# Aggressive Research Intelligence Facility (ARIF)

ARIF was a specialist unit based at the University of Birmingham whose role was to improve the incorporation of research findings into population level health care decisions in the NHS in the West Midlands.

*Meta study of Sex-Reassignment health benefits.*

This is a brief summary of the evidence available at the time. Readers should not use the comments made in isolation and may wish to consult the references provided. Please be aware that new evidence may have become available since the request's completion in April 1997 and Update in July 2004.

The Problem Submitted for ARIF to Advise Upon: What are the effects of gender reassignment surgery, and does the balance of positive and negative effects suggest that this procedure is clinically effective overall?

Question Reformulated A detailed consideration of the main elements of the question was undertaken: Reviews Identified An extensive bibliography of relevant studies was compiled; the list below represents those references most pertinent to the comments section.

INTERVENTION: Do different surgical procedures have different effects and has the technical skill with which the procedure is generally performed improved over time?

 POPULATION: Does the nature of the effects depend on characteristics of the person submitted for surgery? It would be expected that the following would have an important bearing: Whether the original biological sex is male or female. The degree of certainty about the diagnosis, distinguishing between the general condition of gender dysphoria and recognised causes of this such as transvestitism, homosexuality and primary transsexualism. Other characteristics of the patient beyond the primary diagnosis, such as previous treatment and coexisting conditions.

 OUTCOMES: In the case of gender reassignment the following outcomes would be expected to be important: Immediate success of surgery - complications of surgery, cosmetic/aesthetic effect, requirement for reoperation. Health outcomes for the individual - especially suicide. Psychological outcomes for the individual - measures of adjustment, happiness, regret or satisfaction with the operation. Social outcomes for the individual - ability to work, maintain relationships and generally contribute to society. Health/psychological/social outcomes for other family members. Societal outcomes - especially use of health care resources.

 Reviews Identified

An extensive bibliography of relevant studies was compiled; the list below represents those references most pertinent to the comments section.

Brown GR. A review of clinical approaches to gender dysphoria. Journal of Clinical Psychiatry 1990; 51: 57-64

Other Literature Identified

Snaith P et al. Sex reassignment surgery. A Study of 141 Dutch transsexuals. British Journal of Psychiatry 1993; 162: 681-5 Meyer JK, Reter DJ. Sex reassignment: follow up. Archives of General Psychiatry 1979; 36: 1010- 1015 Abramowitz SI. Psychosocial outcomes of sex reassignment surgery. Journal of Consulting and Clinical Psychology 1986; 54: 183-189 Williams G. Gender reassignment today. British Medical Journal 1987; 295: 1348 Mate-Kole KC et al. A controlled study of psychological and social change after surgical gender reassignment in selected male transsexuals. British Journal of Psychiatry 1990; 157: 261-4Kuiper B, Cohen-Kettenis P. Sex reassignment surgery: a study of 141 Dutch transsexuals. Archives of Sexual Behaviour 1988; 17: 349-457

The overall conclusion reached by ARIF was: The degree of uncertainty about any of the effects of gender reassignment is such that it is impossible to make a judgement about whether the procedure is clinically effective. This was based on the following observations on the literature identified:

Brown GR. A review of clinical approaches to gender dysphoria. Journal of Clinical Psya. Journal of Clinical Psychiatry 1990; 51: 57-64 Snaith P et al. Sex reassignment surgery. A Study of 141 Dutch transsexuals. British Journal of Psychiatry 1993; 162: 681-5 Meyer JK, Reter DJ. Sex reassignment: follow up. Archives of General Psychiatry 1979; 36: 1010- 1015 Abramowitz SI. Psychosocial outcomes of sex reassignment surgery. Journal of Consulting and Clinical Psychology 1986; 54: 183-189 Williams G. Gender reassignment today. British Medical Journal 1987; 295: 1348 Mate-Kole KC et al. A controlled study of psychological and social change after surgical gender reassignment in selected male transsexuals. British Journal of Psychiatry 1990; 157: 261-4 Kuiper B, Cohen-Kettenis P. Sex reassignment surgery: a study of 141 Dutch transsexuals. Archives of Sexual Behaviour 1988; 17: 349-457

There is no systematic review of the available research literature, thus even the better reviews identified (Brown GR, 1990) do not give sufficient detail about the review method to assure that bias has been avoided. Making a judgement about the clinical effectiveness of gender reassignment surgery is immediately made difficult without unbiased review of the available research. There seem to have been at least 30 research assessments of the effects of gender reassigment surgery (Brown GR, 1990). The number of these particularly dictates that some sort of systematic review is necessary to make a balanced judgement about what the effects actually are. Further, the development of research in the field suggests that criticisms of early studies have only been reacted to more recently (Snaith P et al, 1993). This emphasizes that any reviews must not only be systematic, but up-to-date. Although the research published generally states that the effects are beneficial, it would be incorrect to say that this finding has been universal (Meyer JK, Reter DJ, 1979). This study has been heavily criticised on grounds of method, but given that most of the research designs used to answer the question are highly susceptible to bias, its results cannot be easily discounted on this basis (Abramowitz SI, 1986). Further, individuals involved in providing gender reassignment surgery have actually voiced their concern that the results of available research are misleading (Williams G, 1987). One should not overstate the importance of an opinion, but a challenge to the "face validity" of the results should prompt closer scrutiny of whether there are grounds to suspect that the "researchers might have got it wrong".

Most research designs employed to investigate the effects of gender reassignment surgery have not employed a control group. This means that it is very difficult to ascribe any effects identified to the surgery performed. The alternative explanation that improvements would have occurred anyway, because as time passes the individual adjusts better to their circumstances, is plausible and has received support from a study which did contain a control group (Meyer JK, Reter DJ, 1979). The results of this on its own are not sufficient to overturn the results of other studies performed, but it does raise doubts about the true nature of the effect of gender reassignment surgery, which should at least have been more intensively investigated than has been the case. The only study (Mate-Kole et al, 1990) to have taken up this challenge compared outcomes in 20 patients having immediate surgery with 20 patients awaiting surgery. Its results seem to reinforce the existence of benefit observed in the studies without controls, but the correct comparison is between one small controlled study (Meyer JK, Reter DJ, 1979) which showed little effect of surgery against another similarly small study (Mate-Kole et al, 1990) showing benefit. Further, the latter study is also not without flaws. A particular concern is bias in the assessment of outcome. It would have been clear to both the participants and the investigators whether they were in the treatment or control group and in such circumstances it is highly likely that questions using the options, "more active/same/less active" could have received biased responses. Results obtained for those in the treatment group will have a tendency to overestimate the effect of the surgery, and results for those in the control group will have a tendency to underestimate the effect of "usual" treatment.

The final basis for the assertion that there is considerable uncertainty about the effects of gender reassignment surgery is the high rates of loss to follow-up in many studies, over 50% in some cases (Kuiper B, Cohen-Kettenis P, 1988). Although loss is inevitable to some degree, high rates are important sources of bias, particularly where there is no control group. The reason for this is that it may be the surgery itself and the consequences of it, e.g dissatisfaction or even suicide, causing the drop-outs. Thus those patients who are examined to obtain the results are self-selected towards those who have better outcomes.

The points above, by raising significant problems in the conduct of much of the research claiming to show that gender reassignment surgery is beneficial, suggests that the true conclusion from the available research is that we genuinely cannot be certain about what its effects are. A systematic review could help reduce this uncertainty, but because of the flawed nature of the majority of the research it is likely that the only way to reduce the level of uncertainty is to undertake more research using more rigorous designs with a control group, ideally randomly assigned, and blind independent assessment of outcomes (Abramowitz SI, 1986). Request Carried Out: April 1997

Updated: July 2004 The search for literature conducted in 1997 was up-dated following media interest in this topic, and direct contact concerning our original request. We re-ran searches on the Cochrane Library, MEDLINE and PsycINFO as well as interrogating websites of key organisations involved in health technology assessment such as NICE, CCOHTA, AHRQ and NZHTA. [Further details of locations searched and search terms used are available on request].

The search was conducted on 5/7/04. Although many narrative reviews have been published since 1997, there were only two satisfying criteria for being systematic e.g. statement of sources searched: These identified no randomised controlled trials or controlled trials to the end of 2001 and mostly based their conclusions on cohort studies and case-series. Both reviews while recognising net benefits to carefully selected individuals remained concerned about the quality of evidence on effectiveness (particularly adverse outcomes) and the biases to which available studies were open. [In particular see discussion in section 5.2 of the report by Best and Stein.] Our searches confirm absence of randomised controlled trials and controlled trials to December 2001, and have identified none since then to the end of June 2004. Further cohort studies and case-series appear to have been published eg Lawrence AA. Factors associated with satisfaction or regret following male-to-female sex reassignment surgery. Archives of surgery with 20 patients awaiting surgery. Its results seem to reinforce the existence of benefit observed in the studies without controls, but the correct comparison is between one small controlled study (Meyer JK, Reter DJ, 1979) which showed little effect of surgery against another similarly small study (Mate-Kole et al, 1990) showing benefit. Further, the latter study is also not without flaws. A particular concern is bias in the assessment of outcome. It would have been clear to both the participants and the investigators whether they were in the treatment or control group and in such circumstances it is highly likely that questions using the options, "more active/same/less active" could have received biased responses. Results obtained for those in the treatment group will have a tendency to overestimate the effect of the surgery, and results for those in the control group will have a tendency to underestimate the effect of "usual" treatment. The final basis for the assertion that there is considerable uncertainty about the effects of gender reassignment surgery is the high rates of loss to follow-up in many studies, over 50% in some cases (Kuiper B, Cohen-Kettenis P, 1988). Although loss is inevitable to some degree, high rates are important sources of bias, particularly where there is no control group. The reason for this is that it may be the surgery itself and the consequences of it, e.g dissatisfaction or even suicide, causing the drop-outs. Thus those patients who are examined to obtain the results are self-selected towards those who have better outcomes.

Best L, Stein K. Surgical gender reassignment for male to female transsexual people. Development and Evaluation Committee Report No 88. Southampton: Wessex Institute for Health Research & Development, 1998

Day P. Trans-gender reassignment surgery. NZHTA Tech Brief Report 2002 Vol 1 No 1. Christchurch: New Zealand Health Technology Assessment (NZHTA), 2002

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 eg Lawrence AA. Factors associated with satisfaction or regret following male-to-female sex reassignment surgery. Archives of Sexual Behaviour .2003 ;32(4):299-315.

 We have not assessed in detail whether all these studies are open to the level of bias which gave rise to the uncertainty in the DEC and NZHTA reports, although the concerns about loss to follow-up do apply to the specific article quoted where only 232 out of 727 persons undergoing surgery were represented in the main results.

If a parallel control group is not feasible, as proponents of gender reassignment surgery suggest, follow-up studies must convince readers that they have identified a representative cohort of individuals (particularly with respect to likelihood of experiencing benefits or disbenefits) and represented all of these in the final results. The logistics of following patients up over long periods and achieving a cohort which is not influenced by the immediate results (i.e. individuals with good/very poor outcomes most likely to remain in touch with surgeon) strongly suggest that the cohort studies should also be conducted prospectively (study planned and organised before data collection begins).