

Cost-effectiveness of early intervention services for psychosis and fidelity to national policy implementation guidance.

Muralikrishnan Radhakrishnan¹ PhD, Paul McCrone¹ PhD, Louise Lafortune² PhD, Linda Everard³ BSc, David Fowler⁴ PhD, Tim Amos⁵ MBBS, MRCPsych, Nick Freemantle⁶ PhD, Swaran P Singh⁷ MBBS, MD, FRCPsych, DM, Max Marshall⁸ MBBS, MD, Vimal Sharma⁹ MD, FRCPsych, PhD, Anna Lavis¹⁰ PhD, Peter B. Jones¹¹ MBBS, PhD and Max Birchwood¹² PhD, DSc, CPsychol, FBPsS

Authors affiliations:

¹ King's Health Economics, King's College London, UK

² Institute of Public Health, Forvie Site, University of Cambridge School of Clinical Medicine

³ The Early Intervention Service, Birmingham and Solihull Mental Health NHS Foundation Trust, UK

⁴ Department of Psychology, University of Sussex, UK

⁵ Academic Unit of Psychiatry, University of Bristol, Bristol, UK

⁶ Department of Primary Care and Population Health, UCL Medical School (Royal Free Campus), London, UK

⁷ Mental Health and Wellbeing, Warwick Medical School, University of Warwick, Coventry, UK

⁸ School of Medicine, University of Manchester, Manchester, UK

⁹ Early Intervention Service, Cheshire and Wirral NHS Foundation Trust & University of Chester, UK

¹⁰ Institute of Applied Health Research, College of Medical and Dental Science, University of Birmingham, UK

¹¹ Department of Psychiatry, University of Cambridge and CAMEO, Cambridge and Peterborough NHS Foundation Trust, Cambridge, UK

¹² Mental Health and Wellbeing, Warwick Medical School, University of Warwick, Coventry, UK

Correspondence :

Muralikrishnan Radhakrishnan PhD King's Health Economics ,King's College London, Institute of Psychiatry, Psychology & Neuroscience
Box 024, The David Goldberg Centre, De Crespigny Park, Denmark Hill
London SE5 8AF, UK
Tel: 020 7848 5081
Fax: 020 7848 0458
Email: muralikrishnan.radhakrishnan_kartha@kcl.ac.uk

Abstract

Introduction

Early Intervention Services (EIS) for psychosis are being implemented, internationally. It is important to learn from established examples and define the components and intensity of services that provide good value for money. This study aims to assess the cost-effectiveness of EIS according to how closely they adhered to the recommendations of the English Department of Health 2001 Policy Implementation Guide (PIG).

Methods

EIS from the National Eden Study were assessed using a measure of fidelity to the PIG that rated the presence or absence of 64 recommended items relating to team structure and practice. EIS were then classified into three groups: those with fidelity of 75-80 %, 81%-90 %, and 91-95 %. Patient-level resource use and outcomes were measured one year following inception into the service; costs were calculated and combined with quality-adjusted life years (QALYs) gained.

Results

At a threshold of £20,000 per QALY, the 81-90% fidelity group had a 56.3% likelihood of being the most cost-effective option followed by 75-80% fidelity at 35.8% and 91-95% fidelity group (7.9%).

Conclusions

The results from England suggest that striving to maximise fidelity may not be warranted, but that dropping below a certain level of fidelity may result in inefficient use of resources.

Key words : Psychotic Disorders, Early Medical Intervention, Economic Evaluation, Quality-Adjusted Life Years, Costs and Cost Analysis

Introduction

During the past decade, the development of early intervention services (EIS) for young people with first-episode psychosis has become a priority in a number of countries, including England, Canada, Denmark, Australia and Scandinavia (Lester et al 2009). England was the first country to mandate national coverage in the early 2000s, with a second round of service development currently underway. Thus, the provision of EIS has steadily increased, and in 2009 there were 145 EIS operating in England, serving about 15,750 individuals (Bird et al 2010). Two randomized control trials conducted in the UK (LEO trial) and Denmark (OPUS trial) and several effectiveness studies of 'routine' early intervention services shows that specialised early intervention services are superior to generic care in managing the critical early phase of psychosis (Craig et al 2004, Petersen et al 2005, Garety et al 2006, Singh 2010, Nordentoft et al 2014). EIS are also highly valued by consumers and engage users effectively (Lester et al 2009).

Economic evidence from the England (McCrone et al 2010) and other countries including Australia (Mihalopoulos et al 1999, Mihalopoulos et al 2009), Sweden (Cullberg et al 2006), Italy (Serretti et al 2009) and Denmark (Hastrup et al 2013) supports the cost-effectiveness case of EIS, and close liaison between EIS and primary care (Perez et al 2015). Since the national implementation of EIS in England during the first decade of the 21st century, concerns over continued funding for mental health services has seen some disappear or be diluted within non-specialist teams. There are tensions between providing a good quality service as mandated in the Policy Implementation Guidance (PIG) (DOH 2001) and meeting case-load targets linked to future funding; there are gaps between the PIG and actual practice (Lester et al 2009).

In a national setting of economic austerity and an international context where EIS are being considered in very different types of economic and health systems (McDaid et al 2016, Csillag et al 2015), it is important to determine the level of service intensity and breadth at which EIS provides good value for money. This study aims to assess the costs and cost-effectiveness of degrees of fidelity to a gold-standard (DOH 2001).

Methods

Participants and Intervention

Data come from the National EDEN study described in detail by *Birchwood et al* (2014). Briefly, the National EDEN (2005–09) study describes a cohort of recruited referrals to EIS with measures of their baseline characteristics, their outcomes at one year, and an assessment of the service in which individuals were treated. EIS were from five socioeconomically diverse sites across England: Birmingham, Cornwall, Cambridgeshire, Norwich, and Lancashire/Cheshire chosen to reflect urban/rural differences and EIS team structures. Fourteen EISs participated across the five sites; each within a defined geographical catchment area, from where they accepted all new cases of first episode psychosis in people aged 14–35. Lester et al (2009) used the implementation guidance from the national policy on early intervention teams PIG (DOH 2001) to populate items on the (64 item) fidelity scale, each item measured on a 4-point scale and consisting of core elements of the national early intervention teams. The fidelity scale drew items that focused on team structure, function and treatment availability. The scales were then administered to the early intervention service team managers to assess team fidelity relative to national guidance. Fidelity scores were available for five EIS sites (distributed across the 5 geographical regions). We used the available fidelity scores to group the EIS sites for cost-effectiveness analysis. Firstly, we classified the 14 participating EISs in the National Eden dataset into five geographic clusters (based on their respective mental health trusts-being the administrative body for the EIS sites), and fidelity scores were imputed from the five original sites to the other EIS teams within each mental health trust (service) . The imputation of the scores was done only after consultation with the original researchers who reasoned the imputation was reasonable since the EIS teams were similar in structure and under the same administrative body. Since original fidelity scores was not available for one of the mental health trusts, the three EIS sites under the trust were excluded from the analysis. Further, fidelity experts felt that it was not reasonable to impute scores from the nearby trusts for the excluded EIS sites. The included sites (n=11) were then classified as those with a fidelity score ranging from 75-80 %, 81%-90 %, and 91-95 %. The fidelity % was calculated using the fidelity scores with the maximum score (256) as the denominator.

Service use and costs

A wide (health care, social care, informal care and criminal justice) perspective was adopted for the calculation of costs. Service use was measured using an adapted version of the Client Service Receipt Inventory (CSRI) (Beecham & Knapp 2001). The CSRI has been used in numerous economic evaluations of mental health services in the UK and internationally (McCrone et al 2010, Mohan et al 2006). Service use captured in the CSRI included hospital-based care (in-patient and out-patient), community & primary care services, social care, contacts with the criminal justice system and informal care. Participants were asked whether they had used specific services during the 3-month (12 months for inpatient services) period prior to baseline assessment; 6-month follow-up; and 12-month follow-up.

Service use data were combined with appropriate unit cost information for 2011-12, primarily obtained from a nationally recognised source (Curtis 2012). Other sources, along with personal communication with the police were used to cost the criminal justice services (Finn et al 2000, Harries 1999, MOH 2011). The cost of a psychiatric assessment was derived from the average hourly cost of a forensic medical examiner (equivalent to a medical consultant) and an approved mental health practitioner (equivalent to a social worker) (Curtis 2012). Unpaid informal care from family/friends was valued at £13 per hour based on national mean gross hourly earnings (ONS 2013). The cost per user session for voluntary agencies was assumed to be same as the average of local authority social services and private sector day care for people with mental health problems (Curtis 2012). Specific types of medication (antidepressants, anxiolytics, antipsychotics and hypnotics) were recorded and average costs assumed for each type (HSCIC 2013).

Outcome measures

The primary outcome measure used was quality-adjusted life years (QALYs) generated from the EuroQol five dimensions (EQ-5D) health-related quality of life questionnaire at baseline, and at 12 months. The EQ-5D consists of a general health measure based on five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and are characterized by three levels (i.e. no problems, some problems and extreme problems). In total 243 possible health states can be described using this instrument, which can be further assigned with utilities based on country-specific algorithms. The EQ-5D has been tested for validity and responsiveness and has been found to be appropriate for use to measure improvements in psychosis (Barton et al 2009). The accrual of QALYs was calculated using area under the curve, using UK-specific utility weights (Dolan

et al 1995) , assuming a linear change between each available time point. Differences in baseline utility scores were controlled for when making comparisons between groups (Manca et al 2005).

Cost-effectiveness

Twelve-month follow-up costs and QALYs were compared conditional upon baseline utility, costs and individual characteristics using a bootstrapped regression model to account for the expected skewed distribution of the residuals. Cost-effectiveness of different fidelity levels was assessed using the net-benefit approach and interpretation of the cost-effectiveness results was made using cost-effectiveness acceptability curves (Briggs 2001). For each QALY value, regression models were used to determine the difference in net benefit between the three fidelity groups controlling for baseline utility, baseline costs and individual characteristics. Bootstrapping with 1000 resamples allowed the proportion of resamples showing the three fidelity groups as having the highest net benefit (and to be most cost-effective) to be computed and plotted.

A first set of analysis was performed including patients who did not have any missing costs/outcomes. As there were missing(at random) EQ5D data (35%) either at baseline or 12 months and cost data (6%) at 12 months, a separate analysis imputing costs and QALYs using regression methods was also undertaken. Observations with missing EQ5D values at both baseline and 12 month were dropped from the analysis.

Results

Participant characteristics

The participants consisted of 1,027 people between the ages of 14 and 35 recruited to the National Eden study between 2005 and 2009. Of these, 57 participants were with EIS sites that had no fidelity score, leaving a sample of 970 (94.4%) to be analysed. Further, 53 (5.5%) did not have EQ5D data at baseline or 12 months and were dropped from analysis. Of the remaining 917 participants, 593 (64.7%) were included for complete data analysis. The remaining 324 (35.3%) had missing data on either EQ5D at baseline or 12 months or costs, and these were analysed after imputation.

Baseline demographic characteristics are presented in Table 1. There were statistically significant differences in ethnicity and educational levels of the patients across fidelity groups. The mean age of the participants was 22.8 years (s.d 4.91), they were predominantly female (674, 69.48%) and single/unmarried (831, 85.76%). In terms of ethnicity, the majority of the participants were white (686, 72.06%) and the difference between groups was statistically significant. Differences in

educational levels were also statistically significant, with most of them having secondary/general education (475, 50.53%). As for employment status, only a small proportion (176, 18.18%) was in paid/self-employment.

Service use and cost

Baseline service use for the fidelity groups is presented in Table 2. Across the whole sample, about one-third had psychiatric inpatient stays and these had on average 49 days in hospital. Under one-fifth had psychiatric outpatient visits or accident and emergency visits over the previous 3 months. However, two-thirds did have contacts with psychiatrists in the community, while one-fifth had contacts with psychologists and over 80% had mental health nurse contacts. Under half had GP contacts. About one-third of the participants reported receiving informal care from friends/relatives at baseline.

Service use at 12-month follow-up for each fidelity group is reported in Table 3. Among all fidelity groups, the proportion receiving psychiatric inpatient care was lower than at baseline. The proportion of participants who received psychiatric outpatient care and had accident and emergency visits remained similar to baseline. Compared to baseline, contacts with psychologists, general practitioners, and community psychiatric nurse increased slightly in the 12-month follow-up period.

Mean unadjusted costs of service use at baseline and follow up are reported in Table 4. Adjusting for baseline utility, costs and individual characteristics (Table 5), total costs were higher by £1,735 (95% CI 1,643 to 1,827) for the 91-95% fidelity group when compared to the 81-90% fidelity group and lower by £1,465 (95% CI -1,661 to -1,270) when compared to the 75-80% fidelity group. Total costs were lower by £1,929 (95% CI -2,111 to -1,748) for the 81-90% fidelity group when compared to the 75-80% fidelity group.

Outcomes

All fidelity groups resulted in improvements in health related quality of life (measured with the EQ5D) (Table 6). After accounting for baseline utility, costs and individual characteristics (Table 5), the difference was only 0.0075 (95% CI 0.0066 to 0.0083) for the 91-95% fidelity group compared to the 81-90% fidelity group. However, the differences between the 91-95% fidelity group (-0.0471, 95% CI -0.0485 to -0.0458) and the 81-90% fidelity group (-0.0571, 95% CI -0.0582 to -0.0560) when compared to the 75-80% fidelity group showed the 91-95% group doing worse.

Cost effectiveness

The incremental cost and QALYs for the complete and imputed data are reported in Table 5. For the complete data analysis, at a threshold of £20,000 per QALY, the 81-90% fidelity group had a 56.3% likelihood of being the most cost-effective option followed by the 75-80% fidelity at with a 35.8% likelihood (Figure 1). The 91-95% fidelity group had a 7.9% likelihood of being the most cost-effective. In the imputed data analysis (Figure 2), the likelihood of cost-effectiveness at a threshold of £20,000 per QALY for the 81-90% fidelity group was 51.5%, followed by the 75-80% fidelity at 42.4% and the 91-95% fidelity group at 6.1%.

Fidelity analysis

Here we present an analysis of the fidelity scores in order to interpret these data in terms of the actual structure and function of the teams. We have the benefit of data on these teams as they evolved over the life of the project. There are 64 items each with a 4-point scale; the maximum score is 256. We present descriptive fidelity scores for the teams in each of the four years in Table 7.

All sites appeared to improve fidelity over the four years with changes from year one between 7% and 26%. The 'fidelity gap' overall between services however widened with time- from 26 points in year 1 between the lowest and highest scoring services, to 39 points in year 4. This largely reflects Cornwall's outlier status since the change from years 1 to 4 in the other four sites is from 26 points to 18 points i.e. the gap in fidelity narrowed.

We then examined the criteria which appeared in *all* services over time (the 'lowest common denominator') and those criteria scoring >3.9 but <4.0 over time.

There were 5 criteria with complete fidelity from year 1 to year 4 in all sites:

1. The EIS is a stand alone service composed of staff whose sole or main responsibility is to the EIS
2. The EIS includes a formal assessment of psychiatric history, mental state examination, risk, social functioning, family and significant others
3. The EIS completes an assessment on 90% of clients referred to the team
4. Almost all of service time (excluding admissions) is spent in the community
5. 90% of EIS clients are under the age of 35 years

The following 8 criteria scored 3.9/3.95 across all sites with no outliers from year 1-4:

1. The EIS has one general adult whole time equivalent (wte) psychiatric nurse for every 250,000 head of population

2. 90% of referred clients begin assessment within 3 weeks of initial referral
3. Risk of suicide is routinely and formally assessed according to protocol
4. No patient in the EIS has a duration of untreated psychosis (DUP) of greater than 5 years
5. The EIS team uses assertive outreach on a case sharing basis for those who are difficult to engage
6. The EIS has one wte support worker per 250,000 total population
7. The EIS team contains two formally trained and accredited cognitive therapists
8. The EIS team maintains contact with at least 95% of accepted clients for 12 months

The 8 lowest scoring criteria across sites were:

1. Within the last 12 months, the EIS has been involved in continuous community based programmes to reduce stigma associated with mental illness
2. The EIS should have specialist support from Child and Adolescent Mental Health Services(CAMHS) when prescribing for under 16 year olds
3. The EIS includes a programme of health promotion as part of its psychoeducation package
4. The EIS has an emphasis on finding employment or resuming work
5. The EIS runs psychosis identification training programmes which are continuously audited and adjusted
6. The EIS monitors all clients who are assessed but not accepted onto caseload for 12 months after initial assessment
7. The EIS assesses and treats symptoms of post traumatic stress disorder linked to the illness or its treatment
8. The EIS controls access to separate age-appropriate inpatient and crisis facilities

Discussion

This analysis adds to the literature by using EQ5D as an outcome measure for assessing the cost-effectiveness of EIS, which was recommended in an earlier analysis of EIS in England(McCrone et al 2010). A potential problem is that existing measures are not sensitive to change in mental health status. However, *Barton et al* have suggested that EQ-5D scores do vary in ways that reflect different levels of psychosis symptomatology (Barton et al 2009). The total cost for EIS over 12 months (£9,777) compares with that reported (£11,685) for 18 months in UK. Inpatient costs form the main component of cost in both studies. The results suggest that EIS result in improvements in health related quality of life over a 12 month period. Fidelity (91-95%) resulted in the higher QALYs, followed by 81-90% fidelity and 75-80% fidelity. The 75-80% fidelity group had a significantly lower

baseline utility compared to 81-90% and 91-95% fidelity groups. However, this issue of different fidelity groups starting with different baseline utilities was addressed by conditioning on baseline utility in the cost-effectiveness analysis, which subsequently estimated that 81-90% fidelity group was the most cost-effective. The proportion of participants using acute psychiatric inpatient services also reduced from 35% at baseline to 17% at 12 months follow-up. The finding that EIS results in reduced hospital admission has already been reported in literature (Bird et al 2010) and our results strengthen the evidence base.

Evidence on the cost-effectiveness of EIS when compared to standard care in UK has already been established (McCrone et al 2010). This study has taken the next step to establish the cost-effectiveness of fidelity levels to national PIG and will be helpful to commissioners and policy planners. In both set of cost-effectiveness analysis (complete and imputed data), 81-90% fidelity remained the most cost-effective option, followed by 75-80% fidelity and 91-95% fidelity. The imputed analysis results being similar to complete analysis can be attributed to the fact that imputed estimates were generated using regressions based on complete data. The results also show that striving for very high fidelity services may not result in improved cost-effectiveness. However, in order to understand these scores and their meaning in terms of service structure and function, we presented an analysis of the fidelity scores by site and over time and listing those criteria that were common denominators across services. These were: stand alone services, operating in an assertive community-based fashion, maintaining a high level of contact with prescribed staff ratio and skills and providing prompt access. The eight lowest scoring criteria across all sites are important and represented those that contributed to fidelity variability. These high fidelity elements included: specialist support from CAMHS, employment interventions (Individual placement and support) and efforts to reduce stigma and improve access and DUP. This analysis showed that the modal level of fidelity was high in terms of the core concept of EIS: dedicated, stand alone services operating in an assertive outreach format, with an emphasis on prompt referral and treatment and with a skill mix to provide NICE approved care. It may be argued that these high fidelity elements impaired cost-effectiveness. However, IPS is a NICE approved intervention to access employment and has been shown to be cost-effective in first episode psychosis (Knapp et al 2013) and over the longer term will reduce costs of state support. We recently showed in an analysis of the Birmingham site (Birchwood et al 2013) that pathways via CAMHS, tend to prolong DUP, supporting the PIG requirement for services to be integrated with CAMHS. In the UK context, there are quality standards in place that include a 2 week maximum delay between referral and first assessment for psychosis; again in our analysis of the Birmingham EDEN site, we showed that such delays occur when patients first contact with services is a generic CMHT supporting the stand alone EIS.

Adhering to fidelity levels of 81-90% to early intervention policy implementation guidance was more cost-effective than adhering to lower or higher levels. This suggests that striving to maximise fidelity to the 2001 guidelines may not be warranted, but that dropping below a certain level of fidelity may also result in an inefficient use of resources; however, our data showed that these 'high fidelity' elements have additional longer-term cost benefit (eg employment) and facilitate prompt access to care, now the subject of UK service standard in first episode psychosis

Limitations

The study used self-reported information on service use and informal care. There may be issues of accuracy with this approach but it was largely unavoidable given the need for a comprehensive perspective. Generally, such an approach of using self-reported information is an accepted method (Calsyn et al 1993, Goldberg et al 2002, Patel et al 2004). For medication, average costs were assumed for the cost periods. However, medication costs are small compared to other service and the use of average costs seems reasonable. This study used national mean gross hourly earnings to value informal care. There is disagreement around the most appropriate way of valuing informal care (Koopmanschap et al 2008) since alternative approaches to valuing informal care can provide different results. Alternative approaches have not been tested in this study; the differences they might make to the cost-effectiveness results are unclear. The study has considered only short-term results over 12 months and we cannot be certain about the longer-term cost-effectiveness of these different fidelity groups. Indeed, egregious deviations from the 2001 PIG, such as restricting services to two, rather than three years due to budget cuts, are not modelled in the definitions of fidelity used in our study. Another important limitation is the imputation of the fidelity scores from the original EIS sites to other sites under the same mental health trusts. Though this was done after consultation with EIS fidelity experts, we could expect some variations in the services provided by the EIS sites. This was addressed by the inclusion of baseline costs (captures difference in service structure for EIS sites) in the regression model and reasonably addresses the issues of imputing fidelity scores. The limitation of subjective reporting of fidelity responses by EIS team managers used in the original fidelity study (Lester et al 2009) is acknowledged. Overall, our findings provide support the idea of aiming high when designing and implementing EIS in any setting, but remind the field that the best should not become the enemy of the good. Further health economic evaluation of new services in a variety of settings internationally will help policy makers, managers and clinical leaders make good judgments.

Funding

This work was supported by grants from the UK Department of Health (RDD/ARF2) and the National Institute of Health Research (NIHR) under the Programme Grants for Applied Research Programme (RP-PG-0109-10074). The views expressed in this publication are those of the authors and not necessarily those of the NHS, NIHR, or the Department of Health.

Professors Birchwood and Singh are part funded by the National Institute for Health Research (NIHR) through the Collaborations for Leadership in Applied Health Research and Care for West Midlands (CLAHRC-WM). Professor Jones is part funded by the NIHR CLAHRC East of England. As such, the research was carried out under the auspices of these National Institute of Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care but the views expressed are not necessarily those of the NHS, NIHR or Department of Health.

Acknowledgements & Authors Contributions

MB was the CI and grant holder, LE, PJ, DF, TA, NF, VS, SS, AL & MM contributed to the study design and execution. The data were analysed by MR, PM, LF and with MB and PJ drafted the manuscript. MB acts as guarantor. The University of Birmingham (UK) acted as the study sponsor. We thank Prof Helen Lester (deceased) for making available the EIS fidelity scores and providing expert consultation to the study design. We thank the UK Mental Health Research Network for their support and assistance and all National EDEN participants.

Conflict of interest

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

References

- Barton GR, Hodgekins J, Mugford M, Jones PB, Croudace T, Fowler D (2009). Measuring the benefits of treatment for psychosis: validity and responsiveness of the EQ-5D. *Br J Psychiatry* 195:170-7.
- Beecham J, Knapp M. Costing psychiatric interventions (2001). In *Measuring Mental Health Needs* (ed G Thornicroft): 200–24. Gaskell.
- Bird V, Premkumar P, Kendall T, Whittington C, Mitchell J, Kuipers E (2010). Early intervention services, cognitive-behavioural therapy and family intervention in early psychosis: systematic review. *Br J Psychiatry* 197:350-6.
- Birchwood M, Connor C, Lester H, Patterson P, Freemantle N, Marshall M, Fowler D, Lewis S, Jones P, Amos T, Everard L, Singh SP (2013). Reducing duration of untreated psychosis: care pathways to early intervention in psychosis services. *Br J Psychiatry* 203:58-64.
- Birchwood M, Lester H, McCarthy L, Jones P, Fowler D, Amos T, Freemantle N, Sharma V, Lavis A, Singh S, Marshall M (2014). The UK national evaluation of the development and impact of Early Intervention Services (the National EDEN studies): study rationale, design and baseline characteristics. *Early Interv Psychiatry* 8:59-67.
- Briggs AH (2001). A Bayesian approach to stochastic cost-effectiveness analysis. *Int J Technol Assess Health Care* 17: 69–82.
- Calsyn RJ, Allen G, Morse GA, Smith R, Templehoff B (1993). Can you trust self-report data provided by homeless mentally ill individuals? *Evaluation Rev* 17: 353–366.
- Craig TK, Garety P, Power P, Rahaman N, Colbert S, Fornells-Ambrojo M, Dunn G (2004). The Lambeth Early Onset (LEO) Team: randomised controlled trial of the effectiveness of specialised care for early psychosis. *BMJ* 329: 1067.
- Csillag C, Nordentoft M, Mizuno M, Jones PB, Killackey E, Taylor M, Chen E, Kane J, McDaid D (2015). Early intervention services in psychosis: from evidence to wide implementation. *Early Interv Psychiatry* [Epub ahead of print]
- Cullberg J, Mattsson M, Levander S, Holmqvist R, Tomsmark L, Elingfors C, Wieselgren IM (2006). Treatment costs and clinical outcome for first episode schizophrenia patients: a 3-year follow-up of the Swedish 'Parachute Project' and two comparison groups. *Acta Psychiatr Scand* 114: 274–81.
- Curtis L (2012). Unit costs of health and social care. Canterbury: PSSRU.
<http://www.pssru.ac.uk/project-pages/unit-costs/2012/>
- Department of Health (2001). Early intervention in psychosis. In *The Mental Health Policy Implementation Guide*: London: Department of Health 43–61. <http://www.iris-initiative.org.uk/silo/files/mh-policy-implementation-guide-2003.pdf>

- Dolan P, Gudex C, Kind P, Williams A (1995). A social tariff for EuroQol: results from a UK population survey. York: University of York.
- Finn W, Hyslop J, Truman C (2000). Mental Health, Multiple Needs and the Police. Revolving Doors Agency.
- Garety PA, Craig TKJ, Dunn G, Fornells-Ambrojo M, Colbert S, Rahaman N, Read J, Power P (2006). Specialised care for early psychosis: symptoms, social functioning and patient satisfaction. Randomised controlled trial. *Br J Psychiatry* 188:37–45.
- Goldberg RW, Seybolt DC, Lehman A (2002). Reliable self-report of health service use by individuals with serious mental illness. *Psychiatr Serv* 53: 879–881.
- Harries R (1999). 'The Cost of Criminal Justice' in Home Office Research – Development and Statistics Directorate Research Findings 103.
<http://webarchive.nationalarchives.gov.uk/20110314171826/http://rds.homeoffice.gov.uk/rds/pdfs/r103.pdf>
- Hastrup LH, Kronborg C, Bertelsen M, Jeppesen P, Jorgensen P, Petersen L, Thorup A, Simonsen E, Nordentoft M (2013). Cost-effectiveness of early intervention in first-episode psychosis: economic evaluation of a randomised controlled trial (the OPUS study). *Br J Psychiatry* 202:35-41
- Health & Social Care Information Centre (2013). Prescription cost analysis England 2012
<http://www.hscic.gov.uk/catalogue/PUB10610>
- Knapp M, Patel A, Curran C, Latimer E, Catty J, Becker T, Drake RE, Fioritti A, Kilian R, Lauber C, Rössler W, Tomov T, van Busschbach J, Comas-Herrera A, White S, Wiersma D, Burns T (2013). Supported employment: cost-effectiveness across six European sites. *World Psychiatry* 12:60-8.
- Koopmanschap MA, van Exel JN, van den Berg B, Brouwer WB (2008). An overview of methods and applications to value informal care in economic evaluations of healthcare. *Pharmacoeconomics* 26: 269–280.
- Lester H, Birchwood M, Bryan S, England E, Rogers H, Sirvastava N (2009). Development and implementation of early intervention services for young people with psychosis: case study. *Br J Psychiatry* 194: 446–50.
- Manca A, Hawkins N, Sculpher MJ (2005). Estimating mean QALYs in trial based cost-effectiveness analysis: the importance of controlling for baseline utility. *Health Econ* 14: 487–496.
- McCrone P, Craig TKJ, Power P, Garety PA (2010). Cost-effectiveness of an early intervention service for people with psychosis. *Br J Psychiatry* 196:377–82.
- McDaid D, Park A, Lemmi V, Adelaja B, Knapp M (2016). Growth in the use of early intervention for psychosis services: an opportunity to promote recovery amid concerns on health care sustainability. Personal Social Services Research Unit, London, UK.
<http://eprints.lse.ac.uk/65630/>

Mihalopoulos C, McGorry PD, Carter RC (1999). Is phase-specific, community oriented treatment of early psychosis an economically viable method of improving outcome? *Acta Psychiatr Scand* 100: 47–55.

Mihalopoulos C, Harris M, Henry L, Harrigan S, McGorry P (2009). Is early intervention in psychosis cost-effective over the long term? *Schizophr Bull* 35: 909–18.

Ministry of Justice (2011). Costs per place and costs per prisoner by individual prison. National Offender Management Service Annual Report and Accounts 2010-11: Management Information Addendum.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/218347/prison-costs-summary-10-11.pdf

Mohan R, McCrone P, Szmukler G, Micali N, Afuwape S, Thornicroft G (2006). Ethnic differences in mental health service use among patients with psychotic disorders. *Soc Psychiatry Psychiatr Epidemiol* 41:771–776

Nordentoft M, Rasmussen JO, Melau M, Hjorthøj CR, Thorup AA(2014). How successful are first episode programs? A review of the evidence for specialized assertive early intervention. *Curr Opin Psychiatry* 27:167-72

Office for National Statistics (2013). EARN08 part 1: Distribution of gross hourly earnings of all employees. Labour Market Statistics. <http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcM%3A77-276583>

Patel A, Rendu A, Moran P, Leese M, Mann A, Knapp M (2004). A comparison of two methods of collecting economic data in primary care. *Fam Pract* 22: 323–327

Petersen L, Jeppesen P, Thorup A, Abel MB, Ohlenschlaeger J, Christensen TO, Krarup G, Jørgensen P, Nordentoft M (2005). A randomised multicentre trial of integrated versus standard treatment for patients with a first episode of psychotic illness. *BMJ* 331: 602.

Perez J, Jin H, Russo DA, Stochl J, Painter M, Shelley G, Jackson E, Crane C, Graffy JP, Croudace TJ, Byford S, Jones PB (2015). Clinical effectiveness and cost-effectiveness of tailored intensive liaison between primary and secondary care to identify individuals at risk of a first psychotic illness (the LEGs study): a cluster-randomised controlled trial. *Lancet Psychiatry* 2:984-93.

Singh SP (2010). Early intervention in psychosis. *Br J Psychiatry* 196:343-5.

Serretti A, Mandelli L, Bajo E, Cevenini N, Papili P, Mori E, Bigelli M, Berardi D (2009). The socio-economical burden of schizophrenia: a simulation of cost-offset of early intervention program in Italy. *Eur Psychiatry* 24: 11–6.

Table 1 - Baseline demographics

	75-80% Fidelity	81-90% Fidelity	91-95% Fidelity	p value
N	126	715	129	
Age, Mean(SD)	22.6(5.20)	22.7(4.77)	23.7(5.28)	
Sex, n(%)				
Male	39(30.95)	215(30.07)	42(32.56)	0.847
Female	87(69.05)	500(69.93)	87(67.44)	
Marital Status, n(%)*				
Single/unmarried	111(88.10)	609(85.29)	111(86.05)	0.553
Married/Cohabiting	14(11.11)	87(12.18)	13(10.08)	
Divorced/Separated	1(0.79)	18(2.52)	5(3.88)	
Ethnicity, n(%)*				
Asian		146(20.65)	6(4.80)	<0.001
Black		64(9.05)	4(3.20)	
White	116(96.67)	459(64.92)	111(88.80)	
Mixed/Others	4(3.33)	38(5.37)	4(3.20)	
Education, n(%)*				
Primary education or less	9(7.32)	94(13.60)	14(11.11)	0.030
Secondary/general education	78(63.41)	336(48.63)	61(48.41)	
Tertiary/further education	36(29.27)	261(37.77)	51(40.48)	
Employment, n(%)*				
In paid/self employment	20(15.87)	123(17.25)	33(25.58)	0.060
Others	106(84.13)	590(82.75)	96(74.42)	
* Total do not add upto total sample size due to missing data				

Table 2 - Service use at baseline

Service	Number(%) of participants using services			Mean(SD) number of service contacts		
	75-80% Fidelity (n=126)	81-90% Fidelity (n=715)	91-95% Fidelity(n=129)	75-80% Fidelity (n=126)	81-90% Fidelity (n=715)	91-95% Fidelity(n=129)
Inpatient Services(days)^a						
Acute psychiatric ward	40(31.7)	234(32.7)	65(50.4)	46.9(54.8)	54(52.7)	32(26.7)
Psychiatric rehabilitation ward	2(1.6)	7(1.0)	1(0.8)	15.5(7.8)	46.9(35.8)	55(-)
Long-stay ward	0(0)	4(0.6)	0(0)		62.5(91.8)	
Emergency/crisis ward	4(3.2)	6(0.8)	1(0.8)	1(0)	1.7(1.2)	1(-)
General medical ward	9(7.1)	32(4.5)	10(7.8)	12.6(16.4)	13.5(23)	11.3(18.2)
Outpatient Services(visits)^b						
Accident and Emergency	24(19.0)	107(15.0)	32(24.8)	1.1(0.34)	1.3(0.88)	1.3(0.93)
Psychiatric	39(31.0)	104(14.5)	29(22.5)	1.9(0.92)	2.5(1.8)	2.7(1.8)
Others	9(7.1)	46(6.4)	14(10.9)	1.4(0.72)	1.9(2.7)	1.2(0.58)
Day hospital	3(2.4)	9(1.3)	0(0)	1.3(0.58)	2.2(1.7)	
Community based Day Services(attendances)^b						
Community mental health centre	6(4.8)	53(7.4)	0(0)	3.3(2.9)	2.7(2.3)	
Day care centre	0(0)	7(1.0)	0(0)		17.9(18)	
Group therapy	3(2.4)	5(0.7)	1(0.8)	8.3(4.7)	3.4(3)	1(-)
Sheltered workshop	2(1.6)	1(0.1)	1(0.8)	5.5(6.4)	1(-)	2(-)
Specialist education	1(0.8)	3(0.4)	0(0)	6(-)	3(2.6)	
Primary and Community Care(contacts)^b						
Psychiatrist	75(59.5)	497(69.5)	82(63.6)	2.4(2.7)	3(3)	3.8(3.2)
Psychologist	19(15.1)	173(24.2)	20(15.5)	1.7(1)	3.3(2.7)	6.3(6.8)
General practitioner	80(63.5)	287(40.1)	59(45.7)	2.3(1.1)	2.8(2.8)	2.6(1.7)
Counsellor	6(4.8)	11(1.5)	4(3.1)	3(1.8)	6.4(4)	4(3.2)
District Nurse	2(1.6)	6(0.8)	3(2.3)	6.5(5)	5.5(7.2)	2.3(1.2)
Community psychiatric nurse	113(89.7)	569(79.6)	97(75.2)	10.3(8.7)	10.9(12.3)	7.8(6.2)
Social worker	9(7.1)	125(17.5)	8(6.2)	5.8(4.3)	5.8(5.5)	4.3(4)
Occupational therapist	11(8.7)	55(7.7)	5(3.9)	3.2(3.1)	4.2(3.3)	4.4(3.4)
Home care worker	24(19.0)	4(0.6)	3(2.3)	5.8(5.1)	4.8(5.2)	8(6)
Others	20(15.9)	176(24.6)	13(10.1)	3.3(2.3)	7.9(9.3)	16.8(23.8)
Criminal Justice Services(contacts)^b						
Police contacts	28(22.2)	100(14.0)	26(20.2)	1.6(0.9)	1.6(1.9)	1.3(0.6)
Police cell or prison nights	11(8.7)	28(3.9)	15(11.6)	6.5(17.7)	11(35.1)	7.2(23.1)
Psychiatric assessment	16(12.7)	28(3.9)	12(9.3)	1.5(0.6)	1(0.2)	1.9(2.9)
Civil court appearances	2(1.6)	5(0.7)	3(2.3)	4(1.4)	1.4(0.5)	2(1)
Criminal court appearances	3(2.4)	10(1.4)	2(1.6)	2.3(0.6)	2.2(1.9)	2(0)
Informal Care^b						
Friends and Relatives (weekly hours)	74(58.7)	202(28.3)	40(31.0)	25.1(20)	13.6(21.8)	12.6(11.6)
Voluntary Agencies (contacts)	26(20.6)	38(5.3)	10(7.8)	5.4(8)	8.5(12.1)	5.6(5.6)

^a Service use are for past 12 months, ^b Service use are for past 3 months

Table 3 - Service use at 12 months follow-up

Service	Number(%) of participants using services			Mean(SD) number of service contacts		
	75-80% Fidelity (n=106)	81-90% Fidelity(n=645)	91-95% Fidelity(n=113)	75-80% Fidelity (n=106)	81-90% Fidelity(n=645)	91-95% Fidelity(n=113)
Inpatient Services(days)						
Acute psychiatric ward	11(10.3)	105(16.2)	37(32.7)	59.5(64.1)	59.2(66.3)	42.7(44.7)
Psychiatric rehabilitation ward	5(4.7)	5(0.8)	0(0)	64.2(70.7)	50.8(27.8)	
Long-stay ward	0(0)	4(0.6)	0(0)		57.3(40.4)	
Emergency/crisis ward	0(0)	2(0.3)	1(0.9)		1(0)	1(-)
General medical ward	5(4.7)	27(4.2)	3(2.7)	39.2(69.2)	13.5(34.8)	1.3(0.6)
Outpatient Services(visits)						
Accident and Emergency	8(7.5)	101(15.6)	13(11.5)	1.4(0.7)	1.7(1.8)	1.3(0.9)
Psychiatric	43(40.5)	88(13.6)	27(23.9)	2.4(1.7)	3.9(3.5)	6.3(10)
Others	21(19.8)	72(11.2)	17(15.0)	2.1(1.2)	2.9(4.1)	1.5(0.7)
Day hospital	2(1.9)	18(2.7)	0(0)	1.5(0.7)	3.1(3.8)	
Community based Day Services(attendances)						
Community mental health centre	0(0)	24(3.7)	3(2.7)		13.6(19.3)	4(3)
Day care centre	1(0.9)	12(1.8)	0(0)	10(-)	12.5(22)	
Group therapy	10(9.4)	10(1.6)	4(3.5)	6.3(5.2)	12.3(13.3)	29(24.8)
Sheltered workshop	14(13.2)	2(0.3)	1(0.9)	9.3(10)	24(0)	13(-)
Specialist education	2(1.9)	11(1.7)	2(1.8)	9.5(7.8)	6.5(5.7)	3(0)
Primary and Community Care(contacts)						
Psychiatrist	86(81.1)	532(82.4)	91(80.5)	2.9(3.3)	4.9(4.7)	5.5(5.1)
Psychologist	19(17.9)	317(49.1)	47(41.6)	2(2.8)	7.3(7.6)	13(10.7)
General practitioner	72(67.9)	302(46.8)	58(51.3)	4(2)	4.5(5.1)	4.3(5.4)
Counsellor	2(1.9)	7(1.0)	5(4.4)	2(1.4)	9.3(7.2)	3.8(4.6)
District Nurse	3(2.8)	9(1.4)	4(3.5)	1.7(0.6)	5.8(6.6)	1.5(0.6)
Community psychiatric nurse	105(99.0)	590(91.5)	105(92.9)	24.2(13.7)	26(21.1)	29.2(20.8)
Social worker	6(5.6)	126(19.5)	12(10.6)	5.7(3.6)	13.4(13.5)	9.2(8)
Occupational therapist	6(5.6)	153(23.7)	8(7.0)	6.3(7.3)	11.4(13.5)	11.6(13)
Home care worker	54(50.9)	12(1.8)	3(2.7)	14.2(12.2)	28.3(50.5)	7.3(3)
Others	42(39.6)	274(42.5)	34(30.0)	11(16.2)	13.5(13)	23.7(20)
Criminal Justice Services(contacts)						
Police contacts	24(22.6)	83(12.9)	17(15.0)	2.1(1.9)	2.8(8.5)	1.8(0.8)
Police cell or prison nights	8(7.5)	28(4.3)	5(4.4)	2.1(1.6)	4.2(6.8)	2.6(2.5)
Psychiatric assessment	3(2.8)	14(2.2)	5(4.4)	1(0)	1.4(0.5)	1(0)
Civil court appearances	1(0.9)	17(2.6)	1(0.9)	1(-)	1.3(0.6)	2(-)
Criminal court appearances	6(5.6)	16(2.4)	5(4.4)	2.5(1.8)	2(0.8)	1.6(0.5)
Informal Care						
Friends and Relatives (weekly hours)	65(61.3)	165(25.6)	30(26.5)	19.5(19)	11.9(15)	9.5(11)
Voluntary Agencies (contacts)	54(50.9)	77(11.9)	22(19.5)	10.3(21)	10.4(21.9)	9.7(11.4)

Table 4 -Service costs at baseline and follow-up.

Service	Mean (SD) baseline cost (2011/12 UK pounds)			Mean (SD) 12 months cost (2011/12 UK pounds)		
	Low Fidelity (n=126)	Medium Fidelity (n=715)	High Fidelity(n=129)	Low Fidelity (n=108)	Medium Fidelity(n=686)	High Fidelity(n=123)
Inpatient Services^a						
Acute psychiatric ward	15,469(18,074)	17,869(17,385)	10,519(8,778)	19,650(21,160)	19,523(21,880)	14,083(14,761)
Psychiatric rehabilitation ward	4,464(2,240)	13,495(10,306)	15,840(-)	18,490(20,368)	14,630(8,006)	
Long-stay ward		14,313(21,029)			13,110(9,258)	
Emergency/crisis ward	330(0)	550(400)	330 (-)		330(0)	330(-)
General medical ward	6,767 (8,824)	7,293(12,363)	6,091(9,854)	21,129(37,293)	7,286(18,780)	719(311)
All inpatient services	16,044(17,945)	17,115(17,705)	10,869(9,024)	21,802(31,076)	18,253(23,410)	13,778(14,799)
Outpatient Services^b						
Accident and Emergency	126(38)	148(98)	147(104)	154(83)	186(201)	146(96)
Psychiatric	318(157)	417(300)	457(312)	407(283)	661(597)	1,077(1,701)
Others	201(101)	266(377)	169(80)	298(160)	402(575)	204(100)
Day hospital	133(58)	222(172)		150(71)	311(386)	
All outpatient services	285(186)	323(310)	323(283)	444(346)	493(618)	733(1,378)
Community based Day Services^b						
Community mental health centre	166(247)	91(76)			844(1,521)	290(187)
Day care centre		1,142(949)		1,110(-)	1,384(2,810)	
Group therapy	63(35)	65(99)	5(-)	79(69)	108(131)	196(159)
Sheltered workshop	109(140)	17(-)	42(-)	204(258)	625(177)	203(-)
Specialist education	15(-)	12(3)		123(145)	110(181)	26(5)
All community based day services	142(204)	206(449)	23(26)	200(312)	792(1,767)	239(218)
Primary and Community Care^b						
Psychiatrist	773(818)	859(1,006)	857(547)	956(924)	1,317(1,261)	1,508(1,643)
Psychologist	209(123)	378(332)	645(531)	243(376)	938(1,006)	2,041(1,828)
General practitioner	157(89)	162(196)	132(108)	272(143)	256(303)	277(496)
Counsellor	200(126)	386(259)	260(206)	146(115)	415(188)	228(312)
District Nurse	341(338)	205(215)	45(37)	56(27)	167(199)	19(13)
Community psychiatric nurse	540(483)	438(515)	411(352)	1,190(685)	1,042(946)	1,494(1,096)
Social worker	1,302(1144)	1,035(1,233)	1,255(1,818)	1,019(744)	2,602(2,669)	1,889(1,847)
Occupational therapist	165(132)	214(209)	260(221)	386(456)	794(2,174)	535(390)
Home care worker	141(149)	73(106)	115(61)	322(270)	1,133(1,920)	238(131)
Others	108(93)	220(375)	670(855)	410(556)	399(494)	1,142(1,372)
All primary and community care	1,338(1,217)	1,446(1,476)	1,301(1,096)	2,594(1,754)	3,548(3,113)	4,308(2,953)
Criminal Justice Services^b						
Police contacts	85(47)	83(98)	70(29)	111(100)	146(443)	92(43)
Police cell or prison nights	700(1,897)	1,185(3,757)	770(2,481)	227(166)	451(732)	278(269)
Psychiatric assessment	174(73)	120(22)	222(333)	116(0)	157(58)	116(0)
Civil court appearances	5,268(1,863)	1,844(721)	2,634(1,317)	1,317(-)	1,704(774)	2634(-)
Criminal court appearances	3,073(760)	2,897(2,468)	2,634(0)	3,293(2,319)	2,634(1,075)	2,107(721)
All criminal justice services	1,125(2,046)	783(2,843)	1,043(2,026)	1,036(1,908)	1,066(1,677)	835(1,140)
Informal Care^b						
Friends and Relatives	4,255(3,379)	2,302(3,676)	2,127(1,963)	6,578(6,436)	4,010(5,059)	3,222(3,748)
Voluntary Agencies	188(277)	298(425)	196(197)	361(735)	365(766)	342(400)
All informal care	3,947(3,466)	2,195(3,582)	1,852(1,941)	5,386(6,427)	3,432(4,842)	2,481(3,450)
Medication^b						
	125(165)	139(222)	107(149)	873(903)	609(783)	623(726)
Total Cost(Health and social care)^c						
	7,035(13,308)	8,125(13,996)	7,448(8,634)	7,603(16,179)	8,004(14,184)	9,803(11,467)
Total Cost	9,854(13,573)	8,920(14,700)	8,363(9,021)	12,065(17,342)	9,225(14,794)	10,786(11,917)

^a Baseline costs are for past 12 months, ^b Baseline costs are for past 3 months, ^c Excludes criminal justice and informal care

Table 5 - Cost-effectiveness results			
	91-95% vs 81-90%	91-95% vs 75-80%	81-90% vs 75-80%
Complete Data Analysis			
Incremental effect (95%CI)	0.0075(0.0066 to 0.0083)	-0.0471(-0.0485 to -0.0458)	-0.0571(-0.0582 to -0.0560)
Incremental total costs(95%CI)	1735 (1643 to 1827)	-1465(-1661 to -1270)	-1929(-2111 to -1748)
Incremental cost-effectiveness ratio	231,333	31,104	33,783
Imputed Data Analysis			
Incremental effect (95%CI)	0.0022 (0.0016 to -0.0027)	-0.0390(-0.0399 -0.0381)	-0.0468(-0.0477 to -0.0461)
Incremental total costs(95%CI)	1287 (1213 to 1362)	-1351 (-1511 to -1190)	-831(-972 to -690)
Incremental cost-effectiveness ratio	585,000	34,641	17,756

Table 6 - EQ5D utilities and QALYs accrued

	75-80% Fidelity		81-90% Fidelity		91-95% Fidelity	
	n	Mean(s.d.)	n	Mean(s.d.)	n	Mean(s.d.)
Baseline	94	0.57(0.29)	630	0.73(0.28)	120	0.77(0.27)
12 Months	85	0.85(0.19)	501	0.81(0.24)	83	0.84(0.21)
QALYs accrued	71	0.72(0.16)	445	0.76(0.22)	80	0.81(0.19)

Table 7 Fidelity scores in each site over the four years of the study

	Year1	Year2	Year3	Year4	% change year 1 to year 4	% of total score in year 4
Lancashire	179	209	215	226	26	88
Cornwall	186	185	203	198	7	77
Norfolk	194	213	215	219	13	86
Cambridge	203	204	214	237	17	93
Birmingham	205	234	225	230	12	90

Fig 1 - Cost-effectiveness acceptability curves(Complete data)

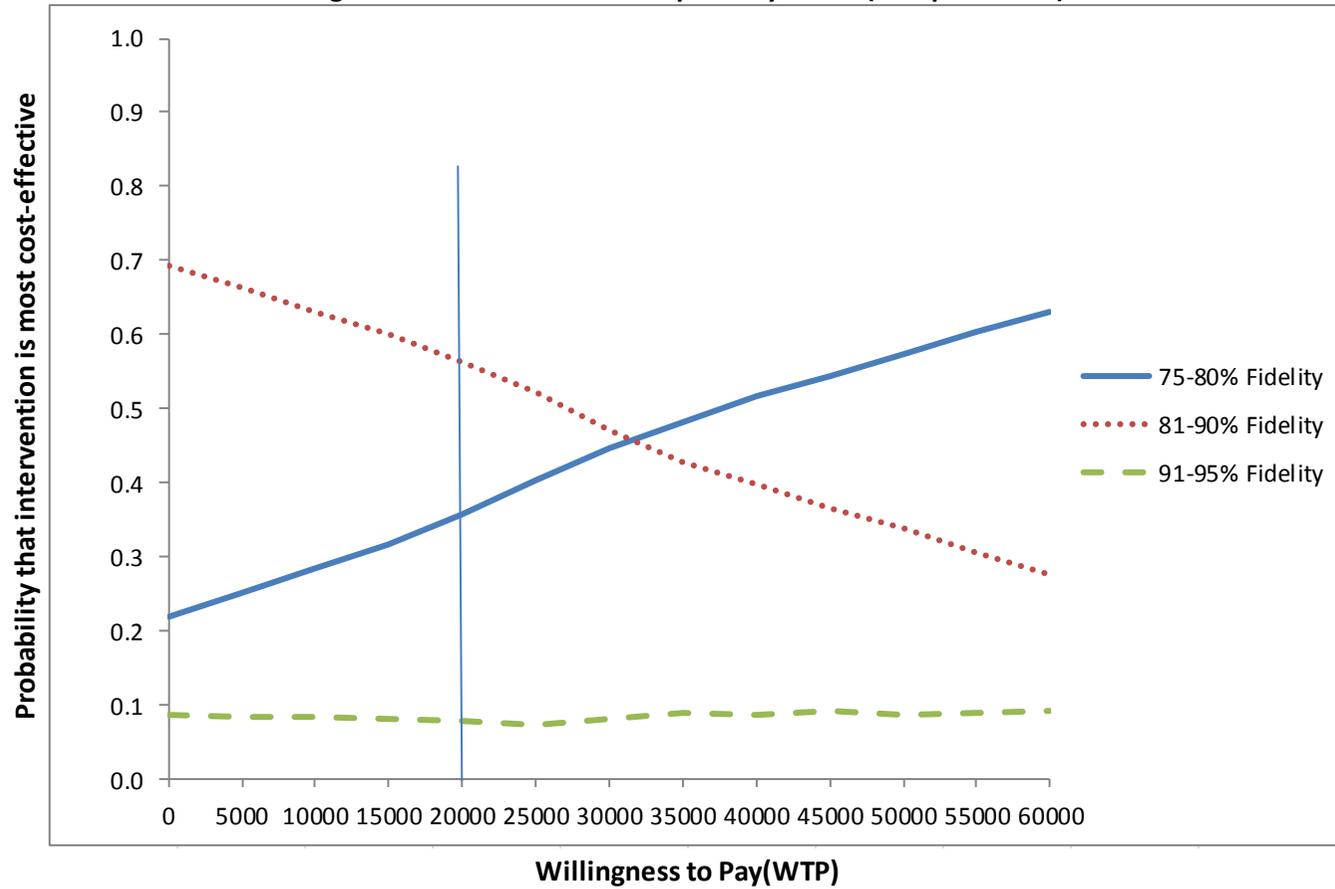


Fig 2 - Cost-effectiveness acceptability curves(Imputed data)

