by international master trainer/supervisor (as observed in the trial) and 2) PM+ delivery by
280 lay health workers supervised by local supervisor. The second scenario will be the case for scale-up of
281 the intervention package in real world setting. The additional costs associated with the intervention led
282 to a relative improvement in outcomes, e.g. the mean cost per unit score improvement in anxiety and
283 depression on HADS was PKR 2957 (95% CI: 2262, 4029) or US\$ 28 with an international
284 trainer/supervisor. This would be PKR 588 (95% CI: 434, 820) or US\$ 6 with a national
285 trainer/supervisor; with an international supervisor, each 1-point improvement on WHODAS costed
286 PKR 4097 (95% CI: 2978, 6046) or US\$ 40 and with a national supervisor it was estimated to be PKR
287 815 (95% CI: 576, 1225) or US\$ 8. We plotted 1,000 resampled estimates of costs and outcomes on a
288 cost-effectiveness plane for the primary and secondary outcomes. The results show that all the
289 resampled estimates fall in the upper-right quadrant, i.e. PM+ intervention is ‘more effective but
290 costlier’ in all of the resampled estimates.

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

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

302 **Discussion**

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

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

332 intervention for post-natal depression versus EUC in community settings of rural Pakistan. The
333 intervention was costlier as compared to EUC but was effective in improving the severity of post-natal
334 depression (costs per unit improvement in PHQ-9 score of US \$15.50 (9.59 to 21.61) for the whole
335 study period. The intervention had a 98% probability of being cost-effective over a willingness-to-pay
336 threshold of US\$ 60 per unit of improvement on PHQ-9 score compared to EUC [35]. Although it is
337 difficult to compare the results of cost-effectiveness evaluations across studies due to differences in
338 analytical approaches, treatment conditions and different outcome measures, the results of these studies
339 demonstrate cost-effectiveness of brief psychological intervention using a task-shifting approach.

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

348 **Limitations**

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

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

367 **Conclusions**

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

377

378

379

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

		Group	Baseline			Endpoint			
			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)	---	---
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* **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)

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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)*				Difference in LS mean (95%CI)	p-value
Cost of Services	Time point	Intervention (N=172)		EUC (N=174)			
		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)

Endpoint	International specialist supervisor		Local specialist supervisor	
	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 with 1000 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

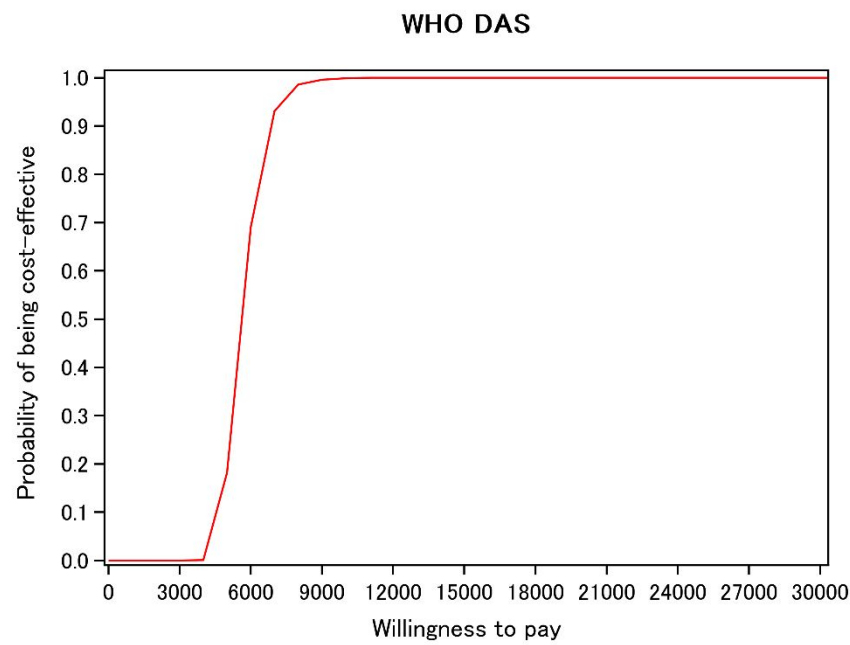
Figure 1a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

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

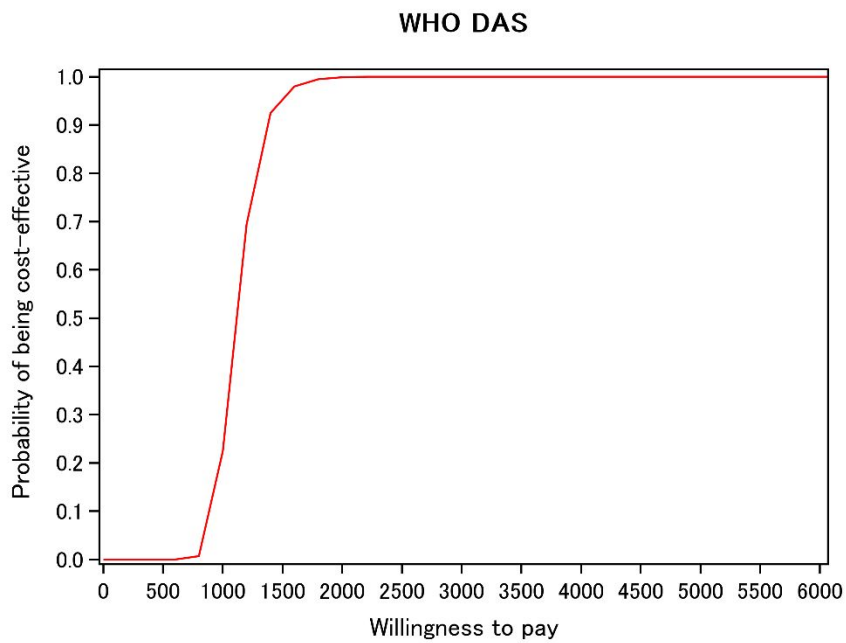
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Figure 2a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)



Review

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



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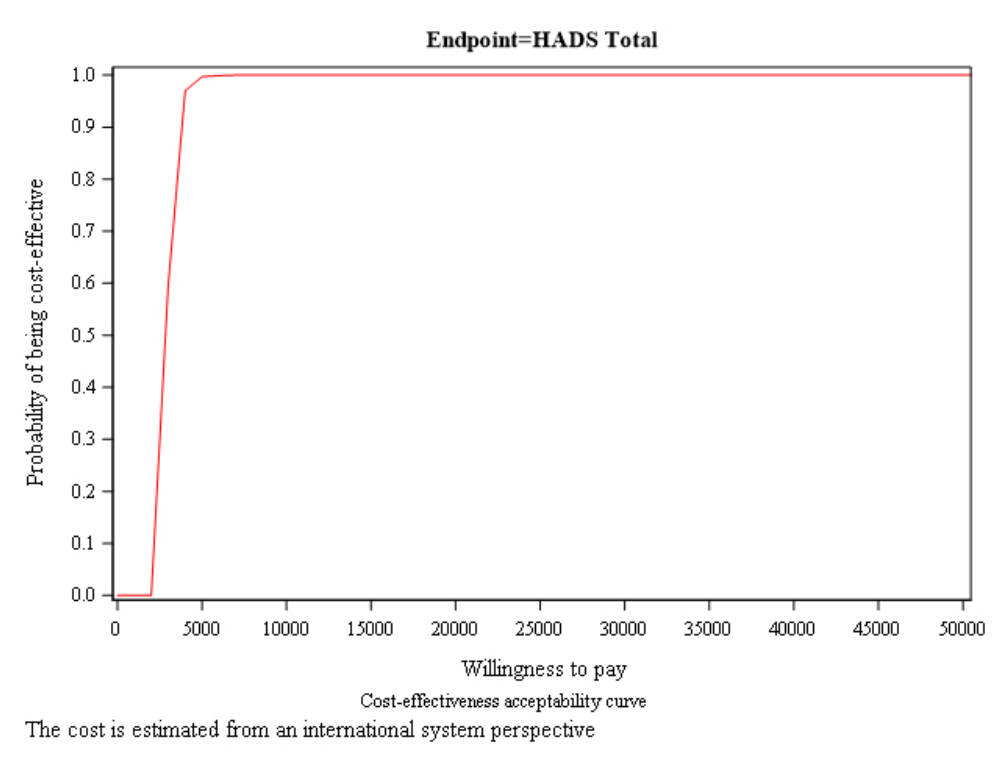


Figure 1a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

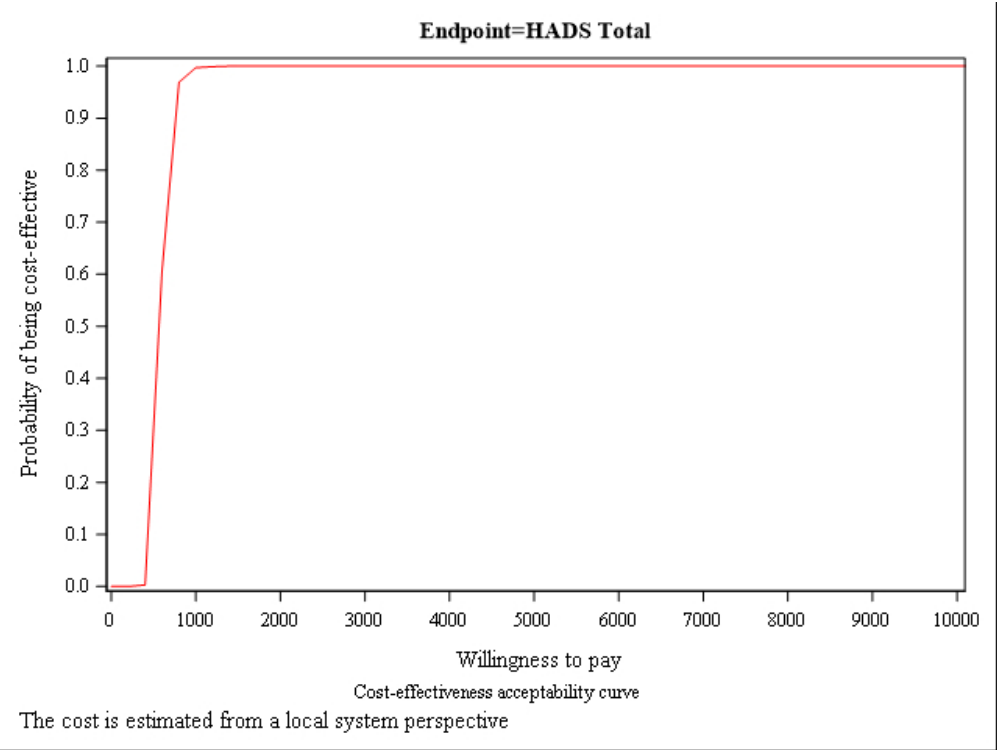


Figure 1b: Cost-effectiveness acceptability curve for PM+ - with local trainer (in PKR) (1 USD = 104 PKR; 2016)

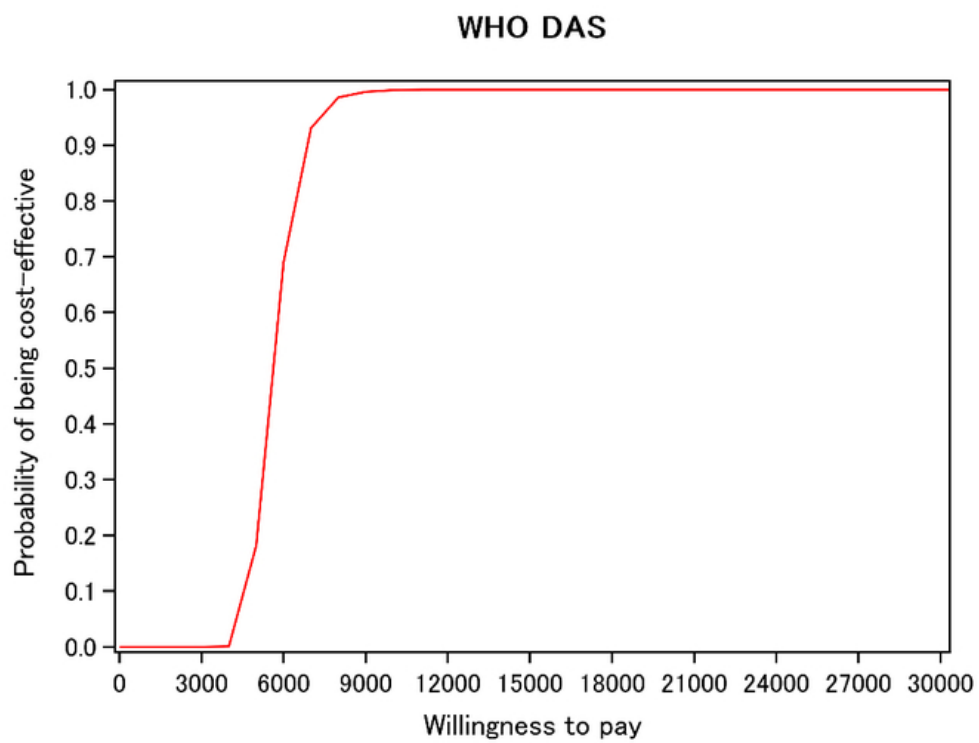


Figure 2a: Cost-effectiveness acceptability curve for PM+ with international supervisor (in PKR) (1 USD = 104 PKR; 2016)

114x88mm (150 x 150 DPI)

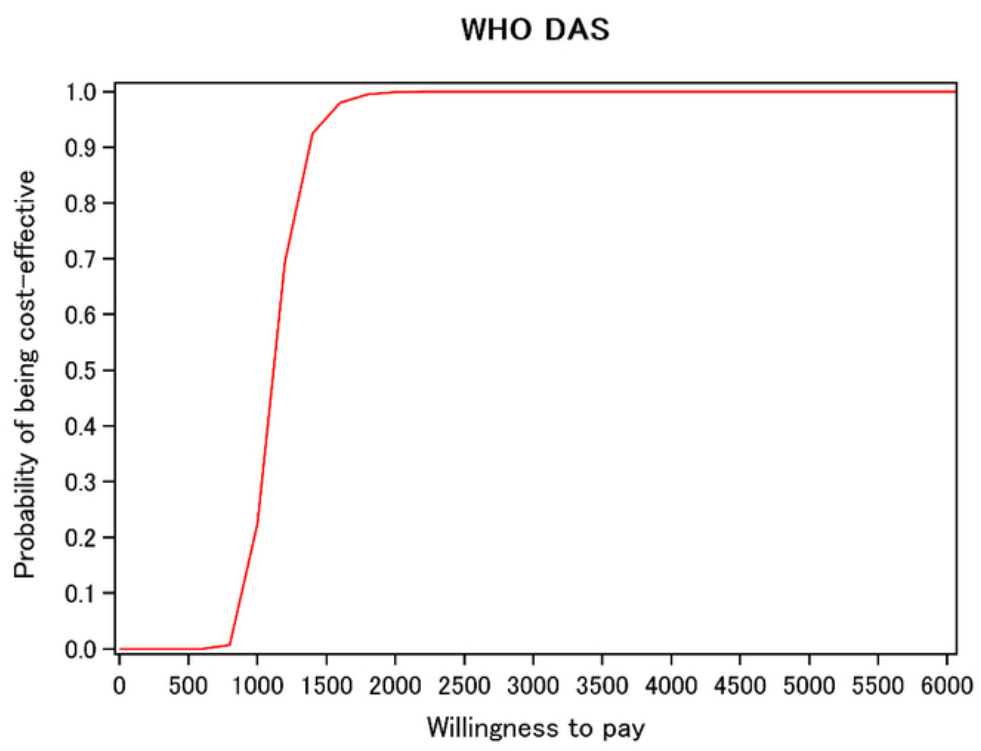


Figure 2b: Cost-effectiveness acceptability curve for PM+ with local supervisor (in PKR) (1 USD = 104 PKR; 2016)

114x88mm (150 x 150 DPI)