

<p>Institution: The University of Manchester</p>
<p>Unit of Assessment: 4</p>
<p>Title of case study: ReduceDUP: Socio-economic impact of reducing the duration of untreated psychosis</p>
<p>1. Summary of the impact People who develop psychosis (1% of population) typically experience lengthy delays (months to years) before treatment. Researchers at the University of Manchester (UoM) established a concrete and significant association between delay in treatment of the first episode of psychosis and outcome. We demonstrated that outcome of psychosis could be improved considerably if these lengthy delays were reduced. This research influenced policy and practice in the UK and abroad. Policy changes included the establishment of early psychosis teams dedicated to early detection and treatment (50 in England alone). Practice changes included amendments to clinical guidelines in the UK and abroad that now require clinicians to respond urgently to a first episode of psychosis. These changes to clinical practice have increased the proportion of patients with a short DUP from 55.6 to 77.4%.</p>
<p>2. Underpinning research <i>See section 3 for references 1-6. UoM researchers are given in bold.</i> The impact is based on research that took began at UoM in 1995 and continues to date. The research was part of a continuing programme of work on early psychosis, funded by the Department of Health (DH), the Medical Research Council and the National Institute of Health Research, which has included: systematic reviews, clinical trials, follow-up studies and qualitative studies. The first major publication was in 2000. The key researchers were:</p> <ul style="list-style-type: none"> • Max Marshall (Senior Lecturer, 1995-2001; Professor, 2001-date) • Shôn Lewis (Professor, 1994-date) • Richard Drake (Clinical Research Fellow, 1996-2001; Clinical Lecturer, 2002-2004; Senior Lecturer, 2004-date) • Austin Lockwood (Research Nurse, 1995-2007) • Shahid Akhtar (Clinical Lecturer, 1995-2001) • Clifford J Haley (Clinical Lecturer, 1995-2001) <p>Our research focussed on the duration of untreated psychosis (DUP) in determining the prognosis of schizophrenia. DUP is the time from the appearance of the first psychotic symptom until initiation of adequate treatment. For many years debate raged in the research community between those who believed that untreated psychosis was harmful (in the sense of actually causing permanent damage to the chances of recovery from psychosis) and those who did not. The importance of the debate rested on the fact that if DUP were indeed harmful, then reducing it would be a key way to improve the outcome of an otherwise intractable and expensive condition.</p> <p>Our research settled this debate by demonstrating a clear association. In 2000, we published our first contribution by reporting results from a large cohort study (SOCRATES) funded by the Medical Research Council (1). This research established a strong association between DUP and outcome, and indicated that prognosis was most likely to be improved by urgent intervention. In 2003, we published an expert briefing paper for the DH (2), followed by a narrative review (3) and then a systematic review and meta-analysis of 26 prospective cohort studies involving 4490 first episode patients (4) (funded by NHS nationally commissioned R&D; £43,000, Principal Applicant: Marshall). Our systematic review categorically demonstrated a significant association between DUP and outcomes, including: remission of all symptoms; severity of persistent symptoms (especially, delusions, hallucinations and thought disorder); and social functioning.</p> <p>We also demonstrated that the association between DUP and outcome was present in both the short and long term. Our findings were subsequently confirmed by other researchers and have been summarised in the main international handbook for clinicians working in early psychosis (5). In a more recent review, with our Dutch collaborators, we have also demonstrated an association between DUP and negative symptoms (6).</p>

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3. References to the research

Our research is well documented and highly cited in the top tier of international peer-reviewed journals. For example: in terms of citations, publication 4 is ranked 14th of 1186 papers published in *Archives of General Psychiatry* from 2005-11.

1. **Drake RJ, Haley CJ, Akhtar S, Lewis SW.** Causes and consequences of duration of untreated psychosis in schizophrenia. *The British Journal of Psychiatry.* 2000;177(6):511-5. DOI: 10.1192/bjp.177.6.511
2. **Marshall M.** Early Intervention for People with Psychosis. Expert Briefing Summer 2003. London: Department of Health. <http://www.p3-info.es/PDF/NIMHE.pdf>
3. Norman RMG, **Lewis SW, Marshall M.** Duration of untreated psychosis and its relationship to clinical outcome. *The British Journal of Psychiatry.* 2005;187(48):s19-s23. DOI: 10.1192/bjp.187.48.s19
4. **Marshall M, Lewis S, Lockwood A, Drake R,** Jones P, Croudace T. Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: A systematic review. *Archives of General Psychiatry.* 2005;62(9):975-83. DOI:10.1001/archpsyc.62.9.975
5. **Marshall M,** Harrigan S, **Lewis S.** Duration of Untreated Psychosis: Definition, Measurement and Association with Outcome. In: McGorry P, Jackson H, editors. *The Recognition and Management of Early Psychosis: A preventive approach.* 2nd ed. Cambridge: Cambridge University Press; 2009. pp. 125-46. Available from UoM on request.
6. Boonstra N, Klaassen R, Sytma S, **Marshall M,** De Haan L, Wunderink L, Wiersma D. Duration of untreated psychosis and negative symptoms: A systematic review and meta-analysis of individual patient data. *Schizophrenia Research.* 2012;142(1-3):12-9. DOI: 10.1016/j.schres.2012.08.017

4. Details of the impact

See section 5 for corroborating sources S1-S10.

Context

Psychosis is a serious mental illness characterised by delusions, hallucinations, disordered thinking, disturbed behaviour and poor social functioning. Psychosis is common; about 1% of the population develop psychosis in their lifetime, mostly before the age of 35. Often psychosis becomes a chronic condition and it has substantial economic and social costs. For example, it reduces life expectancy by 15-20 years and costs the UK economy £6.7 billion per year. Typically people who develop psychosis experience lengthy delays (months to years) before receiving treatment. Our research has indicated that the outcome of psychosis could be considerably improved if these lengthy delays were reduced.

Pathways to impact

Our research has arrived at its impact, in the UK and abroad, by influencing:

- (a) national policies that funded early psychosis services to reduce DUP;
- (b) national clinical guidelines that emphasised the need for clinical services to target reductions in DUP;
- (c) radical changes in aspects of best clinical practice at the level of the individual clinician.

Reach and significance of the impact**Impact on mental health policy, leading to improved outcomes****a) England**

Our research was presented to the DH during the implementation of the NHS Plan (2000). The NHS Plan required the establishment of 50 early psychosis services covering the whole of England. A member of the DH mental health policy team (2004-12) confirms that '[t]he research demonstrating the linkage between shorter DUPs and better outcomes was a crucial underpinning of the policy case for early intervention services.' (S1) The research thus contributed to what is described as 'a huge expansion in early intervention services' between 2000 and 2008, 'so that by 2008 the planned comprehensive coverage set out in the NHS Plan of 2000 had been achieved.' (S1) The advisor confirms that support for early intervention services has been maintained under the current government, as evidenced in the cross-government mental health outcomes strategy

Impact case study (REF3b)

published in 2011 (S2). The Chair of the Early Intervention in Psychosis (IRIS) Network, which brings together elected regional early intervention leads, also underlines the importance of the research to recent service development: 'The strengthening evidence base which correlates DUP with improved outcomes has been vital in energising the whole direction of service development' (S3). The 2012 IRIS Guidelines, which cite our research, describe in detail how to organise an Early Intervention Service and are endorsed by Rethink, the national mental health charity and the NHS Confederation (S3). In 2010-11 in England alone, Early Intervention Teams served 10,311 new cases of psychosis. Independent research into the economic impact of Early Intervention Services in England has shown a saving of £4972 per year per person treated, due to better outcomes (S4).

Our Expert Briefing Paper (2) was also utilised by the DH in support of one of the key targets of the NHS Plan: reducing DUP to a median of 3 months. Our research from the National Eden project, a large, multi-centre follow up study of new patients being cared for by early intervention teams, shows that as early intervention services are introduced the proportion of patients with a short DUP increases from 55.6 to 77.4% (**Marshall** et al., 2013, submitted) (S5).

The DH requires the reporting of DUP as part of the National Mental Health Minimum Dataset for all NHS Mental Health Trusts.

As a result of the strong link between DUP and outcome, the DH is considering using DUP as a metric in the Quality and Outcomes Framework for Payment by Results. This would ensure that NHS Trusts have a strong financial incentive to respond quickly to a first episode of psychosis. **Marshall** has been acting as an advisor in these deliberations (S1).

b) International reach

The Australian Government's Department of Health and Ageing cited our research in its Early Psychosis Feasibility Study Report, which underpins the Fourth National Mental Health Plan 2009-14. The Australian Government allocates \$AUS 220 million to fund early detection of psychosis services under the 2009-14 National Mental Health Plan (S6).

The US National Institute of Mental Health (NIMH) is considering a national programme to reduce DUP and is currently issuing calls for research into the impact of reducing DUP. **Marshall** is acting as advisor. The director of the Division of Services and Intervention Research at the NIMH confirms that the NIMH committed \$US 2m in the fiscal year 2013 to support initiatives to test reproducible strategies to reduce DUP among those with first episode psychosis in the USA, with plans to commit similar sums for research into DUP in the fiscal years 2014 and 2015. It is noted that the 'seminal meta-analysis of DUP studies (2005)' (ref 4 above) is cited in both recent funding calls (S7).

State Governments in Canada that are promoting Early Intervention Services have cited our research in policy documents, for example the Ontario *Programme Standards for Early Intervention* (S8). This document acknowledges the contribution of the UoM research, noting that 'There is evidence that longer DUP is associated with poorer outcome once treatment is initiated (**Marshall** et al., 2005' [reference 4 above]; Norman et al., 2005)' (p.6). It then identifies as a key objective the need to 'reduce the duration of untreated psychosis through early and appropriate detection and response, thereby potentially reducing the severity of the illness' (p. 7).

Impact on clinical guidelines and practice**a) England**

Our research is cited in the British Association for Psychopharmacology guidelines for the treatment of schizophrenia. New NICE National Schizophrenia Guidelines for Adults (CG82, 2013; currently out for consultation) now recognise the importance of prompt treatment of first-episode schizophrenia. **Marshall** is a member of the Guidelines Development Group, invited for his expertise in this area. Our research is also cited in the NICE guidelines on Psychosis and Schizophrenia in Young People (CG155, 2013). The director of the National Collaborating Centre for Mental Health writes that **Marshall** 'demonstrated that the clinical outcomes for people

following a first episode of psychosis, even up to 15 years later, were harmed by there being a prolonged period during which no treatment was provided. [Marshall's] paper also highlighted the possibility that the early period of psychosis is the most important period during which most of the long term harm associated with psychoses occurs. This understanding, that the duration of untreated psychosis correlates with worse outcomes for people with first episode psychosis, has been highly influential on our overall approach to the treatment of first episode psychosis and on the recommendations for the suite of NICE guideline[s] identified above [CG82, 2013; CG155, 2013]. The duration of untreated psychosis has, since this paper and the various guidelines have been published, fallen substantially'. (S9) Clinicians working in the NHS are required to abide by the NICE guidelines described above.

b) International reach

The research has been cited in: the Italian national guidelines for early intervention in schizophrenia; the World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Schizophrenia, Part 1: Update 2012 on the acute treatment of schizophrenia and the management of treatment resistance; and the National Guidelines for prevention of mental disorders in children issued by National Research Council and Institute of Medicine of the National Academies in United States (S10).

At least 117 professional articles around the world (e.g., Russia, Germany, France, Spain, Japan and the USA) draw on our review to advocate a more urgent response to first episode psychosis. The key international textbook on the clinical management of first episode psychosis devotes a chapter to our research. It is also cited as critical evidence in the *Clinical Manual of Prevention in Mental Health* (Compton 2009): 'DUP is recognized as a critical variable in the light of evidence associating longer DUP with poorer outcomes...Marshall and colleagues (2005)... found a significant association' (p. 144).

5. Sources to corroborate the impact

Sources available from UoM on request.

- S1. Corroborating statement from team member, mental health policy team, 2004-2012.
- S2. HM Government/Department of Health. *No Health without Mental Health: A Cross-Government Mental Health Outcomes Strategy for People of All Ages* (2011).
- S3. Corroborating letter from Chair of IRIS network, GP and carer; IRIS Guidelines (2012).
- S4. Department of Health. Chief Nursing Officer Bulletin, 26 June 2012.
- S5. **Marshall M**, et al. The National Eden Study – Impact of introducing early intervention teams on the duration of untreated psychosis: prospective cohort analysis (submitted 2013).
- S6. Australian Government Department for Health and Ageing, Early Psychosis Feasibility Study Report (2011); Australian Government, Budget 2011-12, Budget Paper No.3, Part 2: Payments for Specific Purposes – Health.
- S7. Corroborating email from the Director, Division of Services and Intervention Research, National Institute of Mental Health (Washington, USA) on impact on policy making at NIH.
- S8. Early Psychosis Intervention Program Standards, Ontario Ministry of Health and Long-Term Care. 2011.
- S9. Corroborating email from the Director, National Collaborating Centre for Mental Health, Royal College of Psychiatrists, Medical Director and Consultant Psychiatrist, Sheffield Health and Social Care NHS Foundation Trust.
- S10. De Masi S, et al. The Italian guidelines for early intervention in schizophrenia: development and conclusions. *Early Intervention in Psychiatry*. 2008; 2(4): 291-302; World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Schizophrenia, Part 1: Update 2012 on the acute treatment of schizophrenia and the management of treatment resistance. *The World Journal of Biological Psychiatry*. 2012;13(5):318 -378; Committee on the Prevention of Mental Disorders and Substance Misuse Among Children, Youth and Young Adults, O'Connell ME et al., editors. *Preventing Mental, Emotional, and Behavioral Disorders Among Young People*. Washington: The National Academies Press; 2009.