Institution: Cardiff University

Unit of Assessment: UoA4

Title of case study: New tools support citizens, governments and health professionals to address effects of infertility

1. Summary of the impact (indicative maximum 100 words)

Around 72 million people worldwide have problems conceiving a child. Research at Cardiff University has led to the development of a suite of self-help tools that help individuals and healthcare professionals to manage the problems that infertility brings. The FertiSTAT tool provides individually tailored fertility guidance and has played a central role in fertility awareness campaigns in Europe and beyond. FertiQoL, a measure of fertility-related quality of life, is used in clinical trials and by clinicians to assess how infertility affects patients' quality of life. Finally, the PRCI tool is used in clinics to help women cope with the stresses involved in fertility treatment.

2. Underpinning research (indicative maximum 500 words)

The World Health Organisation ranks infertility fifth in its list of disabilities affecting the global population aged below 60 years. In 2005 Jacky Boivin (then Senior Lecturer 2003-07, later Reader 2007-10 and Professor 2010-ongoing) began research that has led to the development and evaluation of tools that help patients and professionals across the world to manage fertility issues.

Fertility awareness studies (FertiSTAT)

Boivin and Laura Bunting (postgraduate, 2005-2008) developed a tool to support fertility awareness initiatives and improve fertility knowledge. Unlike other common diseases (e.g., cardiovascular) no validated symptom awareness tool existed for fertility health. The researchers designed FertiSTAT (the Fertility Status Awareness Tool) to be a self-administered tool that takes women through a series of questions about their lifestyle and reproductive profile in order to generate personalised fertility guidance based on their risk profile.[3.1] An evaluation study with over 1000 women showed that the tool could discriminate between medically confirmed fertile and infertile women.[3.1]

Between 2009 and 2010 Boivin and Bunting (postdoc, 2008-2013) surveyed 10,045 people of childbearing age in 18 countries about their knowledge of signs, symptoms and preventable causes of infertility. Participants had poor knowledge, indicating the need for the FertiSTAT tool as a way of stimulating public awareness campaigns.[3.2]

Studies of patient quality of life (FertiQoL)

Between 2005 and 2010 Boivin coordinated research that led to the development of FertiQoL (Fertility Quality of Life). Prior to this work there existed no validated quality of life measure for general fertility problems. FertiQoL was designed to fill this gap and to make it possible for fertility professionals (e.g., clinicians, industry, psychologists) to collect quality of life data in order to inform medical practice, drug development, research, service evaluation and/or policy.

Boivin led this research, together with J. Takefman (McGill University) and A. Braverman (then at University of Medicine and Dentistry of New Jersey). The multidisciplinary research involved 27 experts from 11 countries, patient focus groups, feasibility research across 10 countries, and an international psychometric evaluation with over 1400 volunteers.[3.3]

High stress waiting studies (PRCI)

Between 2006 and 2012 Boivin analysed archival data and showed that waiting for the results of a pregnancy test following fertility treatment was the most stressful stage of treatment. Yet there were no inexpensive, self-help interventions to support infertile women.[3.4] Boivin's team developed the Positive Reappraisal Coping Intervention (PRCI) tool to address this need. The PRCI comprises a two-page self-explanatory leaflet and 10 statements designed to promote the coping strategies that theory and research have shown to be effective in unpredictable, uncontrollable

situations such as the waiting period.[3.5] Women are encouraged to read these statements daily in order to support them during this waiting period.

In a randomised feasibility trial Deborah Lancastle (postgraduate, 2001-2006) showed that fertility patients found the tool practical, easy to use, and helpful in reducing stress during the waiting period.[3.5] Henrietta Ockhuijsen (postgraduate, University Medical Centre Utrecht, 2009-2013) showed that PRCI made the stress of fertility treatment more tolerable in a longitudinal phase III randomised trial of PRCI (N= 375) [3.6] under the supervision of Boivin and medical co-supervisors Nicholas Macklon (Professor, Obstetrics/Gynaecology, University of Southampton) and Agnes van den Hoogen (Nurse, Neonatology, University Medical Centre, Utrecht).

3. References to the research (indicative maximum of six references)

1. **Bunting, L.**, & **Boivin, J.** (2010). Development and preliminary validation of the Fertility Status Awareness Tool: FertiSTAT. *Human Reproduction*, **25**(7), 1722-1733. http://dx.doi.org/10.1093/humrep/deq087
2. **Bunting, L.**, Tsibulsky, I., & **Boivin, J.** (2013). Fertility knowledge and beliefs about fertility treatment: findings from the International Fertility Decision-making Study. *Human Reproduction*, **28**(2), 385-97. http://dx.doi.org/10.1093/humrep/des402
3. **Boivin, J**., Takefman, J., & Braverman, A. (2011). The fertility quality of life (FertiQoL) tool: development and general psychometric properties. *Human Reproduction*, **26**(8), 2084-2091. http://dx.doi.org/10.1093/humrep/der171
4. **Boivin, J.,** & Lancastle, D. (2010). Medical waiting periods: Imminence, emotions and coping. *Women's Health*, **6**(1), 59-69. http://dx.doi.org/10.2217/whe.09.79
5. Lancastle D., & **Boivin J.** (2008). A feasibility study of a brief coping intervention (PRCI) for the waiting period before a pregnancy test during fertility treatment. *Human Reproduction*, **23**(10), 2299–2307. http://dx.doi.org/10.1093/humrep/den257
6. Ockhuijsen, H. D. L, van den Hoogen, A., Macklon, N. S., & **Boivin, J.** (2013). Study protocol for the PRCI study: Design of a randomized clinical trial to evaluate a coping intervention for medical waiting periods in women undergoing a fertility treatment. *BMC Women's Health, 13,* 35. http://www.biomedcentral.com/1472-6874/13/35

Notes: *Human Reproduction* had a 2012 impact factor of 4.670, and is ranked second out of 28 journals in reproductive biology and health, and third out of 78 journals of obstetrics and gynaecology (latest *Journal Citation Reports*, Thomson ISI).

Cardiff researchers in **bold**.

Key funding sources

- Psychosocial factors associated with the initiation, success and termination of fertility treatment. Case studentship to L. Bunting (2005-2008) jointly funded by BBSRC and Merck Serono S.A. £49,864.
- Understanding risk and help-seeking in the context of female fertility. ESRC/MRC Postdoctoral 2-year Fellowship Scheme (Ref. PTA-037-27-0192). Mentors: Professor J Boivin & Professor G Elwyn. £179,035. Nov 2010-July 2013 (no-cost extension for maternity).
- His & her biological clock: Reproductive decision-making and reproductive success in the 21st century. ESRC (Ref. RES-355-25-0038). Boivin, Henwood & Ledger (2009-2010). £177,000.
- Worldwide Infertility Survey. Merck-Serono S.A. educational grant to Boivin (Oct 2008-May 2010). £83,000.
- Development and validation of an international Fertility Quality of Life (FertiQoL) measure. Jointly funded by European Society for Human Reproduction & Embryology, American Society for Reproductive Medicine, and Serono International S.A. Boivin (2006-2007). $66,000 (£34,971).
- Negative feedback, stress, biologic response and outcome in infertility treatment. ESRC (Ref.

RES-000-221-701). Boivin & Walker (1995-1997). £42,000.

4. Details of the impact (indicative maximum 750 words)

The tools achieved the goals of (a) stimulating public awareness of fertility risks, (b) making it feasible to integrate measures of quality of life into fertility care and (c) providing support for patients during fertility treatment.

Stimulating public awareness of infertility risks

FertiSTAT has been and continues to be used by public health authorities and in media campaigns in numerous countries to raise awareness about preventable infertility.

In Belgium, a 2009 media campaign sponsored by the Ministry of Welfare, Health & Family attracted young people to an interactive website that distributed information about preventable causes of infertility using FertiSTAT. Promotional posters were distributed (to clubs, chemists, gynaecology offices) with the tag-line "Test your fertility". In the 6 weeks that followed around 7,500 unique visitors accessed the website and viewed an average of six pages of fertility information.[5.1] In Japan in 2011, *FRaU* magazine (circulation 170,000) used FertiSTAT in a fertility awareness campaign directed at young Japanese career women. A post-publication seminar for nearly 250 women showed that over 70% of them were more aware of and concerned about their fertility health and more than half stated they were now better informed about the behaviours they should change and when to seek timely medical advice in order to safeguard their fertility health.[5.2] In the UK, *Red* magazine (circulation 231,160) listed FertiSTAT as one of the best e-health tools (November 2011); following publication 1434 women visited the Cardiff University website, completed the tool online and received fertility guidance, 26% of whom received guidance about preventable causes that they could immediately address to safeguard their fertility. [5.3] Similar campaigns have been run in Sweden and Portugal and another is planned in Canada.

Integration of tools into medical practice and research

FertiQoL is now available in 30 languages on Cardiff University's website. Every month approximately 70 unique IP addresses download FertiQoL from the website. The tool has been downloaded more than 1,700 times in the past 2 years.

The significance of the FertiQoL tool for fertility professionals is underlined by the efforts of leading fertility societies to promote the tool to their members. The Editors-in-Chief of the two journals serving the American Society for Reproductive Medicine and the European Society for Human Reproduction & Embryology agreed to publish simultaneously the FertiQoL development and validation paper[3.3] to ensure dissemination of the tool to their combined membership of 14,000 persons. The International Federation of Obstetrics and Gynecology (FIGO), which has member associations in 125 countries, included FertiQoL in its "FIGO Infertility ToolBox" which was developed to improve infertility care pathways in both low and high resource countries.[5.4] EMD Serono Inc distributed FertiQoL to clinicians at two consecutive annual fertility conferences (2009, 2010) that were attended by around 8,000 fertility doctors.[5.5] The World Health Organisation (Department of Reproductive Health Research) is also adapting FertiSTAT so that community health workers in its collaborating centres can use it to address poor fertility health habits in low resource health settings,[5.6] and recently awarded a work performance package for this work to be started.[5.7]

The uptake of FertiQoL within the medical community shows an increased awareness of the importance of quality of life and an expansion in the range of clinical outcomes regarded as important. There are now several published FertiQoL validation studies (in Dutch, Hungarian, Spanish, Taiwanese), and studies on correlates of fertility quality of life.

Support for patients during fertility treatment

Cardiff University has granted user permission to 150 professionals, researchers, and clinics internationally who have contacted Boivin's team about using PRCI. These clinics, which have a combined patient population of many thousands, include the Shady Grove Fertility Group (USA) which has adopted PRCI in its 18 clinics (6,000 cycles of treatment per year); this group's service

evaluation has shown that PRCI has benefited patients and staff.[5.8] Merck Serono is offering the PRCI tool on its patient support site.[5.9]

Contribution to policy

In February 2011 Boivin presented results of her research showing poor fertility knowledge among Japanese people to Yūko Obuchi, Minister of State for Social Affairs and Gender Equality, whose responsibility it is to address the declining birth rate in Japan. In June 2012 Boivin's research showing poor fertility knowledge among Japanese people of childbearing age led the Japanese national television channel NHK (Japan Broadcasting Corporation, Nippon Hōsō Kyōkai) to broadcast a documentary featuring Boivin discussing this research. Boivin's research[3.2] was subsequently used to support a recommendation by The Task Force for Tackling the Crisis of Falling Birth Rate by Dr. Hidekazu Saito, a member of the Cabinet Office committee, to fund the creation and distribution of a leaflet to improve fertility knowledge.[5.10]

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. Report prepared for the Belgian Minister of Health. The use of FertiSTAT in the 2009 campaign is corroborated on page 6 and the viewer statistics for the "Test Your Fertility" website reported on page 9 show that there were 7500 unique visitors reading an average of 6 pages of fertility information.
2. Page 1 of the document shows data from the 2011 post-publication seminar with 243 young Japanese women, confirming that 70% felt more aware/concerned about their fertility after reading the article and completing the FertiSTAT published in Japanese *FRaU* magazine (pp. 2-4 of document for the magazine article).
3. Page 1 of the document shows data from 1434 readers who used the Cardiff University fertistat.com website and completed FertiSTAT online in the 6 months following publication of the *Red* magazine feature (November 2011 issue, released October 2011): "20 health websites you need to know about" (page 2 of document shows the magazine article).
4. FIGO Infertility ToolBox for low and high resource countries with page 36 of the document showing inclusion of FertiQoL for measurement of quality of life outcomes.
5. Exhibition panels and distribution cards confirming Merck Serono S.A. distributed FertiQoL at 2009 meeting of American Society for Reproductive Medicine (pages 1-12 for panels; page 13-14 for Merck's letter of interest and request for approval)
6. Corroborative statement by a Research Scientist from the Department of Reproductive Health & Research, World Health Organization (WHO) on the WHO adoption of FertiSTAT
7. Agreement for Performance of Work between WHO Department of Reproductive Health and Research and Prof J. Boivin: Fertility awareness and health care provider tools for research.
8. Written statement by the Director, Psychological Support Services, Shady Grove Fertility Reproductive Science Center about the impact of using PRCI in its clinics.
9. See website of Merck Serono SA incorporating Cardiff University tool http://www.fertility.com/en/stage3/tools/waiting_card/waiting_card.html (also saved as pdf on July 18 2013 and available from HEI).
10. Report to the The Task Force for Tackling the Crisis of Falling Birth Rate in which Dr. Hidekazu Saito (National Center for Child Health and Development), member of the Cabinet Office committee, cites the Boivin research (Section 3, ref. 2) in support of a recommendation to fund the creation of a leaflet to improve fertility knowledge in Japanese women.

All evidence available on request from the HEI.