UROGENITAL FISTULA: STUDIES ON EPIDEMIOLOGY AND TREATMENT OUTCOMES IN HIGH-INCOME AND LOW- AND MIDDLE-INCOME COUNTRIES

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Paul Hilton MB, BS (Newcastle University, 1974); MD (Newcastle University, 1981); FRCOG (Royal College of Obstetricians & Gynaecologists, 1996)

Clinical Academic Office (Guest) and Institute of Health and Society (Affiliate)

Newcastle University, Newcastle upon Tyne, United Kingdom

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Declaration

In accordance with the University 'Rules for submission of work for higher degrees', the candidate declares that:

- This submission is the candidate's own work, save for those collaborations acknowledged in the relevant section below, where the candidate's contribution to the work is estimated.
- No part of the material offered has been previously submitted for a degree or other qualification in this or any other University, save for those publications so annotated, and listed in Appendix B as '*other works put forward as evidence of the scope of the candidate's contribution to the broader field of study - i.e. urogynaecology*'.
- The candidate has no outstanding financial obligations to the University.

Signed: 

Name: Paul Hilton Date: 10/09/2018

Abstract

UROGENITAL FISTULA: STUDIES ON EPIDEMIOLOGY AND TREATMENT OUTCOMES IN HIGH-INCOME AND LOW- AND MIDDLE-INCOME COUNTRIES

It has long been recognised that urogenital fistulas in low- and middle-income countries are predominantly of obstetric aetiology, whereas those in high-income countries usually follow pelvic surgery. This disparity was confirmed in systematic review (*included as paper 1*) and in large cohort studies undertaken in Nigeria (*paper 2*) and the UK (*paper 3*). Whilst there is no standardisation of outcome measures, the same studies report treatment 'success' in approximately 80-90% of cases in low- and middle-income countries (*papers 1 & 2*) and 95% in high-income countries (*papers 1 & 3*).

It is recognised that obstetric fistula patients commonly suffer debilitating stress urinary incontinence even after successful closure of their fistula (*paper 1*). Urodynamic investigation in a cohort of fistula patients in UK also showed a high incidence of functional abnormalities (*paper 4*). Many of these resolved after repair, and most women reported minimal impact on quality of life in the long-term (*paper 5*).

Success rates were found to be lower following second operations than first in cohort studies from Nigeria (*paper 2*) and UK (*paper 3*), and in a UK national cohort study (*paper 8*). This latter study also found idiosyncratic patterns of care, with re-operation rates related to workload, varying between 0% and 50% (*paper 8*).

Evidence is presented to support an increase in risk of iatrogenic (post-hysterectomy) fistulas in high-income countries (*papers 6 & 7*). There also is a growing perception by colleagues in low- and middle-income countries of an increase in urogenital fistulas that may be, in part, iatrogenic in nature. These trends-may reflect supervision and surgical experience accrued in training and workload maintained in independent practice. In both situations, it behoves those responsible for training and workforce planning in healthcare to ensure an appropriately trained and supervised workforce is maintained in the correct working environment.

Dedication

This submission is dedicated, first, to those women whose suffering from adverse effects of maternity and surgical care form the subject matter of this work; second, to those who inspired and encouraged me to undertake this work, who were in turn my respected teachers, supportive colleagues, guiding mentors and dear friends; they each dedicated their professional lives over many decades to the improvement of women's health in under-resourced of areas world where such advocacy comes only at considerable personal cost. They are specifically:

- the late Professor John Bateman Lawson, previously of University of Ibadan, Nigeria, and Newcastle General Hospital, Newcastle upon Tyne, UK (*deceased October 1997*);
- the late Sister Dr Ann Ward, of the Medical Missionaries of Mary and the Pope John Paul II Family Life Centre & VVF Unit, Mbribit Itam, and St Luke's Hospital, Anua, Akwa Ibom State, Nigeria (*deceased May 2016*); and
- the late Sister Dr Maura Lynch, of the Medical Missionaries of Mary and St Anne's Fistula Unit, St Joseph Kitovu Hospital, Masaka, Uganda (*deceased December 2017*).

Acknowledgements

The contributions of the following colleagues are gratefully acknowledged:

The late Sister Dr Anne Ward (Nigeria) of the Medical Missionaries of Mary who introduced me to surgery for obstetric urogenital fistula in low- & middle-income countries during a visit to the Pope John Paul II Family Life Centre & VVF Unit, Mbribit Itam, and St Luke's Hospital, Anua, Akwa Ibom State, Nigeria, in 1989. She generously allowed me to review the outcomes of her fistula work over the period 1970 to 1994 during a subsequent visit in 1995, which formed the basis of paper 2 in this submission.

The majority of surgery reported in paper 2 was carried out by my co-author, Sr Dr Anne Ward, who approved the final version of the manuscript for publication. The protocol development, data collection, analysis and writing of the manuscript were carried out wholly by the candidate; this is estimated as a personal contribution to the publication of 95%.

Dr Lucia Dolan (previously subspecialty trainee in urogynaecology, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; now consultant gynaecologist and subspecialist in urogynaecology, Belfast Health & Social Care Trust, Belfast, Northern Ireland), and Miss Liz Dixon (retired nurse consultant in urogynaecology, Newcastle upon Tyne Hospitals NHS Foundation Trust) for their contributions to paper 5.

The co-authors contributed to the acquisition and analysis of data, drafting and revision of the paper. The candidate conceived and designed the study, contributed to investigations and undertook all surgery; he also contributed to acquisition and analysis of data, and drafting and revision of the paper; all authors approved the final version for publication; this is estimated as a personal contribution of 50%.

Drs David Cromwell and Amit Kiran of the Department of Health Services Research and Policy, London School of Hygiene & Tropical Medicine, and the Lindsay Stewart Centre for Audit and Clinical Informatics, Royal College of Obstetricians and Gynaecologists, London, UK, for their contributions to papers 6, 7 & 8.

The co-authors contributed to data extraction and drafting and approval of the final version of the manuscripts; AK additionally undertook data analysis for paper 7, and DC additionally contributed to each study design; the candidate contributed to study design, data extraction and analysis, and drafting and approval of the manuscript; this is estimated as a personal contribution of 50% to papers 5, 6 and 7.

Drs Chris Hillary and Nadir Osman, and Professor Christopher Chapple of Academic Urology Unit, Royal Hallamshire Hospital, Sheffield, UK for their contributions to paper 1.

Dr Hillary, assisted by Dr Osman, undertook data acquisition and analysis and drafting of the manuscript; Prof Chapple and the candidate conceived and designed the study, provided supervision to the other co-authors, critically revised the manuscript for important intellectual content, and approved the final version for publication; this is estimated as a personal contribution of 30%.

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Abbreviations

BFLUTS	Bristol Female Lower Urinary Tract Symptoms (*questionnaire*)
CI	confidence interval
DOA	detrusor overactivity
DRC	Democratic Republic of Congo
FGM	female genital mutilation
GIT	gastro-intestinal tract
GNI	Gross national income (*per capita*)
HFE	'Hamlin Fistula Ethiopia' (*hospitals*)
HIC/s	high-income country/countries
HDI	Human Development Index
HES	Hospital Episode Statistics
ICD	International Classification of Diseases
ICI	International Consultation on Incontinence
ICIQ	International Consultation on Incontinence questionnaire
ICIQ-FLUTS	ICIQ-Female Lower Urinary Tract Symptoms (*questionnaire*)
ICUD	International Consultation on Urological Diseases
LASH	laparoscopically-assisted subtotal hysterectomy
LAVH	laparoscopically-assisted vaginal hysterectomy
LDC/s	least developed country/countries
LEDC/s	less economically developed country/countries
LMIC/s	low- and/or middle-income country/countries
NHS	National Health Service
NMQCO	non-medically qualified clinical officers
NATO	North Atlantic Treaty Organisation
OAB	overactive bladder
OCEBM	Oxford Centre for Evidence-based Medicine
OPCS	Office for Population Censuses and Surveys

PDG	patient-defined goal
POP	pelvic organ prolapse
QoL	quality of life
RAH	radical abdominal hysterectomy
RCT	randomised controlled trial
SUI	stress urinary incontinence
STH	subtotal abdominal hysterectomy
TAH	total abdominal hysterectomy
TLH	total laparoscopic hysterectomy
UDC/s	underdeveloped country/countries
UN	United Nations
UNDP	United Nations Development Programme
UVF	urethrovaginal fistula
USI	urodynamic stress incontinence
UTI	urinary tract infection
UUI	urgency urinary incontinence
UI	urinary incontinence
VBAC	vaginal birth after caesarean
VH	vaginal hysterectomy
VVF	vesicovaginal fistula
WHO	World Health Organization
YAG	yttrium aluminium garnet (*as in YAG laser*)

Conventions

Abbreviations

Abbreviations are not used in the title, headings or abstract of the submission. They are defined at their first mention in the main text, followed by the abbreviation itself stated in parentheses; thereafter only the abbreviation used.

Classification of countries

The terms '*high-income country*' and '*low- and middle-income countries*' are used throughout this submission, to include the general descriptive, political, economic and developmental categorisations of global society. Hence, they embrace such terms as '*developed*' and '*developing*', '*well-resourced*' and '*poorly resourced*', '*first world*' and '*third world*' *etc*., respectively.

See further detail and justification for this convention on pages 1-5 in: chapter 1 - Background literature – Introduction - Categorisation of countries.

Fistulas *vs*. fistulae

The word '*fistulas'* is used as the pleural of fistula throughout this submission, as opposed to the alternative '*fistulae*', except where previously published work including the alternative form is cited.

References

The 'Newcastle Harvard' style of referencing is employed.

Chapter 1: Background literature

Introduction

CATEGORISATION OF COUNTRIES

The classification of countries on the basis of the level of development of their economic, political and healthcare systems has varied over the last few decades, with terms often used in a purely descriptive sense, or for statistical convenience and not necessarily conveying any objective judgement about the stage reached by a particular country in the processes of human development. Numerous terms have been used with varying degrees of acceptance, acceptability and usefulness (table 1).

A developing country (otherwise described as a low- or middle-income country (LMIC), less developed country, less economically developed country (LEDC), or underdeveloped country (UDC)) is a country with a less developed industrial base and a low Human Development Index (HDI) relative to other countries (United Nations Development Programme, 1990; United Nations Statistics Division, 2017). However, this definition is not universally agreed upon; nor is there any clear agreement over which countries fit this category.

The term '*developing*' describes a currently observed situation and not a changing dynamic or expected direction of progress. Since the late 1990's, many developing countries have tended to demonstrate higher growth rates than developed countries. Developing countries include, in decreasing order of economic growth: newly industrialized countries, emerging markets, frontier markets, and least-developed countries; the latter being the poorest of the developing countries (United Nations Department of Economic and Social Affairs - Development Policy and Analysis Division, 2018).

Developing countries tend to have some characteristics in common. In particular, with regards to health risks, they commonly have: low levels of access to safe drinking water, sanitation and hygiene; energy poverty; high levels of pollution (*e.g.* air pollution, indoor air pollution, water pollution); high proportion of people with tropical and infectious diseases; high number of road traffic accidents. Often, there is also widespread poverty, low educational levels, corruption at all government levels

and a lack of good governance. Effects of global warming (climate change) are expected to impact developing countries more than wealthier countries, as most of them have a high '*climate vulnerability*'.

The so-called '*three-world*' model was used after the second world war to define countries aligned with NATO (the first world), the Communist Bloc (the second world), or neither (the third world) (Leonard, 2006). Since the mid- 1970's the concept has been extended to include stateless, poor, and marginal nations, ancient, indigenous tribal, and non-industrial nations and nation-states (the fourth world) (Manuel and Posluns, 1974).

Hence, the '*third world*' was originally a political, rather than an economic, grouping. Since the end of the Cold War, the term '*third world*' has been used interchangeably with developing countries, although the concept no longer represents the true political or economic state of the world.

The concept of an HDI was introduced by the United Nations Development Programme in 1990 (United Nations Development Programme, 1990; United Nations Development Programme, 2016). It is a summary measure of average achievement in key dimensions of human development *e.g.* health (the ability to lead a long and healthy life as evidenced by average life expectancy at birth), education (the ability to acquire knowledge as evidenced by mean years of schooling), and standard of living (as evidenced by the gross national income (GNI) *per capita*). Hence, the focus of HDI represents a move away from the narrow and misleading attention on a single dimension of human life, whether social, political or economic, to a more holistic approach (figure 1). The most recent UNDP report extends the concept of the HDI further, with additional composite indices, covering inequalities, gender, gender-inequality (highlighting women's empowerment), and non-income dimensions of poverty (United Nations Development Programme, 2016).

The relationship between the dimensions of HDI and the occurrence of obstetric urogenital fistula is self-evident, and the concordance is illustrated in figures 1 and 2. The papers submitted describe (and/or compare) epidemiology and treatment outcomes of urogenital fistulas from the UK (in the highest quartile of HDI), and Nigeria and other countries in sub-Saharan Africa (in the lowest quartile of HDI).

Source (reference) Scale	**Well-resourced**			**Poorly-resourced**	
United Nations (1) Descriptive	developed	developing			
	developed	newly industrialised	emerging markets	under-developed/ least-developed	
NATO & Warsaw pact (2) Political (post-WWII)	1st world NATO aligned	2nd world Soviet Union, China and their allies		3rd world Non-aligned	
George Manuel (3) Political	1st world NATO aligned	2nd world Soviet Union, China and their allies		3rd world Non-aligned	4th world sub-populations excluded from global society
World Bank (4) Gross national income (GNI) per capita (US$)	high-income ≥ $12,056	upper middle-income $3896 to $12,055	lower middle-income $996 to $3895	low-income ≤ $995	
UNDP (5) Human development index (HDI)	highest 25% HDI	> median HDI	< median HDI	lowest 25% HDI	
UNDP (6) Adjusted versions of HDI	Inequality-adjusted HDI	Gender-development Index	Gender Inequality Index	Multidimensional Poverty Index	

1. Millennium development indicators: world and regional groupings. (2017) United Nations Statistics Division. https://unstats.un.org/unsd/mi/worldmillennium.htm
2. Leonard TM. (2006). "Third World". *Encyclopedia of the Developing World*. **3**. Taylor & Francis.
3. Manuel G, Posluns M. (1974) The Fourth World: An Indian Reality. University of Michigan, Free Press.
4. Fantom N, Khokhar T, Purdie E. (2016). The 2016 edition of World Development Indicators is out: three features you won't want to miss. *The Data Blog*. The World Bank.
5. United Nations Development Programme (1990) Human Development Report. http://hdr.undp.org/sites/default/files/reports/219/hdr_1990_en_complete_nostats.pdf.
6. United Nations Development Programme (2016) Human Development Report. http://hdr.undp.org/sites/default/files/HDR2016_EN_Overview_Web.pdf

Table 1: Matrix of classifications of well- and poorly-resourced countries

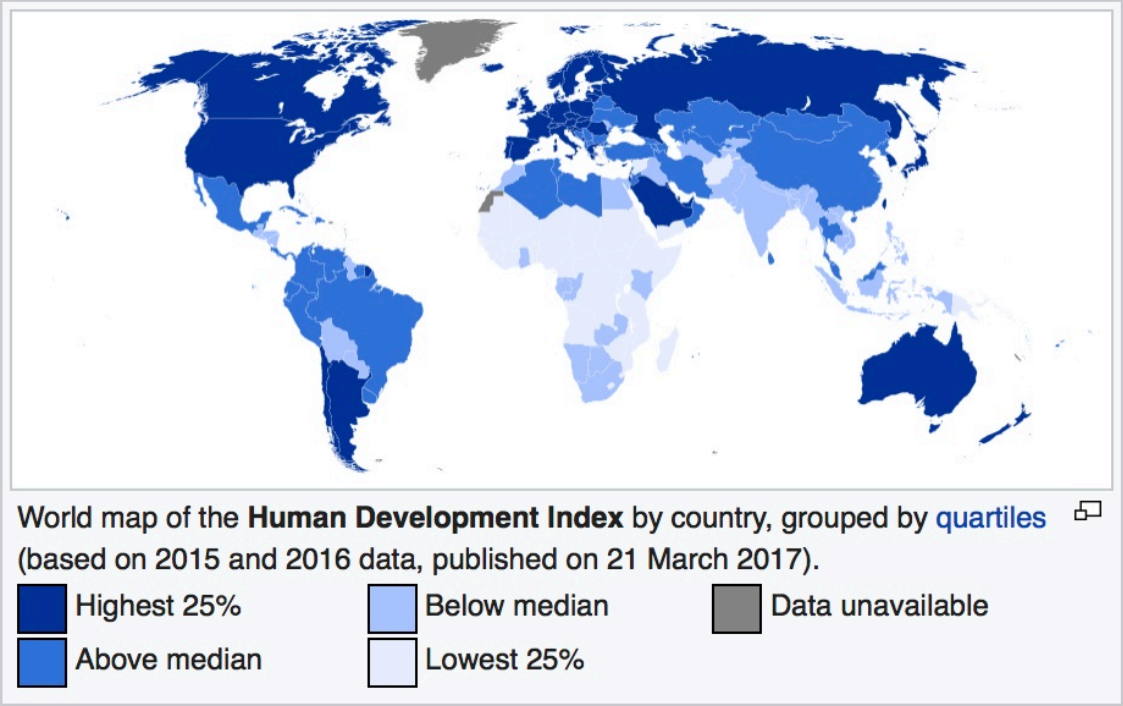


Figure 1: World map of the Human Development Index by country, grouped by quartiles (based on 2015 and 2016 data) (Wikipedia, 2018).

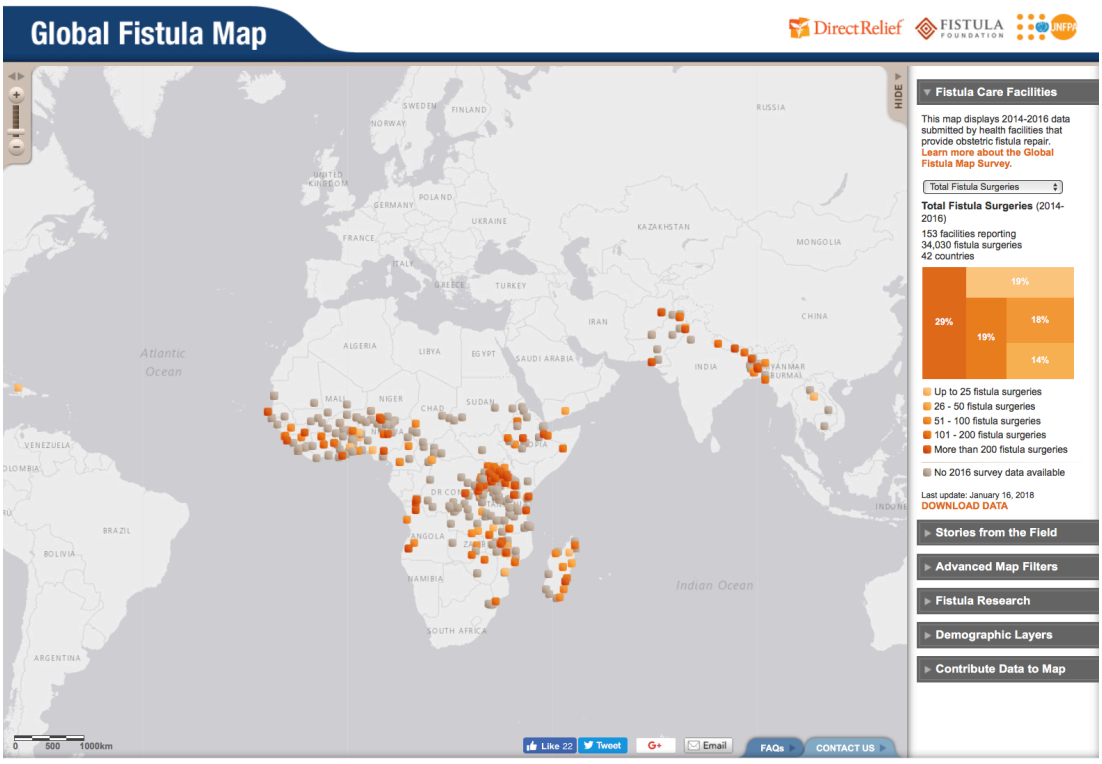


Figure 2: World map of fistula surgeries (based on 2014 and 2016 data) (Fistula Foundation et al., 2018)

Whilst seeking to avoid the pejorative nature of some earlier and simpler terms, yet recognising the, as yet, limited application of more recent composite taxonomy, the terms '*high-income country*' (HIC) and '*low- and middle-income countries*' (LMICs) will be used henceforth throughout this submission, to include the general descriptive, political, economic and developmental categorisations of global society. Hence, they embrace such terms as '*developed*' and '*developing*', '*well-resourced*' and '*poorly resourced*', '*first world*' and '*third world*' etc., respectively.

QUALITY OF AVAILABLE EVIDENCE

Although there is a large body of literature on urogenital fistula, most is of low scientific quality (Abrams *et al.*, 2012; de Ridder *et al.*, 2013; Hillary *et al.*, 2016; Bodner-Adler *et al.*, 2017). The majority of published articles are case series or simple observational data, and would be classified as level III and IV evidence, based on the International Consultation on Urological Diseases (ICUD) modified version of the Oxford Centre for Evidence-based Medicine (OCEBM) grading system (Abrams and Khoury, 2010; Howick *et al.*, 2011a; Howick *et al.*, 2011b) (table 2a). Only seven randomised controlled trials (RCTs) have been identified, concerning causation (Meeks *et al.*, 1997), perioperative antibiotic prophylaxis (Tomlinson and Thornton, 1998; Muleta *et al.*, 2010b), surgical techniques (Safan *et al.*, 2009; Shaker *et al.*, 2011), and duration of postoperative catheterisation (Nardos *et al.*, 2012; Barone *et al.*, 2015). As a result, there are few evidence-based guidelines, and recommendations for practice are limited to grade C, or even D (*i.e. 'no recommendation possible'*) (Abrams and Khoury, 2010; Howick *et al.*, 2011a; Howick *et al.*, 2011b) (table 2b). Recent World Health Organisation (WHO) guidance on the duration of bladder catheterisation after surgical repair of simple obstetric urinary fistula, whilst based on two RCTs and 684 treated women (Nardos *et al.*, 2012; Barone *et al.*, 2015), described their outcomes as reflecting low or very low quality evidence (World Health Organization, 2018).

Level of evidence	Description
I	Meta-analysis of RCTs or high quality RCT
II	Low quality RCT or good quality prospective cohort study
III	Good quality retrospective case-control study or cohort study
IV	Expert opinion

Grade of recommendation	Description
A	Usually consistent with level I evidence
B	Consistent with level II or III evidence or 'majority evidence' from RCTs
C	Level IV evidence or 'majority evidence' from level II or III studies
D	No recommendation possible because of inadequate or conflicting evidence

Table 2: (a) Summary of IUCD modified OCEBM systems for levels of evidence (above) and (b) grades of guideline recommendation (below).

Epidemiology of urogenital fistulas

AETIOLOGY

Urogenital fistulas rarely occur congenitally (Dolan *et al.*, 2004), and are most often acquired from obstetric, iatrogenic (surgical), radiation and malignant causes. Most reports suggest that whilst approximately 70% of fistulas reported from HICs are of iatrogenic aetiology (Moir, 1973; Lawson, 1978; Hilton, 2001), less than 10% of those reported from LMICs follow pelvic surgery. In contrast, over 90% of fistulas reported from LMICs are of obstetric aetiology (most following neglected obstructed labour) (Waaldijk, 1989; Danso *et al.*, 1996; Hilton, 2003), whereas less than 10% of cases reported from HICs are associated with pregnancy (most of those following some obstetric surgical intervention). Whilst genital trauma is uncommon as a cause of fistula in HICs, vaginal pessaries for the management of pelvic organ prolapse (POP) or other foreign bodies used for sexual purposes are occasionally seen as aetiological factors. In areas of the world where extreme gender-based violence is used as a strategy of war (Mukwege and Nangini, 2009; Mukwege *et al.*, 2010), fistula may be

seen as part of the broad complex of medical, psycho-social and socio-economic consequences for survivors (Onsrud *et al.*, 2008; Mukwege and Berg, 2016).

INCIDENCE AND PREVALENCE

Obstetric fistula – in low- and middle-income countries

Current estimates of the global prevalence of untreated obstetric fistulas vary from 654,000 to 3,500,000 (Muleta *et al.*, 2012). National and regional community-based estimates of prevalence are more consistent at between 1.2 and 1.7 per 1,000 women surveyed in Ethiopia (Muleta *et al.*, 2007), Malawi (Kalilani-Phiri *et al.*, 2010), Bangladesh (Walz *et al.*, 2003) and south-east Asia (Adler *et al.*, 2013). Reports of the incidence of obstetric fistula show much greater variation, with a difference between estimates of approximately ten-fold. The only prospective population-based study found an overall incidence of 0.10 per 1,000 births, and an incidence in rural areas of 1.24 per 1,000 births in West Africa (Vangeenderhuysen *et al.*, 2001). On the basis of this work these authors estimated a minimum of 33,451 (95 % confidence interval (CI) 4,050 – 120,413) new cases annually in rural sub-Saharan Africa. Whilst the global incidence of obstetric fistula has been expressed as 0.1 to 1.5 per 1000 births (de Ridder *et al.*, 2013), hospital-based reports give figures approximately four times higher, at between 0.4 and 6.5 per 1,000 births (Muleta *et al.*, 2012).

Non-obstetric fistula – in high-income countries

There are few robust data available on the prevalence of non-obstetric fistula in HICs. Data from Hospital Episode Statistics (HES) for England over the last 25 years indicate an average of 104 (95% CI 100.0, 107.5) procedures for the treatment of VVF, and 13 (95% CI 12.0, 14.4) for urethrovaginal fistula (UVF) annually. These are for procedures undertaken as the patient's '*main procedure*'; the equivalent figures for '*all*' procedures are 127 (95% CI 122.4, 132.4) and 18 (95% CI 16.3, 19.0), giving a national annual incidence of 145 operations for lower urogenital fistula (figure 3). Assuming a population of 20,000,000 women aged 15-64 years, this gives an incidence of 0.73 fistula per 100,000 women per year, or approximately 1 in 140,000 – *candidate's own calculations based on HES downloaded 1992-2017 from* (Department of Health, 2018).

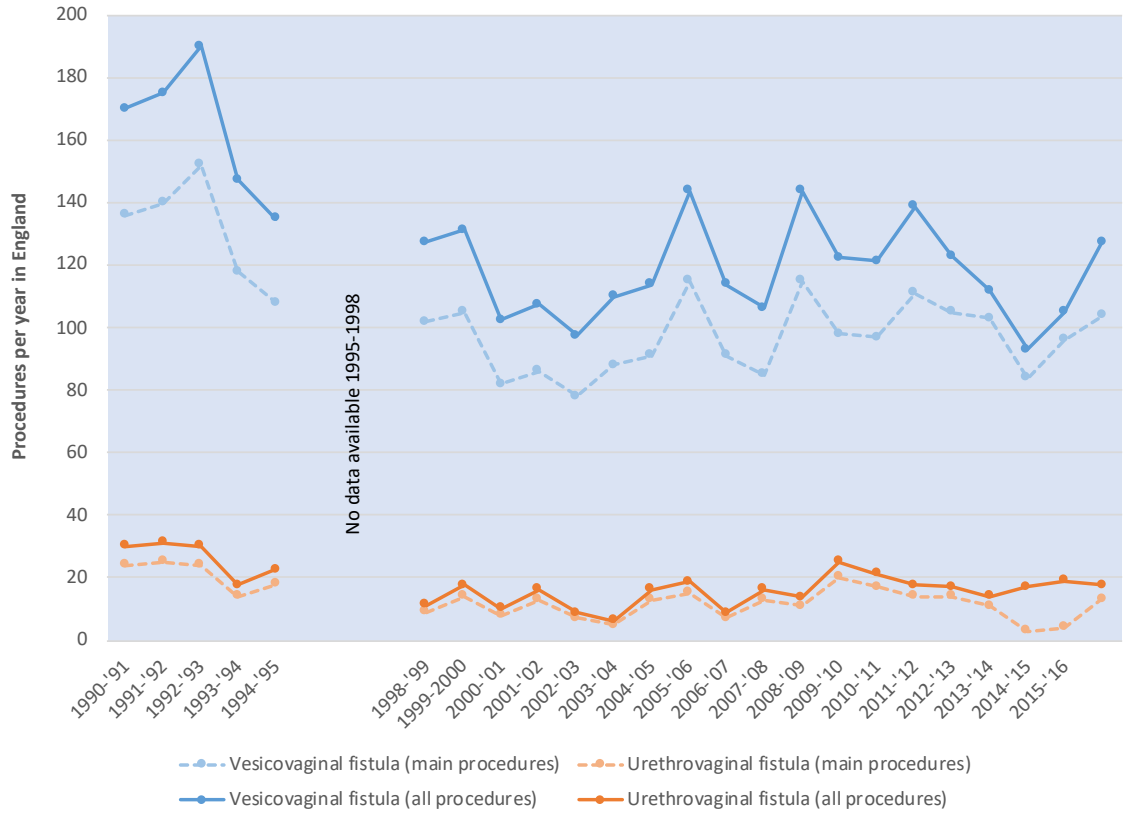


Figure 3: 'Main' and 'all' annual procedures for VVF (OPCS P25.1) and UVF (OPCS P25.2) repair in NHS in England, 1990-91 to 2015-16.

RISK OF LOWER URINARY TRACT FISTULA AFTER HYSTERECTOMY

Although injury to the lower urinary tract and subsequent fistula formation can occur at any pelvic surgery, it is with hysterectomy that the risks appear to be greatest, and have been reported to be between 0.1% and 4% (Forsgren and Altman, 2010). In a national study from Sweden the rate of women undergoing fistula surgery of any type was reported as 0.26% in women who had undergone hysterectomy, compared to 0.0007% in those not exposed to hysterectomy, the '*number needed to harm*' being estimated at 5700 (Forsgren *et al.*, 2009).

The previous largest series describing bladder injury and/or fistula in association with hysterectomy is that from Harkki-Siren *et al.*, examining 62,379 hysterectomies in Finland (Harkki-Siren *et al.*, 1998), although it is highly likely that this significantly underestimates the rate of cystotomy, since they describe only 30 (0.05%) cystotomies, yet 52 (0.08%) fistulas. A number of other studies have reported the rate of unintentional cystotomy at pelvic surgery and the subsequent rate of fistula

formation (Hadley *et al.*, 1994; Mehra *et al.*, 1996; Mathevet *et al.*, 2001; Duong *et al.*, 2011). Meta-analysis of these series indicates an average rate of cystotomy of 1.9% with 7% of those, *i.e.* 0.13% or approximately 1 in 750 overall, going on to develop a VVF (de Ridder *et al.*, 2013).

RISK OF URETERIC INJURY AFTER HYSTERECTOMY

Ureteric injury is an uncommon but serious complication of gynaecological surgery; iatrogenic trauma is the commonest cause of ureteric injury. In the Finnish series cited above the incidence of ureteric injury associated with hysterectomy for benign disease was 0.2%, with the lowest rate being associated with vaginal hysterectomy (Harkki-Siren *et al.*, 1998). A registry study from the USA found the overall incidence of ureteric injury during radical hysterectomy to be 0.8% (Likic *et al.*, 2008). Recent systematic reviews have reported that gynaecological and colorectal surgery may be associated with ureteric injury in up to 6% of cases (Brandes *et al.*, 2004; Summerton *et al.*, 2012; de Ridder *et al.*, 2013).

It is often stated that the majority of iatrogenic ureteric injuries follow what was thought at the time to have been straightforward operations. Presumed risk factors include those contributing to abnormal anatomy, abnormal tissue adhesion or major intraoperative haemorrhage. Risks are higher in surgery for pelvic malignancies, and this may reflect one or more of these factors.

Injury to the ureter at hysterectomy most typically occurs in the lower third, the most common mechanisms being, in descending order of frequency, ligation, kinking by suture, transection/avulsion, partial transection, crush, and devascularization (Brandes *et al.*, 2004). It is perhaps because of these mechanisms that the diagnosis of iatrogenic ureteric injury is often delayed, and identified only after the index procedure, in 65–80% of cases. The delay in diagnosis results in more common and serious complications including renal unit loss.

Patterns of care for fistula

Although attempts have been made to formulate treatment algorithms for lower urinary tract and ureterovaginal fistula of both surgical and radiation aetiologies (de Ridder *et al.*, 2013), there have never been widely accepted national or international pathways for the care of women with urogenital fistula.

OBSTETRIC FISTULA – IN LOW- AND MIDDLE-INCOME COUNTRIES

Women with obstetric fistula commonly report delay or difficulty in accessing essential healthcare services both for emergency obstetric care and for obstetric fistula services. This may reflect long distances to reach care, difficult terrain, poor transportation networks, lack of money, lack of family support or permission, the view that parturition is something that can be managed at home, or the wish to try traditional remedies before recourse to modern medicine (de Vries *et al.*, 2012). These delays, in the decision to seek care, in arrival at a health-care facility, and in the provision of adequate care in hospital have been termed '*Maine's delays*' (Thaddeus and Maine, 1991). Amongst reported series of obstetric fistula patients, up to 96% of women laboured for more than 24 hours (Ndiaye *et al.*, 2009), and 24% for more than 96 hours (Muleta *et al.*, 2010a).

Whilst there may be specific local or regional beliefs and practices influencing access to emergency obstetric care, similar issues may also affect women's access to fistula care. In keeping with this conjecture, one study from northern Nigeria found that women with a longer duration of suffering with fistula also had a longer duration of labour (Tahzib, 1983). In other reports the median length of time living with obstetric fistula varies between eight months (Muleta *et al.*, 2010a) and eight years, being longer in more rural environments (Muleta *et al.*, 2007; Bangser *et al.*, 2011).

NON-OBSTETRIC FISTULA – IN HIGH-INCOME COUNTRIES

In high income settings, whilst waiting times for treatment vary by country, by region, and by specialty, in general the development of a urogenital fistula would be seen as justifying urgent care. Delays in seeking or obtaining care, as described for obstetric fistula, would be most unusual.

In UK, although over 80% of urogenital fistulas develop following gynaecological surgery, 75% of fistula repair procedures carried out in the 1990s were undertaken by urologists (Hilton, 1997). Although only 150 fistula repair procedures were reported in HES annually at that time, over 80 hospitals returned data on repair procedures, undertaken by surgeons who, in most cases, carried out between one procedure every 5 years (gynaecologists) and one procedure per year (urologists) (Hilton, 1997). Such idiosyncratic patterns of care are contrary to what is known about the relationship between workload and outcome of treatment.

Although the evidence on surgical and other interventional procedures tends to suggest that higher procedure volume is associated with better outcomes, the consistency and size of the effect varies for different procedures. A systematic review of 135 studies found a significant association between higher volume (hospital or surgeon) and better outcomes in about 70% of studies; none of the studies found a significant association between higher volume of any type of surgery and poorer outcome (Halm *et al.*, 2002). In these studies, the definition of low or high volume varied between procedures, with median low volumes of up to 100–200 for coronary angioplasty or coronary artery bypass graft surgery; and median low volume values ranging from 1 to 73 for other procedures described (mainly in the region of 10–30).

No previous studies have reported the outcomes of fistula surgery according to the volume of surgery undertaken, although there are some comparable data in relation to other continence surgery. One case series of retropubic '*bottom-up*' mid-urethral tapes considered the cure rates for each of the ten surgeons who undertook the retropubic '*bottom-up*' tape procedure, which ranged from 72% to 92% and were not significantly associated with the number of procedures performed (11–250 per surgeon) (Holmgren *et al.*, 2005). From Finnish national data on retropubic 'bottom-up' tapes, it was estimated that the incidence of complications was 40% in hospitals where 15 or fewer operations had been undertaken, and 14% in centres performing more than 15 operations (Kuuva and Nilsson, 2002).

Although the UK retropubic '*bottom-up*' mid-urethral tape (TVT™)/colposuspension RCT (Ward and Hilton, 2002; Ward and Hilton, 2004; Ward and Hilton, 2008), was not powered for subgroup analysis, evaluation of recruitment numbers and outcome was undertaken (Hilton, 2002). It is difficult to put the numbers into context because

recruited cases may have represented only a proportion of the continence surgery undertaken in respective centres. Notwithstanding, objective cure rates were higher for centres recruiting more patients; the categories analysed being more than 30 patients, 21–30, or fewer than 20. While it must be conceded that the effect of drop-outs on an intention-to-treat analysis is greater on units recruiting small numbers of patients, it was felt nevertheless that there may be a minimum workload consistent with optimal surgical outcome (Hilton, 2002).

Other studies have reflected on the '*learning curve*' with the retropubic '*bottom-up*' mid-urethral tape procedure, each showing that the complication rate, or specifically bladder injury, was relatively higher during the surgeon's training period, the threshold/definition for which differed across the studies, from the first 5, 10–20, 50 or 100 procedures (Lebret *et al.*, 2001; Neuman, 2004; McLennan and Melick, 2005; Schraffordt Koops *et al.*, 2005; Maguire *et al.*, 2013; Hilton and Rose, 2016).

With these latter data in mind, the pattern of care provided to women with urogenital fistula in the UK described above, with a large number of surgeons each undertaking small numbers of procedures annually, might be seen as idiosyncratic, and likely to be associated with suboptimal outcomes.

Outcomes of treatment for lower urinary tract fistula

DEFINITION OF CURE

There is no universally accepted definition of success or scale of outcome in the treatment of urogenital fistula, and definitions applied vary considerably between studies. Historically, outcomes have been evaluated dichotomously on the basis of '*success*' or '*failure of anatomical closure*' of the fistula. In most LMICs this has been based on observed or patient-reported leakage, or on vaginal examination findings at the time of catheter removal or discharge from hospital. In HICs it has been common practice to perform imaging, using cystography or video-cystourethrography, prior to catheter removal following surgery, and to use this as a measure of immediate outcome.

The definition of success may be different when seen from the patient perspective, and a woman whose fistula is closed but who remains incontinent may be just as

debilitated as a woman whose repair failed. Estimates of persistent urinary incontinence (UI) after successful closure of obstetric fistula are likely to be significantly underestimated in epidemiological literature, but range from 16% to 33% depending on the sample size and case complexity (Mourad *et al.*, 2012).

With the recognition of this so-called '*continence gap*' (Wall and Arrowsmith, 2007), authors have expanded outcome scales to include functional in addition to structural outcomes. Hence, a scale incorporating '*anatomical closure of fistula without residual incontinence*', '*anatomical closure with residual incontinence*', and '*failed repair*', is seen as more appropriate.

The need for further surgery – either repeat fistula repair, or secondary urinary diversion – has been used to imply failure of initial surgical management. Perhaps such a scale could usefully be expanded to include the need for surgery for urgency urinary incontinence (UUI) or stress urinary incontinence (SUI), thus incorporating the concept of the '*continence gap*' into a surgical outcome scale.

In the evaluation of treatment outcome for other causes of UI there has been an increasing move towards the incorporation of patient-defined treatment goals (Elkadry *et al.*, 2003). Although little used to date in surgical or fistula literature, the use of composite outcomes, reflecting the overall worth of treatment and the patient's individual experience and interaction with the healthcare system, should also be considered (Hilton and Robinson, 2011). In the context of the obstetric fistula patient this might include not only the achievement of urinary and/or faecal continence, but also social re-integration, economic stability, role definition, restoration of fertility and/or sexual function, and the attainment of pregnancy and motherhood, as desired by the woman (de Ridder *et al.*, 2013).

The WHO published a classification of obstetric fistula that divided fistula in simple or complex fistula (de Bernis, 2007); this has been adapted by adding radiation fistula to the complex fistula group (de Ridder *et al.*, 2013) (table 3).

Simple fistula with good prognosis	Complex fistula with uncertain prognosis
• Single fistula	• Multiple fistulae
• Fistula <4cm diameter	• Fistula >4cm diameter
• Vesicovaginal fistula	• Rectovaginal or cervical fistula
• Closing mechanism not involved	• Closing mechanism involved
• No circumferential defect	• Circumferential defect
• Minimal tissue loss +/- scarring	• Extensive tissue loss +/- scarring
• Ureters not involved	• Intravaginal ureters
• No previous attempt at repair	• Failed previous repair/s
	• Radiation fistula

Table 3: Adapted WHO fistula classification (de Bernis, 2007; de Ridder *et al.*, 2013)

The categorical and continuous definitions of cure and scales of outcome are summarised overleaf (table 4).

Scale (categories/sub-groups)	Success		Failure	
Anatomical **Visual (2)**	Successful anatomical closure		Failure of anatomical closure	
Imaging (2)	Negative cystourethrogram		Positive cystourethrogram	
Anatomical/functional (2/3)	Successful anatomical closure		Failure of anatomical closure	
	No incontinence	Residual incontinence	Residual leakage via fistula	
Surgical (2/4)	Successful closure		Failure of repair	
	No further surgery	Surgery for UUI or SUI	Repeat fistula repair	Secondary diversion
Symptomatic/PROM (2/4)	No leakage	Leakage persists		
		Urgency UI	Stress UI	Continuous UI
Quality of life (continuous)	Improvement in individual domain scores and/or total score		No improvement in scores	
Patient-defined goals (PDG's) (continuous)	Achievement of PDG's *e.g.* urinary and faecal continence; reintegration into society; restoration of sexual function and fertility; achievement of pregnancy and motherhood		Failure to reach any or all PDG's	
Scale (continuous)	**Success**		**Failure**	

Table 4: Summary of outcome measures for fistula treatment

CLASSIFICATION OF FISTULA AND TREATMENT OUTCOME

Historically, classification systems for fistula have been based largely on the size and site of the fistula (Moir, 1967; Lawson, 1968), with Moir particularly recognising the importance of circumferential tissue loss. More recent classification systems have incorporated position in relation to fixed reference points (as opposed to an anatomical description), the extent of scarring and urethral involvement, and type of surgical intervention or anticipated surgical difficulty (Goh *et al.*, 2009). The most widely used systems for classification of obstetric fistulas in LMICs have been those described by Waaldijk (Waaldijk, 1989) and Goh (Goh, 2004).

Classification of fistula might be said only to be useful if it can be shown to determine aspects of treatment (*e.g.* optimal surgical approach) or outcome. A significant increase in post-fistula repair UI has been found in association with both circumferential fistula (Bird, 1967), and the markedly stenosed vagina (Gray, 1970). In a postoperative follow-up study of 987 women assessed preoperatively by the Goh classification, those women with high (type 1) or small (type a) fistulas were more likely to be continent after repair, whereas those with circumferential fistulas or with previous unsuccessful repair (type iii) were more likely to have failed closure or post-fistula repair UI (Goh *et al.*, 2008).

In the initial description of his classification system, Waaldijk documented the occurrence of SUI after repair of fistulas of varying types, describing 1% incidence where there was no sphincter involvement in the fistula, and 16% where there was both sphincter involvement and tissue loss (Waaldijk, 1989). More recently the same author has reported the rates of fistula closure and postoperative SUI in a consecutive series of 1716 women undergoing early repair of obstetric fistula, and confirmed these to show rank association with the degree of urethral involvement (Waaldijk, 2009) (table 5).

It should be noted that these two classification systems (Waaldijk, 1989; Goh, 2004), with their focus on the urethra and bladder neck (*i.e.* the area at greatest risk from compression in labour), are appropriate for the evaluation of obstetric fistulas in LMICs; they are however of limited value in the grading of fistulas in HICs, where the largest proportion involve the vaginal vault, reflecting the predominance of iatrogenic surgical (especially post-hysterectomy) aetiology.

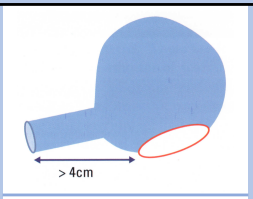
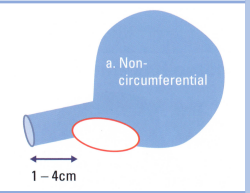
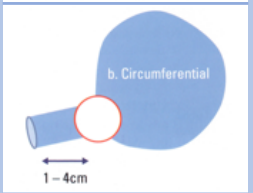
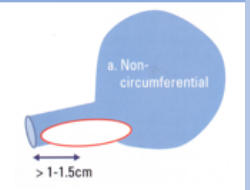
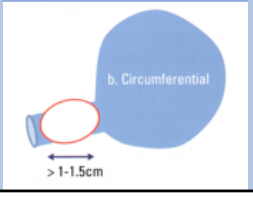
Waaldijk classification	Diagrammatic	N	Closed at 1st operation	Incontinent
I		243	238 (98%)	1 (0%)
IIAa		888	868 (97%	11 (1%)
IIAb		366	333 (91%)	30 (9%)
IIBa		87	80 (96%)	14 (16%)
IIBb		132	114 (86%)	59 (49%)

Table 5: Waaldijk classification of obstetric fistula showing postoperative closure and incontinence rates in 1716 consecutive women undergoing early closure of type I & II fistulas (Waaldijk, 2009; de Ridder *et al.*, 2012).

URINARY TRACT FUNCTION IN ASSOCIATION WITH FISTULA AND FISTULA REPAIR

In the above seminal works on classification by Waaldijk and Goh, sphincter involvement was determined on a purely anatomical basis (Waaldijk, 1989; Goh, 2004), and treatment outcome on a purely symptomatic basis (Goh *et al.*, 2008; Waaldijk, 2009). Waaldijk has emphasised the importance of functional assessment prior to repair, especially in those patients with a long delay between fistula development and treatment, where bladder compliance is at risk. However, given the resource-poor settings in which he practices, and lack of available dynamic

assessments, he has described measurement of bladder length as a surrogate for bladder capacity, indicating poorer outcome in women with a longitudinal bladder diameter of <6cm. (Waaldijk, 2008).

The application of cystometry in the evaluation of women with residual symptoms after surgical closure of obstetric fistula (Schleicher *et al.*, 1993; Murray *et al.*, 2002; Goh *et al.*, 2013) confirms the high rate of urodynamic stress incontinence (USI) and mixed USI and detrusor overactivity (DOA) postoperatively, the latter authors in particular emphasising the need for greater consideration of medical treatment. Whilst not carrying out urodynamic investigations, Ekwedigwe *et al.,* reported on the high incidence (45%) of bladder spasm in women immediately following repair of obstetric fistula, and found this symptom to be associated with poor outcome from surgery (Ekwedigwe *et al.*, 2017).

The application of urethral pressure measurement, and identification of intrinsic sphincter deficiency in association with UVF has been reported previously (Sand and Ostergard, 1995), although its clinical usefulness remains in doubt (Hilton, 1990). There are no previous reports of cystometry in fistula patients before repair surgery. Recording detrusor pressure during cystometry depends on the ability to record intravesical pressure as distinct from intra-abdominal pressure. Conventionally the latter is determined from rectal or vaginal pressure. The feasibility of carrying out cystometry in patients with communication between the urinary and the genital tract may therefore be questioned (Abrams and Hilton, 2002).

TREATMENT OUTCOMES

Conservative management

Before epithelialisation is complete an abnormal communication between viscera will tend to close spontaneously, provided that the natural outflow is unobstructed. Normal urinary continence mechanisms, however, involve the physiological contraction and intermittent relaxation of urethral sphincter mechanisms (or anal sphincters in the case of anal continence). As a result, although completely spontaneous closure of genital tract fistulas does occur, it is the exception rather than the rule. Bypassing the sphincter mechanisms, or diverting flow around the fistula, for example by urinary catheterisation or percutaneous nephrostomy (or by

colostomy in the case of colo- or recto-vaginal fistula), may however encourage closure. Recent systematic and non-systematic reviews found closure with catheter drainage alone in 13% (95%CI 0%, 36%) and 31% (95%CI 7%, 81%) of included surgical fistulas, respectively (Bazi, 2007; de Ridder *et al.*, 2013).

In large series of obstetric fistulas where a consistent approach to conservative management has been applied, spontaneous healing has been reported in 15-28% of cases (Waaldijk, 1997; Waaldijk, 2004). Patients with ongoing, continuous vaginal leakage despite a functioning indwelling catheter are unlikely to have resolution of a VVF without surgery. Such patients should be spared prolonged catheter drainage and proceed with more definitive repair as soon as medically appropriate.

Within their systematic review of the management of VVF following benign gynaecological surgery, Bodner-Adler and colleagues evaluated the outcomes from '*conservative*' treatments (Bodner-Adler *et al.*, 2017). Only 16% women were reported to have undergone prolonged catheter drainage, with only 8% resolving.

The same authors also included what might be more appropriately considered as minor surgical treatments *e.g.* endovaginal application of cyano-acrylic glue or platelet-rich fibrin glue, transvaginal injection of fibrin sealant, neodymium/holmium yttrium-aluminium-garnet (YAG) laser welding, electrocoagulation/fulguration, curettage of the track and the use of a rubber/metal ball. They described success rates between 67% and 100%, although a total of only 50 women were included, with between 1 and 18 highly selected women being treated by these various techniques.

Surgical management

The literature relating to the management of surgical fistula is extensive, but of limited quality. Chassar Moir and Lawson reviewed the position with regard to urogenital fistulas in Britain in the 1970's (Moir, 1973; Lawson, 1978), and Lee *et al*., in the USA in the 1980's (Lee *et al.*, 1988). However, little has been published on the subject since that time, apart from small case series, and descriptions of surgical techniques; the largest recent UK series was of 41 cases managed in tertiary practice by Ockrim *et al*., in 2009 (Ockrim *et al.*, 2009).

Only 107/124 (86%) of the identified studies in the Bodner-Adler *et al*., review documented a success rate (Bodner-Adler *et al.*, 2017). Interpretation of their meta-analysis of outcome is difficult; they report '*success*' rates of 92.9% for '*conservative*'

(minor surgical) treatments and 98.0% for surgical treatments; 97.0% (abdominal), 93.8% (vaginal), 98.9% (laparoscopic/robotic) and 100% (others). However, only 87/1359 (6.4%) of women were apparently completely symptom-free, and 754/1359 (55.5%) completely dry. Only 406 (30.0%) were reported to be healed or cured; it is not stated, but one assumes this means that these fistulas were anatomically closed, but the women experienced some residual symptoms.

No studies have randomised cases by route of surgery, and clearly few surgeons would consider themselves to have equipoise on this point. The candidate's preference has always been for the vaginal approach where possible, accepting that the abdominal route has a place where access vaginally is limited (by virtue of the patient's nulliparity, or previous surgery or other pelvic pathology) or where there is concurrent ureteric involvement requiring re-implantation. Hence, it is not surprising that there are no studies randomising patients between route of surgery. Neither Bodner-Adler *et al*., (Bodner-Adler *et al.*, 2017), nor the International Consultation on Incontinence (ICI) review (*candidate's own analysis*) (de Ridder *et al.*, 2013) found any difference between abdominal and vaginal approaches, nor between transvesical and transperitoneal approaches.

Given the wide variation in case mix, definitions of cure, and duration of follow-up, and the overall poor quality of research on fistulas in LMICs alluded to earlier in this chapter, the interpretation of reports on the outcome of treatment of fistula is even more problematic. '*Success rates*' between 45% and 100% are reported.

Long-term outcomes

The majority of studies involving fistula patients in LMICs have defined the success of a procedure at the time of catheter removal or discharge from hospital; only one study has reported later outcomes, albeit that at only six months postoperatively (Browning and Menber, 2008). Reports from HICs have usually reserved the definition of success until clinic follow-up. In the review by Bodner-Adler *et al.,* only 79/124 (64%) studies provided information on length of follow-up; in this sub-set follow-up averaged 20 months (Bodner-Adler *et al.*, 2017).

Chapter 2: Group I publications[1]

(***Works upon which a candidate primarily bases his claim to have satisfied the standards for the award of the degree***)

This submission for '*degree by publication*' includes eight papers, comprising:

- One systematic review, examining:
    - aetiology and treatment comparing HICs and LMICs (*paper 1*)
- Two retrospective, individual surgeon, cohort studies describing the epidemiology and treatment outcome in:
    - fistula patients managed in south-east Nigeria over a 25-year period (*paper 2*)
    - fistula patients managed in north-east England over a 25-year period (*paper 3*)
- Two prospective cohort studies examining:
    - urodynamic findings in women with lower urinary tract fistulae, and their association with treatment outcome (*paper 4*)
    - long-term treatment outcome following fistula repair, based on symptoms and quality of life (*paper 5*)

[1] The candidate's publications are categorised as group I, IIa and IIb, as follows:

Group I - Works upon which a candidate primarily bases his claim to have satisfied the standards for the award of the degree (*Chapter 2*);

Group II - Other works put forward as evidence of the scope of the candidate's contribution:

IIa - to the specific field of study in which the primary submissions lie - *i.e.* urogenital fistula (*see Appendix A*);

IIb - to the broader field of study - *i.e.* urogynaecology (*see Appendix B*).

- Three retrospective national cohort studies based on HES data, examining:
    - the risk of lower urinary tract fistula following hysterectomy (*paper 6*)
    - the risk of ureteric injury and fistula following hysterectomy (*paper 7*)
    - patterns of care and outcomes of treatment of lower urinary tract fistula in the NHS in England (*paper 8*)

These publications are listed below, including details of the candidate's contribution to the work in each case; the contribution of other authors is recognised in the acknowledgements section on page xi; photocopies of individual publications follow.

1. Hillary C, Osman N, Chapple CR, Hilton P. The aetiology, treatment and outcome of urogenital fistulae managed in well- and low-resourced countries: a systematic review. **Eur Urol** 2016; 70(3): 478-492.

Personal contribution 25%: specific systematic reviews on the epidemiology, and management of urogenital and intestine-genital fistula following surgery and radiotherapy were carried out by the candidate, as well as drafting of these aspects of the manuscript; other searches and writing were carried out by co-authors; all authors approved the final version of the manuscript for publication.

2. Hilton P, Ward A. Epidemiological and surgical aspects of urogenital fistulae: a review of 25 years' experience in southeast Nigeria. **Int Urogynecol J & Pelvic Floor Dysfunct** 1998; 9: 189-194.

Personal contribution 95%: protocol development, data collection, analysis and writing of the manuscript were carried out wholly by the candidate; the majority of surgery was carried out by my co-author, Sr Dr Anne Ward, who approved the final version of the manuscript for publication.

3. Hilton P. Urogenital fistula in the UK – a personal case series managed over 25 years. **BJU Int** 2012; 110(1): 102-110.

Personal contribution 100%: protocol development, urodynamic studies, surgery, data collection, analysis and writing of the manuscript were carried out wholly by the candidate.

4. Hilton P. Urodynamic findings in patients with urogenital fistulae. **BJU Int** 1998; 81: 539-542.

Personal contribution 100%: protocol development, urodynamic studies, surgery, data collection, analysis and writing of the manuscript were carried out wholly by the candidate.

5. Dolan LM, Dixon WE, Hilton P. Urinary symptoms and quality of life in women following urogenital fistula repair: a long-term follow-up study. **BJOG** 2008; 115(12): 1570-1574.

Personal contribution 50%: protocol development, urodynamic investigation, data collection, analysis and all surgery were carried out by the candidate. Some urodynamic investigations were carried out by one of my co-authors and drafting of the manuscript by the other. All contributors approved the final version of the manuscript for publication.

6. Hilton P, Cromwell D. The risk of vesicovaginal and urethrovaginal fistula after hysterectomy performed in the English National Health Service – a retrospective cohort study examining patterns of care between 2000 and 2008. **BJOG** 2012; 119(12): 1447-1454.

Personal contribution 50%: protocol development and writing of the clinical aspects of the manuscript were carried out by the candidate; coding and analysis of the database analysis and writing the epidemiological aspects of the manuscript were carried out by my co-author, Dr David Cromwell; both authors approved the final version of the manuscript for publication.

7. Kiran A, Hilton P, Cromwell DA. The risk of ureteric injury associated with hysterectomy: a 10-year retrospective cohort study. **BJOG** 2016; 123(7): 1184-1191.

Personal contribution 50%: protocol development and writing of the clinical aspects of the manuscript were carried out by the candidate; coding and analysis of the database analysis, and writing the epidemiological aspects of the manuscript were carried out by my co-authors, Drs Amit Kiran and David Cromwell; all authors approved the final version of the manuscript for publication.

8. Cromwell D, Hilton P. Retrospective cohort study on patterns of care and outcomes of surgical treatment for lower urinary-genital tract fistula among English National Health Service hospitals between 2000 and 2009. **BJU Int** 2013; 111(4b): E257-E262.

Personal contribution 50%: protocol development and writing of the clinical aspects of the manuscript were carried out by the candidate; coding and analysis of the database analysis and writing the epidemiological aspects of the manuscript were carried out by my co-author, Dr David Cromwell; both authors approved the final version of the manuscript for publication.

Paper 1: The aetiology, treatment and outcome of urogenital fistulae managed in well- and low-resourced countries: a systematic review

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European Association of Urology

Review – Reconstructive Urology

The Aetiology, Treatment, and Outcome of Urogenital Fistulae Managed in Well- and Low-resourced Countries: A Systematic Review

Christopher J. Hillary [a], *Nadir I. Osman* [a], *Paul Hilton* [b], *Christopher R. Chapple* [a,*]

[a] *Academic Urology Unit, Royal Hallamshire Hospital, Sheffield, UK;* [b] *Department of Urogynaecology, Newcastle University, Newcastle, UK*

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Abstract

Context: Urogenital fistula is a global healthcare problem, predominantly associated with obstetric complications in low-resourced countries and iatrogenic injury in well-resourced countries. Currently, the published evidence is of relatively low quality, mainly consisting retrospective case series.
Objective: We evaluated the available evidence for aetiology, intervention, and outcomes of urogenital fistulae worldwide.
Evidence acquisition: We performed a systematic review of the PubMed and Scopus databases, classifying the evidence for fistula aetiology, repair techniques, and outcomes of surgery. Comparisons were made between fistulae treated in well-resourced countries and those in low-resourced countries.
Evidence synthesis: Over a 35-yr period, 49 articles were identified using our search criteria, which were included in the qualitative analysis. In well-resourced countries, 1710/2055 (83.2%) of fistulae occurred following surgery, whereas in low-resourced countries, 9902/10 398 (95.2%) were associated with childbirth. Spontaneous closure can occur in up to 15% of cases using catheter drainage and conservative approaches are more likely to be successful for nonradiotherapy fistulae. Of patients undergoing repairs in well-resourced countries, the median overall closure rate was 94.6%, while in low-resourced countries, this was 87.0%. Closure was significantly more likely to be achieved using a transvaginal approach then a transabdominal technique (90.8% success vs 83.9%, Fisher's exact test; $p = 0.0176$).
Conclusions: It is difficult to conclude whether any specific route of surgery has advantage over any other, given the selection of patients to a particular procedure is based upon individual fistula characteristics. However, surgical repair should be carried out by experienced fistula surgeons, well versed in all techniques as the primary attempt at repair is likely to be the most successful.
Patient summary: Urogenital fistulae are a common problem worldwide; however, the available evidence on fistula management is poor in quality. We searched the current literature and identified that 95% of fistulae occur following childbirth in low-resourced countries, whereas 80% of fistulae are associated with surgery in well-resourced countries, where successful repair is also more likely to be achieved. The first attempt at repair is often the most successful and therefore fistula surgery should be centralised to hospitals with the most experience.

* Corresponding author. Room H26, H-Floor, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK. Tel. +44 (0)114 271 3048; Fax: +44 (0)114 279 7841.
E-mail address: c.r.chapple@sheffield.ac.uk (C.R. Chapple).

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1. Introduction

Urogenital fistula represents a major global health problem, responsible for significant physical, social, and psychological morbidity. In low-resourced countries (LRC), it is estimated that at least 3 million women worldwide have an untreated fistula, while between 30 000 and 130 000 new fistulae develop annually in Africa alone [1]. Vesico-vaginal fistula is the most common type and in LRC most often results from neglected prolonged obstructed labour, which is associated with tissue ischaemia resulting from compression of the bladder and vagina by the foetal presenting part against the bony pelvis. In contrast, urogenital fistulae are relatively uncommon in well-resourced countries (WRC) and in the UK it is estimated that approximately 120 repairs are carried out on an annual basis [2]. Hence, the literature on fistula repairs in WRC relates to case series or retrospective cohorts from relatively few centres. In comparison to fistulae in LRC, which are largely of obstetric aetiology, those that occur in WRC are associated with iatrogenic factors (surgery or radiotherapy) in almost three quarters of cases [2].

In response to the growing public health issues surrounding obstetric vesico-vaginal fistulae, various charitable and nongovernmental bodies are involved in the development of management programmes and in establishing specific treatment centres [3]. As a result, most fistula repairs are performed by relatively few fistula surgeons in areas of high fistula prevalence, each with their own favoured methods for repair. Therefore, much of our knowledge results from the opinions of comparatively few, borne out of large case series rather than a trial setting. Consequently, there is wide variation in the definitions of fistula location and complexity with little standardisation of treatment protocols and outcome measures.

We aimed to systematically review the current literature on urogenital fistulae in economically less-resourced and WRC, with emphasis on the aetiology, approach to treatment, and the outcomes of fistula management, in order to allow conclusions to be made about the most appropriate management of fistulae worldwide.

2. Evidence acquisition

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement, a prospective search protocol was developed and registered with the PROSPERO database (ID number: CRD42015019021). Published evidence was identified through a search of the PubMed and Scopus databases using the following search terms: "obstetric fistula", "vaginal fistula", "bladder fistula", "urethral fistula", "urinary fistula", "vesicovaginal fistula", "genital fistula", and "fistula", which yielded 12 626 articles. The search was limited to women and the English language and further refined by excluding the following MeSH headings "infant", "child", "neonate", "male", "penile", "Crohn's disease", "hypospadias", "anal", "rectal", "arterial", and "venous". The search was limited to the period between January 1980 and March 2015 and further excluded case reports, which yielded 680 articles (Fig. 1). Forty-seven additional records were identified through searching the references of included articles and other review texts. Abstract screening followed by full text screening was performed.

The primary outcome was to report fistula aetiology; secondary outcomes included surgical technique and surgical outcomes. Each article was rated following the Oxford Centre for Evidence-Based Medicine levels of evidence scale (Fig. 2) [4].

3. Evidence synthesis

After screening these abstracts and excluding articles with fewer than 20 patients (for quality purposes), 98 full texts were identified, which includes four articles found through reviewing the references of other included articles. Of these, 49 were excluded for not reporting fistula aetiology, not clearly reporting outcomes, or excluding those that describe a significant proportion of recto-vaginal fistulae or ureterovaginal fistulae. Table 1 demonstrates that from 49 studies, 15 studies reported on fistula repair in WRC [2,5–18], while 34 studies reported on fistula management in LRC [19–52]. In all, two studies were randomised controlled trials (RCTs) and two were feasibility cohort studies that compared new treatments. RCTs compared outcomes for patients randomised to use fibrin glue compared with Martius flap interpositioning [42] and to trimming versus no trimming of the fistula tract [43]. The two cohort studies included in this review investigated the use of Floseal haemostatic matrix (Baxter Healthcare Corp., IL, USA) [19] and porcine small intestinal submucosa (Surgisis Biodesign, Cook Medical, Bloomington, IN, USA) [25] as interposition materials. Eleven studies included prospective data, while 34 were retrospective series.

3.1. *Fistula aetiology*

3.1.1. *Surgery/radiotherapy*

The 15 included articles reporting data from WRC included 2055 fistulae, of which 1710 (83.2%) were of a surgical aetiology; in contrast, the 34 included articles reporting data from LRC included 10 398 fistulae, of which only 459 (4.4%) were of a surgical aetiology (Table 2). Of the 2055 fistulae in WRC, 46.2% were associated with simple abdominal hysterectomy and hysterectomy by any route was an aetiological factor in 62.7% of all fistulae and 75.4% of the 1710 cases of fistulae resulting from surgery. Some cases were associated with other types of pelvic surgery (12.7%), including benign and malignant colorectal, urological, and gynaecological procedures that were otherwise unspecified in the included articles.

Of the 2055 fistulae reported from WRCs, 268 (13.0%) followed radiotherapy (with or without previous radical surgery); in comparison, only 17/10 015 (0.2%) of fistulae seen in LRCs followed radiotherapy.

3.1.2. *Childbirth*

Of fistulae reported from LRCs, 9902/10 398 (95.2%) cases were of an obstetric aetiology. Prolonged neglected

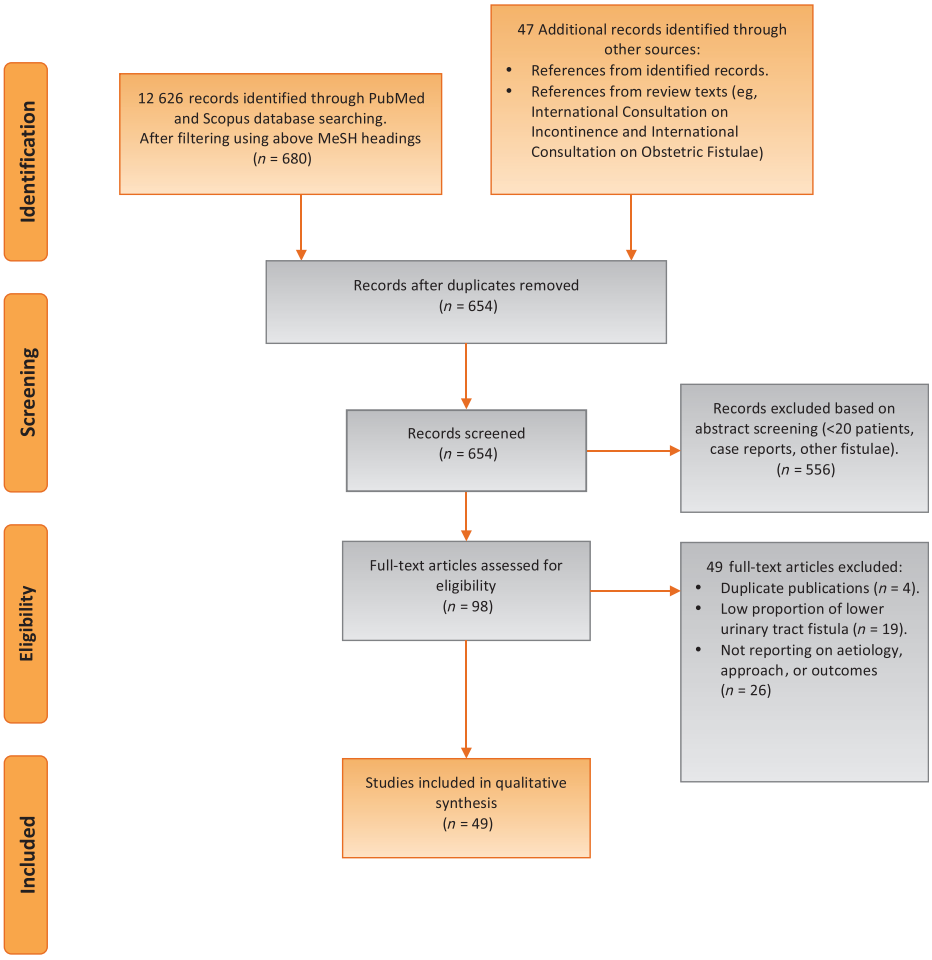

Fig. 1 – Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow-diagram to demonstrate progress of articles through the review.

Level	Type of evidence
1a	Systematic review with homogeneity of randomised control trials
1b	Individual randomised control trial with a narrow confidence interval
1c	All or none related outcome
2a	Systematic review with homogeneity of cohort studies
2b	Individual cohort study (including low-quality randomised control trials, eg, <80% follow-up)
2c	"Outcomes" research; Ecological studies
3a	Systematic review with homogeneity of case–control studies
3b	Individual case–control study
4	Case-series (and poor-quality cohort and case–control studies)
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or "first principles"

Fig. 2 – Evidence-based medicine levels of evidence scale [4].

Table 1 – Available articles included in the review

Well-resourced countries										
Study	Design	Population	Sample size	Aetiology	Outcome definition	Exposure of interest	Approach	Outcomes	Follow up or study duration	CEBM levels of evidence
Blaivas et al., 1995 [5]	Retrospective	All VVF	24	12 TAH 3 TVH 2 anterior colporrhaphy 2 urethral diverticulectomy 1 Colposuspension 1 bladder rupture 3 no details provided	Not given	Transvaginal repair vs transabdominal repair	Transvaginal in 15, transabdominal in 8, conservative in 1	23/24 success (96%) 1 SUI	6 mo to 4 yr	4
Brandt et al., 1998 [6]	Prospective	All benign VVF	80	68 TAH 5 TVH 7 anterior colporrhaphy	Not given	Use of bladder mucosa autograft via vaginal approach	All vaginal	77/80 overall success (96%) 1 SUI	1 yr	2b
Cromwell and Hilton 2012 [2]	Retrospective	All VVF and genitourinary tract fistula	1194	177 malignant gynaecological conditions 328 benign gynaecological conditions 171 bladder/colon malignancies 518 others (426 hysterectomy, 33 caesarean sections)	Need for repeat repair		Not specified 294 ileal conduit	797/905 overall success (88.1%)	10 yr retrospective analysis Re-op rates for trusts performing >3 procedures/yr 7.4% vs 13.2% for less	2c
Eilber et al., 2003 [7]	Retrospective	All VVF repaired transvaginally	207	172 TAH 17 TVH 8 DXT 10 obstetric causes/ colporraphy Total of 159 recurrent fistulae	Need for repeat procedure	Transvaginal repair using interposition ing 120 - peritoneum/ Martius/full-thickness labia flap	Transvaginal In 120 patients with complex/recurrent fistulae, peritoneum flap in high fistulae, Martius in low, labia used if sufficient vaginal epithelium not available.	201/207 overall success (97%) 99% success for those not requiring interposition 96%, 97%, 33% for peritoneum, Martius, and labial flaps respectively	10 yr retrospective analysis	2b
Evans et al., 2001 [8]	Retrospective	All VVF repaired transabdominally	37	20 TAH 1 D&C 1 obstetric 2 caesarean section 1 tubo-ovarian abscess 4 trauma 4 gynaecological DXT 3 radical gynaecological surgery and DXT 1 radical gynaecological surgery Total of 12 redo procedures	Completely dry by patient report	Transabdominal - interposition (omentum) vs no flap	Transabdominal	28/37 overall success (75.8%) 100% success when interposition flap used 63% success no flap (benign) 67% no flap (malignant)	>6mo	4
Hadzi-Djokic et al., 2008 [9]	Retrospective	All primary or recurrent VVF	220	138 benign hysterectomy 67 radical hysterectomy 13 caesarean section 2 obstetric injuries	Need for repeat repair		129 transvesical, 59 transvaginal, 32 transperitoneal with omentum/ peritoneum interposition flap	208/220 overall success (94.6%)		4

Table 1 (*Continued*)

Well-resourced countries										
Study	Design	Population	Sample size	Aetiology	Outcome definition	Exposure of interest	Approach	Outcomes	Follow up or study duration	CEBM levels of evidence
Hilton 2012 [10]	Prospective	All genitourinary tract fistula	283	132 TAH 19 radical hysterectomy 15 urethral diverticulectomy 7 midurethral tape 9 TVH 12 colporrhaphy 45 other pelvic procedure 15 caesarean section 8 uterine rupture 5 instrumental delivery 4 caesarean hysterectomy 2 prolonged labour 4 other obstetric 28 DXT 11 pessary 6 congenital 25 others	Absence of urinary leakage at 2–3 mo follow-up		82 transabdominal procedures, including 66 transperitoneal (15 with ureteric reimplantation), 16 transvesical, 201 transvaginal	267/283 overall success (95.4%) (83.3% success for transabdominal, 96.1% for transvaginal) 93.5% continence rate		4
Kochakarnand Pummangura 2007 [11]	Retrospective	All VVF	45	28 laparoscopic hysterectomy 10 TAH 4 TVH 3 RH	Subjective dry		19 transvaginal, 26 transabdominal	42/45 overall success (93.3%) (89% of transvaginal dry, 96% of transabdominal dry)	8 yr retrospective	4
Langkilde et al., 1999 [12]	Retrospective	All VVF	37	30 pelvic surgery 7 DXT	Subjective dry		25 transabdominal, 12 transvaginal	28/37 overall success (76%) 90% success for benign fistulae, 14% for fistulae following DXT		4
Lee et al., 2014 [13]	Retrospective	All nonradiated VVF	66	28 hysterectomy unknown route 5 TAH 1 TVH 1 laparoscopic hysterectomy 2 obstetric 5 other	Absence of leakage on postoperative UDS	Primary vs recurrent	50 transvaginal, 16 transabdominal	64/66 overall success (97%) (failures all transvaginal and underwent successful transabdominal repair. No significant difference between primary and multiple surgical repairs 8 SUI	Mean follow-up 55 mo (6–198 mo)	4
Milicevic et al., 2013 [14]	Retrospective	All VVF	24	4 DXT 19 TAH 1 caesarean section	Need for further repair		All routes	23/24 overall success (96%). 75% following primary repair (100% with transvaginal and transperitoneal each, 68% with transvesical)		4
Mondet et al., 2001 [15]	Retrospective	All VVF treated by trans peritoneal transvesical repair	28	19 hysterectomy nos 1 obstetric 4 caesarean-section 2 DXT 2 pelvic surgery nos	Complete repair of communication and absence of symptoms		Transperitoneal, transvesical	24/28 overall success (85%) 0/2 success for patients with history of DXT	Mean follow-up 30 mo (23 d to 14.6 yr)	4

Ockrim et al., 2009 [16]	Retrospective	All VVF and UVF	37	16 TAH 3 caesarean section 2 caesarean hysterectomy 2 cystoplasty 1 bladder neck closure 1 colposuspension 2 DXT 1 obstructed labour 2 urethral diverticulectomy 3 autologous fascial sling 2 MUT 2 urethropexy	Subjective and objective (UDS) cure		Transabdominal and transvaginal	34/37 overall success (92%) 73% success after initial procedure	6 mo	4
Pushkar et al., 2009 [17]	Retrospective	All VVF following DXT	210	Radical hysterectomy and DXT	Absence of urinary leakage		Transvaginal	169/210 overall success (80.4%) 48.1% success after initial repair	40 yr retrospective	4
Pushkar et al., 2006 [18]	Retrospective	All urethrovaginal fistulae	71	19 obstetric 16 periurethral cyst 12 anterior colporrhaphy 9 autologous fascial sling 8 periurethral bulking agents 4 midurethral tape 3 other	Absence of fistulae recurrence		Transvaginal (9 with Martius flap interpositioning)	70/71 overall success (98.59%) 90.14% success after initial repair SUI 37/71 (52%)	21 patients with mean follow-up of 99.6 mo (84–103 mo)	4

Low-resourced countries

Study	Design	Population	Sample size	Aetiology	Outcome definition	Exposure of interest	Approach	Outcomes	Follow-up or study duration	CEBM levels of evidence
Abou-Elela et al [19]	Cohort study	Supratrigonal and complex VVF	20	Obstetric trauma	Not given	Use of Floseal matrix and parasagittal abdominal approach with bladder flap		20/20 overall success (100%) after initial repair	Not given	4
Ahmad et al., 2005 [20]	Retrospective	All obstetric genitourinary fistulae	1086	790 obstructed labour 83 caesarean hysterectomy 79 caesarean section 48 forceps delivery 46 foetal destructive procedures 40 uterine/bladder rupture	Not given		1002 transvaginal 84 transabdominal	918/1086 overall success (84.5%) 5% SUI	25 yr retrospective	4
Amr 1998 [21]	Retrospective	All VVF	132	30 obstructed labour 16 caesarean-section 18 uterine rupture 14 forceps delivery 25 TAH 8 TVH 3 anterior colporrhaphy 11 others	Absence of urinary leakage following catheter removal		123 transvaginal 9 transabdominal	108/132 overall success (82%) 45% success after initial repair	24 yr retrospective	4
Dalela et al., 2006 [22]	Prospective	Supratrigonal VVF	26	22 obstructed labour 2 TVH 2 TAH	Absence of urinary leakage following catheter removal	Modified O'Connor's transperitoneal repair	Transperitoneal (24 omentum interpositioning 2 paravesical peritoneum)	26/26 overall success (100%) 1 SUI	21 followed up 1–5 yr	4
El-Lamie 2008 [23]	Retrospective	All genitourinary fistulae (VVF 22, VUF 4)	26	(VVF) 10 obstructed labour 6 TAH 3 radical hysterectomy + DXT 1 vaginoplasty, 2 cystolitholapaxy (VUF) 4 elective caesarean section	Subjective absence of urinary leakage		16/22 of VVF underwent transvaginal approach (Martius flap following DXT) 6 transabdominal	26/26 overall success (100%) 100% success after initial surgery for VUF 91% success after initial surgery for VVF	10 yr retrospective	4

Table 1 (*Continued*)

Low-resourced countries										
Study	Design	Population	Sample size	Aetiology	Outcome definition	Exposure of interest	Approach	Outcomes	Follow-up or study duration	CEBM levels of evidence
Ezzat et al., 2008 [24]	Retrospective	Large VVF using combined abdominal and vaginal approach	35	25 obstructed labour 5 iatrogenic pelvic surgery 3 sling erosion 2 DXT (12 recurrent fistulae)	Combined symptomatic and anatomical absence of leakage	Combined abdominal (O'Connor) and vaginal approach	Interposition type: 5 omentum 2 peritoneum 3 Martius 13 gracillis 12 no flap	35/35 overall success (100%) 88% success after initial surgery, all successfully repaired with vaginal approach 10/12 recurrent fistulae repaired at 1st attempt, 2 at second	27 yr retrospective	4
Farahat et al., 2012 [25]	Cohort study	Complicated VVF: recurrent, large, or with excessive scarring	23	8 obstructed labour 3 anterior colporrhaphy 9 TAH 3 TVH (10 fistula > 1.5 cm)	Symptomatic absence of leakage	Porcine small intestinal submucosa graft	7 transvaginal (low fistulae) 16 transabdominal	21/23 overall success (91.3%) (all transvaginal approaches and 14/16 transabdominal approaches successful)	6 mo	2b
Hilton and Ward 1998 [26]	Retrospective	All urogenital fistulae	2484	(Case notes only available for 2389 patients) 1918 obstructed labour 165 caesarean section 119 uterine rupture 105 gynaecological surgery 42 malignancy 40 miscellaneous 0 DXT	Subjectively dry at last assessment		83% transvaginal 17% transabdominal	Only 2360 patients operated on 2306/2360 overall success (97.7%) 1954/2360 success after initial repair (82.8%)	25 yr retrospective	4
Holme et al., 2007 [27]	Retrospective	All obstetric fistulae	255	All obstetric	Not given	Socio economic status	Not given	186/255 overall success (72.9%) SUI 44/255 = 17.3%	18 mo retrospective	4
Jatoi et al., 2005 [28]	Prospective	All VVF	32	8 vaginal delivery 2 instrumental delivery 10 Caesarean hysterectomy 1 D&C 2 TAH 1 vaginoplasty 1 DXT 2 congenital 1 cystolitholapaxy	Subjective dry following catheter removal at 2 wk		29 operations: 27 transvaginal 2 transabdominal	27/29 overall success (93%)	3 mo	4
Jokhio and Kelly 2006 [29]	Retrospective	All obstetric fistulae	116	98 obstructed labour, 15 pelvic surgery 3 congenital (23 recurrent fistulae)	Absence of urinary leakage		Not specified	93/116 overall success (80%) 6% recurrent fistulae 14% SUI		4
Kayondo et al., 2011 [30]	Prospective	All obstetric fistulae. VVF only included	68	All obstructed labour	Closed on dye test but dry, closed on dye test but incontinent, failed repair	Patient demographics	Not specified	55/68 overall success (79.7%) 13 (23.6%) incontinent		4
Khan et al., 2005 [31]	Retrospective	All VVF	30	19 vaginal delivery 4 caesarean-section 4 hysterectomy 1 forceps delivery 1 bladder calculus 1 DXT (3 recurrent fistulae)	Absence of any urinary leakage		All transabdominal transvesical	24/30 overall success (80%): fistula closure 3/30 failed repair (10%) 3/30 had SUI (10% SUI)	6 yr	4

Kirschner et al., 2010 [32]	Retrospective	All VVF	926	Obstructed labour: 369 caesarean section 303 vaginal delivery 84 forceps delivery 9 foetal destruction 161 unknown	Subjective dry vs wet		90% transvaginal 10% transabdominal	779/926 overall success (84.1%): fistula closure 70% continence	6 yr retrospective	4
Lewis et al., 2009 [33]	Retrospective	All obstetric fistula	505	Obstetric no other details	Subjective dry at discharge		Not given	294/505 overall success (58%) 10% SUI		4
Mathur et al., 2010 [34]	Prospective	All VVF	32	18 obstructed labour 8 caesarean section 14 TAH 4 TVH 2 DXT 4 miscellaneous	No definition given		9 transvaginal 14 transabdominal 5 transabdominal after initial transvaginal 4 conservative	24/32 overall success (76%)	4 yr	4
Nafiou et al., 2007 [35]	Prospective	All obstetric VVF	104	Obstetric no other details	Subjective and objective dry		91% transvaginal 7% transabdominal2% combined	76/104 closed and dry (73%) 14/104 closed and wet (13.5%) 5 unsuccessful (5%) 7 lost to follow up, 2 died	3 mo	4
Nawaz et al., 2010 [36]	Retrospective	All fistulae (VVF only presented)	133	50 obstructed labour 19 caesarean hysterectomy 17 caesarean section 15 instrumental delivery 19 TAH 6 TVH 1 colporrhaphy 3 DXT 2 neglected pessary 1 inflammatory	Anatomical closure of fistula		Not given	117/133 overall success (88%)	3 mo	4
Obi et al., 2008 [37]	Retrospective	All VVF	476	412 obstructed labour: (330 vaginal delivery 35 caesarean section 26 caesarean hysterectomy 21 instrumental delivery) 33 TAH 13 TVH 12 malignancy 6 DXT	Anatomical closure and complete functional continence		Not given	4/18 successful conservative treatment 380/458 overall success (83%)	25 yr retrospective	4
Raashid et al., 2010 [38]	Retrospective	All VVF	61	27 hysterectomy 5 elective caesarean sections 1 forceps delivery 28 obstructed labour (17 spontaneous delivery, 11 caesarean section)	Absence of leakage at 6 wk follow-up		87% transvaginal, 13% transabdominal	53/61 overall success (87%) 46/53 transvaginal success (87%) 7/8 transabdominal success (88%)	2 yr retrospective	4
Raassen et al., 2008 [39]	Prospective	All primary lower genitourinary fistulae	639	581 obstetric nos 45 hysterectomy 9 miscellaneous 4 unknown	Negative dye test	Obstetric VVF only 565	87.6% transvaginal, 12.4% transabdominal	5532/565 overall success (94.1%): closure	<3 mo	4
Rafique 2003 [40]	Retrospective	All obstetric genitourinary fistulae	42	16 obstructed labour 16 obstructed labour, and caesarean section, 2 elective caesarean sections 2 caesarean hysterectomy 5 dilatation and curettage 1 forceps delivery	Subjective dry and gynaecological exam		29 transvesical 10 transvaginal 3 transabdominal for ureterovaginal fistula	36/41 overall success (87%)	<3 mo	4

Table 1 (*Continued*)

Low-resourced countries										
Study	Design	Population	Sample size	Aetiology	Outcome definition	Exposure of interest	Approach	Outcomes	Follow-up or study duration	CEBM levels of evidence
Sachdev et al., 2009 [41]	Retrospective	All obstetric VVF	276	117 obstructed labour 29 caesarean hysterectomy 24 hysterectomy 2 D&C 2 malignancy 1 trauma 2 cystolitholapaxy 1 congenital	Subjective dry		8 conservative 261 transvaginal 7 transabdominal	265/276 overall success (96%)	Retrospective 10 yr	4
Safan et al., 2009 [42]	RCT	All VVF in patients aged 16–50 yr, fistula size < 5 cm, < 3m from occurrence	38	Obstetric nos	Dry at clinic 3/12	Use of fibrin glue vs Martius flap interpositioning	19 transvaginal with fibrin glue 19 transvaginal with Martius flap	13/19 overall success using fibrin (68%) 11/19 overall success using Martius flap interpositioning (58%)	3 mo	2b
Shaker et al., 2011 [43]	RCT	All obstetric VVF aged 16–50 y, any fistula size, <3 mo from occurrence	63	Obstetric nos	Objective during examination at 3 mo follow-up	Trimming or no trimming of fistula edges	31 transvaginal with fistula trimming 32 transvaginal without fistula trimming	23/31 of trimming group overall success (75%) 22/32 of no trimming group overall success (67.6%) 6 SUI (4 trimming, 2 nontrimming)	3 mo	2b
Shoukry et al., 2010 [44]	Retrospective	All obstetric VVF	20	Obstructed labour: (15 vaginal delivery, 5 forceps delivery)	Subjective and objective dry	Use of rectangular vaginal flap using transvaginal approach	Transvaginal vaginal flap technique	20/20 overall success (100%)	Follow-up mean 16 mo (8–28 mo)	4
Singh et al., 2010 [45]	Retrospective	All genitourinary fistulae (37 VVF)	42	22 obstructed labour nos 8 TAH 4 TVH 1 laparoscopic hysterectomy 3 radical hysterectomy 4 miscellaneous	Not described		3 successful conservative management. 28 trans abdominal + peritoneum interpositioning11 transvaginal + Martius flap	34/39 overall success (80.1%) after initial attempt	4–42 mo	4
Singh et al., 2012 [46]	Prospective	All VVF	48	30 obstetric nos 18 gynaecological surgery	Negative postoperative cystogram	Transabdominal approach	Transabdominal	44/48 overall success (91.6%) 87.5% success after initial repair	4 wk	4
Singh et al., 2011 [47]	Retrospective	All VVF	102	78 obstructed labour (64 spontaneous delivery, 14 instrumental delivery) 20 gynaecological procedure nos 4 DXT	Negative postoperative cystogram	Transvaginal approach	Transvaginal Martius (3), gracillis flap (1)	88/102 overall success (86.3%) 10 SUI	Median 48 mo	4
Sjoveian et al., 2011 [48]	Retrospective	All obstetric fistulae	595	470 obstructed labour 69 caesarean section or emergency peripartum hysterectomy 28 gynaecological surgery	Negative dye test at 14 d		Not specified	518/595 overall success (87.1%), of which 15.6% remained incontinent despite closure	2 yr retrospective	4

Tayler-Smith et al., 2013 [49]	Retrospective	All obstetric fistulae	458	Obstetric	Negative dye test at 14 d		Not specified	4/35 had successful conservative management (11%) 394/454 overall success (87%) 76% continent	1 yr retrospective data	4
Vanderputte et al., 1985 [50]	Retrospective	All obstetric fistulae	87	74 obstructed labour, spontaneous delivery 2 caesarean section 7 laparotomy for uterine rupture 2 foetal destructive procedures 2 instrumental delivery	Clinical examination at 2 mo		84 transvaginal 3 transabdominal	77/87 overall success (88.5%), including 4 patients with UUI/SUI > 6mo, 1 patient with total incontinence, 3 patients with failed second repair, and 2 deaths		4
Vyas et al., 2005 [51]	Prospective	All VVF	22	15 Obstetric nos 5 TAH 2 TVH (5 recurrent fistulae)	Leakage following catheter removal	Bladder mucosa autografts	19 transabdominal 3 combined transabdominal and transvaginal	20/22 overall success (91%)		4
Waaldijk 2004 [52]	Prospective	All obstetric VVF <3 mo from occurrence	1716	Obstetric nos	Successful fistula closure		265 conservative 1451 surgical	1690/1716 overall success (98.5%) 94.3% successful closure after initial surgical attempt 93.2% continent	90% of patients were followed-up between 3–6 mo	4

CEBM = Centre for Evidence-Based Medicine; DXT = radiotherapy; D&C = dilatation of the cervix and curettage of the endometrium; MUT = midurethral tape; NOS = not otherwise specified; RH = radical hysterectomy; SUI = stress urinary incontinence; TAH = total abdominal hysterectomy; TVH = total vaginal hysterectomy; UDS = urodynamics; VUF = vesico-uterine fistula; VVF = vesico-vaginal fistula.

Table 2 – Fistula by aetiology

Cause	Well-resourced countries *N* (%)		Low-resourced countries *N* (%)	
Surgical causes				
Abdominal hysterectomy	949	(46.2)	123	(1.2)
Radical hysterectomy	87	(4.2)	3	(0.0)
Vaginal hysterectomy	39	(1.9)	42	(0.4)
Urethral diverticulectomy	19	(0.9)	0	(0.0)
Anterior colporrhaphy	33	(1.6)	7	(0.1)
Laparoscopic hysterectomy	29	(1.4)	1	(0.0)
Midurethral tape	15	(0.7)	3	(0.0)
Colposuspension	2	(0.1)	0	(0.0)
Autologous fascia sling	12	(0.6)	0	(0.0)
Urethropexy	2	(0.1)	0	(0.0)
Vaginoplasty	0	(0.0)	2	(0.0)
Periurethral bulking agent	8	(0.4)	0	(0.0)
Periurethral cyst excision	16	(0.8)	0	(0.0)
Hysterectomy NOS	185	(9.0)	100	(1.0)
Pelvic surgery NOS	262	(12.7)	162	(1.6)
D&C	1	(0.0)	8	(0.1)
Cystoplasty	2	(0.1)	0	(0.0)
Pessary	11	(0.5)	2	(0.0)
Cystolitholapaxy	0	(0.0)	6	(0.1)
Caesarean section (WRC only)	38	(1.8)	–	–
Subtotal	1710	(83.2)	459	(4.4)
Obstetric causes				
Caesarean section (LRC only)	–	–	940	(9.0)
Uterine/bladder rupture	9	(0.4)	184	(1.8)
Instrumental delivery	5	(0.2)	208	(2.0)
Caesarean hysterectomy	4	(0.2)	193	(1.9)
Prolonged obstructed labour	3	(0.1)	4665	(44.9)
Foetal destructive procedures	0	(0.0)	57	(0.5)
Obstetric NOS	50	(2.4)	3655	(35.2)
Subtotal	71	(3.5)	9902	(95.2)
Radiotherapy	268	(13.0)	17	(0.2)
Malignancy	0	(0.0)	14	(0.1)
Congenital	6	(0.3)	6	(0.1)
Total	2055		10 398	

D&C = dilatation of cervix and curettage of endometrium; LRC = low-resourced country; NOS = not otherwise specified; WRC = well-resourced country.

obstructed labour was a causative mechanism in the majority of these, and where specified, caesarean section and instrumental delivery were associated in 9% and 2% respectively. A further 35.2% of fistulae resulted from delivery without any further specific details. Emergency peripartum injury (bladder/uterine rupture, caesarean hysterectomy for bleeding, or foetal destructive procedures) were associated with fistula formation in 1.8%, 1.9%, and 0.5% of cases respectively.

Of so-called 'obstetric fistulae' in LRCs, 940/9902 (9.5%) were associated with caesarean section and 1341/9902 (13.5%) were associated with some surgical intervention. Seventy one out of 2055 (3.5%) fistulae in WRCs were classified as obstetric in origin; however, those fistulae that occur following caesarean section in WRCs were classified as "surgical fistulae."

Miscellaneous causes, such as trauma, foreign bodies, and infection are not included in these data, as they represented only a very small proportion of fistula cases; one of the largest studies [2] could not be included as the exact aetiology of

fistula formation was not apparent and one study included solely radiotherapy induced fistulae [17].

3.2. Fistula management

Six studies directly commented on the conservative treatment of fistulae (two in LRCs and four in WRCs) [5,10,37,45,49,52]. In WRCs, the usual current practice is to perform a delayed repair of the fistula following a period of catheter drainage to allow necrotic tissue to slough and local inflammatory responses to subside. Successful closure rates from this conservative management approach, however, are likely to be underestimated given that successful outcomes in this context are not referred for surgical intervention, and therefore often unreported. A similar "delayed" approach has usually been undertaken in LRCs, although both Waaldijk [52] and Tayler-Smith et al [49] selected patients for conservative management if the time-to-fistula development was short, the fistula itself was small (<3 cm), and the prospects for spontaneous healing were good. In the Waaldijk series [52], catheter drainage was continued in 265/1716 (15.4%) of patients, achieving fistula closure in 264 patients, while Tayler-Smith et al [49] demonstrated spontaneous closure rates in four out of 35 (11%) patients. Patients with a longer history or those in whom the fistula edges were clean were selected for immediate surgery, while those with no evidence of healing following catheterisation underwent repair. In total, 1451/1716 cases in the Waaldijk [52] series were treated with surgery, with anatomical closure in 1369/1451 (94.3%).

Given the heterogeneity in fistula characteristics and locations, it is difficult to comment on the surgical approach. Of studies which specify a particular approach in WRCs, 924/1307 (70.7%) of procedures were performed transvaginally. In comparison, 5376/6369 (84.4%) of patients reported from LRCs, where a specific approach was documented, underwent a transvaginal approach; with 14.6% undergoing a transabdominal procedure and 1% having a combined abdominal/vaginal approach.

A variety of interposition grafts have been used. These include omentum or perivesical peritoneum during abdominal repairs, and the Martius bulbocavernosus muscle/fat graft, or labial skin flap at transvaginal repairs. Peritoneum can be used for high fistulae and gracillis myocutaneous flaps were used in two studies in large or postradiotherapy fistulae [24,47]. No high quality evidence exists to support the use of graft interposition in any context, and anecdotally the use of grafting by obstetric fistula surgeons has declined in LRCs.

The largest series of radiotherapy-induced fistulae, from Pushkar et al [17], describes the transvaginal approach in all patients using either a Martius flap or a Latzko colpocleisis in patients with small, defined fistulae. Many patients with radiation-induced fistula will ultimately undergo urinary diversion either due to the complexity of the fistula itself, poor tissue viability, anaesthetic issues, or surgeon preference [2]. Reporting of patients undergoing diversion are not included in this review; however, urinary diversion is seen as a treatment of choice in many patients with radiotherapy-induced fistulae, owing to the wide field abnormality in this context. Others argue that in carefully selected patients with malignant- or radiotherapy-induced fistulae, repair should be attempted. In Hilton's series [10] reported in 2012, of the 19/36 (53%) patients with malignant- or radiotherapy-induced fistulae who underwent a primary repair operation, 95% were successfully closed after the first surgery.

Two feasibility cohort studies [19,25] investigated the benefit of Floseal haemostatic matrix (Baxter Healthcare Corp.) and porcine small intestinal submucosa (Surgisis Biodesign, Cook Medical) grafts respectively. One RCT investigated the use of autologous fibrin glue versus standard Martius flap interposition grafting [42], while the other assessed the outcomes of patients undergoing trimming versus no trimming of the bladder edge of the fistula [43].

3.3. Definition of success

The definition of surgical success varies between studies. In general, these range from "anatomical closure of fistula", "anatomical closure of fistula but residual leakage", or "failed repair", while others use the "need for a repeat procedure" as the definition of failure. A common practice in studies in WRCs is to perform a cystogram prior to catheter removal following surgery, while those in LRCs opt to perform catheter removal 14 d postoperatively, with catheter reinsertion in the presence of continued urinary leakage. There may therefore be some discrepancy in the reporting of urinary leakage that is due to the closure of the fistula from that caused by stress or urgency urinary incontinence.

The timing of the outcome definition is clearly important. While the majority of studies involving patients in LRCs will define the success of a procedure at the time of catheter removal, those in WRCs will reserve the definition of success until discharge or at clinic follow-up.

3.4. Management outcomes

Of patients managed conservatively, Hilton [10] demonstrated 24 patients in his UK series (6.9% of total) showing spontaneous successful closure following 6–8 wk of catheter drainage; spontaneous closure was not seen in any of the radiotherapy-induced fistulae in this series. While in LRCs, successful conservative management was achieved in 264/1716 patients, constituting 15.6% of patients and 16.2% of fistula closures in the Waaldijk series [52], and in four out of 35 (11%) patients with small necrotic fistulae reported by Tayler-Smith et al [49].

Of patients undergoing surgical closure in WRCs, the median overall closure rate was 94.6% (range, 75.8–98.6%). Studies included with the lowest overall success had a high proportion of radiation-induced fistulae [8,12,17]. In this context a higher success rate was claimed in one small series when interposition grafts were used [two out of two (100%) success rate vs four out of six (67%) when no grafts were used], although these differences are not statistically significantly different [8]. The highest anatomical closure rate of included studies was reported by Pushkar et al [18]

for patients undergoing a transvaginal repair of urethrovaginal fistulae. Of studies that reported postfistula repair stress urinary incontinence (SUI) in WRCs [5,6,10,13,18], the median rate was 6.5% (range, 1.1–51.9%), with the highest rates seen following a transvaginal repair of urethrovaginal fistulae.

Of patients undergoing surgical repair in LRCs, the median overall closure rate was 87.0% (range, 58.0–100%). The median SUI rate for patients with a closed fistula was 10.0% (range, 3.8–30.0%), across all surgical approaches and fistula characteristics.

Abou-Elela et al [19] used Floseal matrix to promote healing and haemostasis and demonstrated 100% success rates following initial attempts at repair in a series of 20 cases. Farahat et al [25] used porcine small intestinal submucosa interposition grafting by either transvaginal or transabdominal approaches in patients with large, complicated vesico-vaginal fistulae. The group demonstrated a 91.3% overall success, with seven out of seven transvaginal procedures and 14/16 transabdominal procedures achieving closure over a follow-up period of 6 mo, with no reported SUI.

In one randomised trial by Safan et al [42], 13/19 (68%) of patients were dry at the 3-mo postoperative follow-up visit following a transvaginal repair using fibrin glue versus 11/19 (58%) of patients (not statistically significant) undergoing a transvaginal repair using a Martius flap. Shaker et al [43] demonstrated that 24/32 (75%) of patients had a closed fistula at the 3-mo postoperative follow-up visit following trimming of the bladder edge of the fistula by 5 mm using a transvaginal approach compared with 21/31 (67.6%) of patients when trimming is not performed. Again, these findings did not reach statistical significance.

There are no randomised studies available that directly compare the outcomes of transabdominal versus transvaginal approaches, given that each surgeon has a particular preference for a certain indication and clearly there would be ethical issues with the conduct of such a study. Of the included studies, three [9,10,16] reported the outcomes of transvaginal versus transabdominal approaches for fistula repair. Amongst these, the overall success rates were 90.8% of 286 vaginal repairs and 83.9% of 250 abdominal repairs (Fisher's exact test; $p = 0.0176$). It must be emphasised that these reports were reviewing nonrandomised cohorts; it is likely that the particular approach used in individual cases was selected based on the preoperative evaluation and dependant on individual surgical bias and it is not therefore valid to carry out a direct comparison of outcomes.

3.5. Discussion

To the best of our knowledge, this is the first review article of its type to compare the aetiologies and management of lower urinary tract fistula in WRCs and LRCs. Most studies included were retrospective case series, while 11 included prospective data, two were nonrandomised cohort studies, and two were RCTs.

We demonstrate that while 83.2% of fistulae in WRCs result from surgical intervention, 95.2% of fistulae in LRCs result from obstetric causes. The large majority of obstetric fistulae seen in LRCs occur as a consequence of prolonged neglected obstructed labour, where sustained pressure necrosis arises due to compression of the bladder base and anterior vaginal wall between the foetal head and symphysis pubis. Furthermore, iatrogenic injury, especially of these devitalised areas during a caesarean delivery may lead to fistula formation subsequently. As the necrotic tissue sloughs off postoperatively, the fistula may become manifest. It is important to note that the fistulae that occur following caesarean section in WRCs are more akin to surgical fistulae, as prolonged obstructed labour is unlikely to be involved in this context.

It must be emphasised that the fistulae that occur after pelvic surgery, are not necessarily a consequence of inadvertent organ injury or surgical misadventure. Tissues may become devitalised as a consequence of extensive dissection or haematoma formation with fistulae forming weeks later. Fistulae that result following ionising radiation may present many months to years later and are thought to occur due to chronic small vessel inflammatory changes leading to tissue ischaemia.

It is apparent that any surgical procedure in the pelvis can lead to fistulae formation. In the current study, 75.4% of postsurgical fistulae resulted following a hysterectomy. Hilton and Cromwell [53] examined Hospital Episode Statistics for English National Health Service hospitals and found that the overall rate of fistula formation following a hysterectomy was one in 788. Furthermore, the study demonstrated a 46% rise in the rate of fistula formation following a hysterectomy from 2000 to 2008, which the authors concluded could reflect the reduced exposure of trainees to these cases associated with a fall in the number of hysterectomies performed.

Spontaneous closure of fistulae is feasible and the rate with which this occurs is likely to be underestimated due to the fact these cases are seldom referred for further treatment. A 6–8-wk period of continuous catheter drainage allows the diversion of urine away from the visceral communication, which can allow spontaneous closure before epithelialisation of the fistula track can occur and this is certainly worth attempting in patients with vesico-vaginal or urethrovaginal fistulae [54]. In patients with a significant degree of necrotic material and slough, catheterisation can allow maturation of the fistulous tract to a sufficient degree that closure can be performed. Rates of spontaneous closure, even for obstetric fistulae, are reported in up to 28% of patients when early catheter drainage is instituted [55]. Radiotherapy-induced fistulae, however, are seldom if ever associated with spontaneous closure and operative management should be performed as appropriate.

There is debate surrounding the optimum timing of repair; immediate or delayed. While the exact definition of what constitutes an "immediate" repair varies between studies, most would consider less than 6 wk. Intuitively, repair should be performed following a period of catheterisation to allow inflammation to settle and necrotic material to slough off whilst providing the opportunity for spontaneous closure and allowing the patient to recover from the initial surgery. Waaldijk [52] using a definition of

"immediate" as within 3 mo of creation, reported 95.2% successful initial closure rates. The rationale behind immediate surgical treatment is to prevent distress to the patient, contain skin irritation, and in LRCs, to minimise stigmatisation.

There is currently an absence of adequate trial data, however, to support immediate repair over a delayed approach. In the experience of the authors, it is certainly more challenging to perform a repair between the 3rd wk and the 3rd mo following fistula formation.

A further area of contention in contemporary fistula surgery surrounds the route of surgery. Clearly, where there is synchronous ureteric involvement, vesico-uterine fistulae, or when access to the vagina is limited, then a transabdominal approach is more likely to be indicated. In the current review, 71% of lower urinary tract fistulae were repaired transvaginally in WRCs compared with 84% in LRCs. The success rates for transvaginal versus transabdominal repairs were 90.8% and 83.9% respectively. While this is a significant finding, clearly these results should be interpreted with caution, given that these approaches are not chosen at random, but based upon specific patient characteristics.

Both laparoscopic- and robot-assisted repair of vesico-vaginal fistula repairs have been performed. Nezhat et al [56] performed the first laparoscopic vesico-vaginal fistula repair in 1994, while Melamud et al [57] reported on the first robot-assisted repair of a vesico-vaginal fistula in 2005. The recent systematic review of the literature performed by Miklos et al [58] including 44 studies and a total of 256 patients, demonstrated that there is an absence of appropriate high level evidence in the contemporary literature and it can therefore be surmised that a significant selection bias exists in these articles. Furthermore, only two of the articles included in this review contained a sample size of >15 cases. With minimally invasive approaches, the same surgical principles as used with open surgery apply: namely separation of the vagina from the bladder and the interposition of well-vascularised tissue between both organs.

Vascularised tissue flaps are used to reinforce a repair, fill dead space, and to improve vasculogenesis following a repair. While this can be useful in complex, radiotherapy-induced, recurrent, or obstetric fistulae, there is no high level evidence to confirm benefit of tissue interposition, particularly as the decision to use tissue transfer techniques is based on specific fistula characteristics. Despite this, a Martius interposition flap is readily available during a transvaginal approach and is therefore commonly performed in this context. During an abdominal procedure, the greater omentum is commonly used as an interposition flap, while a variety of other tissues and materials have been used, including peritoneum [9,22,24,45], gracillis muscle [24,47], porcine small intestinal submucosa [25], Floseal haemostatic matrix [19], and bladder mucosa advancement flaps [6].

4. Conclusions

We have reviewed the English language literature since 1980 relating to lower urinary tract fistula, with a view to highlighting differences in aetiology and management between LRCs and WRCs. Only 49 relevant studies were identified, and most were of low quality.

Over 80% of all fistulae reported in the included studies were of obstetric aetiology, and of those reported from LRCs, childbirth was the causative factor in over 95%. In contrast, of the fistulae reported in the included studies from WRCS, over 80% occurred following pelvic surgery, with hysterectomy being the antecedent operation in over three quarters of these cases.

Closure of a fistula can be achieved in up to one third of cases by conservative management. Whilst the heterogeneity of cases and management pathways makes comparison of reported series difficult, spontaneous closure seems most likely to occur where there has been minimal tissue damage, and is seen more often with obstetric and surgical fistulae than postradiation fistulae.

For similar reasons, comparison between different surgical approaches is also difficult, and is more often based on individual surgeon preference than on evidence-based criteria. There is no proven benefit to delayed repair and surgery can be undertaken once it is clear that conservative measures are not going to be successful, and as soon as any oedema, inflammation, tissue necrosis, and infection are resolved.

There is no high level evidence that any specific route of surgery has an advantage over any other; similar success rates are reported for vaginal and abdominal, and for transvesical and transperitoneal approaches, and for repairs with and without interposition grafting. It has, however, to be borne in mind that series tend to be reported from high-volume centres and as a consequence clinical judgment has been exercised, rendering cohorts highly selected. Clearly an abdominal approach may be appropriate in the context of a complex procedure where the fistula is high in the bladder, close to the ureter(s), associated with radiotherapy, and involving the uterus. There is limited experience with laparoscopic approaches and inevitably this will require the appropriate technical knowledge and definitive statements can only be made when larger series are reported in the literature.

Intuitively, optimum results are more likely if fistula surgery is carried out by surgeons well versed in all available techniques. Limited surgical experience would seem to make failure of a repair more likely and an association between workload and outcome has been shown [2]. Outcomes from first repairs are consistently shown to be better than from repeat procedures. These factors all argue in favour of centralisation of management in areas of high prevalence/workload by an experienced multidisciplinary team. This pragmatic approach to management would seem to be equally applicable to both well and low-resourced settings.

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Study concept and design: Chapple, Hilton.
Acquisition of data: Hillary, Osman.
Analysis and interpretation of data: Hillary, Osman.

Drafting of the manuscript: Hillary, Osman.
Critical revision of the manuscript for important intellectual content: Hillary, Osman, Hilton, Chapple.
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Paper 2: Epidemiological and surgical aspects of urogenital fistulae: a review of 25 years' experience in southeast Nigeria.

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Original Article

Epidemiological and Surgical Aspects of Urogenital Fistulae: A Review of 25 Years' Experience in Southeast Nigeria

P. Hilton[1] and A. Ward[2]

[1]Royal Victoria Infirmary, Newcastle upon Tyne; [2]VVF Unit, Mbribit Itam, Akwa Ibom State, Nigeria

Abstract: The aim of the study was to determine the epidemiological background, clinical details and surgical outcome of patients presenting with urogenital fistulae to St Luke's Hospital, Uyo, and the associated VVF Unit at Mbribit Itam, Akwa Ibom State, Nigeria, between January 1970 and December 1994. A retrospective review of hospital operating theater records and case notes was carried out. Clinical details and outcome were assessed for the total cohort of 2484 patients. Epidemiological data were extracted from the case notes of 715 patients presenting between January 1990 and December 1994. Of these 92.2% were of obstetric etiology, 80.3% following neglected obstructed labor, 6.9% following cesarean section, and 5.0% followed ruptured uterus; 4.4% followed pelvic surgery and the remaining 3.4% of miscellaneous causes included malignancy, coital injury, infection and trauma; 8% had a coexisting rectovaginal fistula or third-degree perineal tear. Only 37.3% of patients were aware of their age; the median age of this group was 28 years. Literacy was difficult to judge reliably, although 29% were able to sign their name. Parity ranged from 0 to 17, and only 31.4% of fistulae related to first pregnancies. Although 73.1% were delivered in hospital, in 97.1% labor was initially managed at home, with a traditional birth attendant, in a maternity home, or in church; 34.1% were delivered by cesarean section, although the live-birth rate was only 10.3% in the causative pregnancy. For a variety of reasons 124 women were not operated upon: 1954 underwent only one operation, giving a presumptive cure rate at first operation of 81.2%; 247 underwent two, 116 three, 32 four, and 11 five operations during the study period. The ultimate closure rate was 97.7%, with only 0.6% undergoing urinary diversion. The type and distribution of fistulae recorded in this series is consistent with previous series of largely obstetric fistulae from the developing world. Surgical cure rates are also comparable. The epidemiological background is at variance with previous reports in several respects; this may reflect biosocial differences in the population studied.

Keywords: Epidemiology; Obstetric trauma; Surgery; Urogenital fistula

Correspondence and offprint requests to: Mr P. Hilton, Consultant Gynaecologist, Royal Victoria Infirmary, Newcastle upon Tyne, NE1 4LP, UK.

Introduction

The prevalence of urogenital fistula is largely unknown, although high levels have been reported especially in areas of sub-Saharan Africa, particularly in Sudan [1], Chad [2], Nigeria [3], Ethiopia [4] and Ghana [5]. An incidence of 1–2 per 1000 deliveries has been estimated, with a worldwide annual incidence of 50 000–100 000 [6] and a prevalence of untreated fistulae of 500 000–2 000 000 [6]. The incidence clearly relates to the level of maternity care provision, those areas with high maternal mortality tending also to have high fistula rates. Danso and colleagues [5] have suggested that a more realistic estimate of the incidence of fistula in any community might be that it approaches the maternal mortality rate. This might indicate an annual incidence worldwide of up to 500 000. Harrison [7,8] reported an overall maternal and perinatal mortality rate of 10 and 90 per 1000, respectively, and 34 and 125 per 1000 in primipara under 16 years of age in northern Nigeria. The majority of fistula patients in developing countries have

been said to be teenage primigravidae [3,6,9–11]. Although obstructed labor is undoubtedly the most significant single etiologic factor, the problems are compounded by many social and cultural factors which may delay referral to specialist care once arrest of labor occurs [12–14]. This study was undertaken to compare the influence of these and other etiologic and epidemiologic factors with earlier reports, and to determine the fistula types and surgical success within the unit.

Patients and Methods

The study was undertaken during the course of two visits made by the first author to St Luke's Hospital, Uyo, and the associated VVF Unit at Mbribit Itam, Akwa Ibom State, Nigeria, in 1989 and 1995. Cases were identified from operating theater record books, and notes were subsequently retrieved from the hospital records department; 2979 operative procedures were initially identified undertaken in 2484 patients between January 1970 and December 1994; 2389 case notes were subsequently retrieved (96%). Details of the causative processes, fistula site and surgical procedure(s) undertaken were well recorded in notes throughout the study period. Epidemiological data were less well recorded in the early part of the study, and it was decided to limit analysis of these aspects to the period between the two visits, i.e. between January 1990 and December 1994: 715 patients were identified during this period, from whom 656 case records (92%) were available for review.

Results

Etiology

The etiologic factors, as far as could be established from case notes, are shown in Table 1: 92.2% of cases were of obstetric etiology. The majority of these (80.3% of the total) resulted from neglected obstructed labor and the remainder from cesarean section or ruptured uterus; assisted vaginal delivery did not seem to be a significant etiologic factor. Previous gynecologic surgery was a factor in 4.4% of cases, and 3.4% arose from miscellaneous causes, including malignancy (1.7%), coital injury (0.9%), other trauma (0.5%), and infection (0.3%); the latter cases related to lymphogranuloma.

Table 1. Etiology in the 2389 cases out of 2484 identified, for whom notes could be retrieved from the hospital records department

Major aetiology Sub-group	No.	Percentage	No.	Percentage
Obstetric	2202	92.2		
Obstructed labour			1918	80.3
Cesarean section			165	6.9
Ruptured uterus			119	5.0
Surgery	105	4.4	105	4.4
Miscellaneous	82	3.4		
Malignancy			42	1.7
Coital injury			22	0.9
Trauma			11	0.5
Infection			7	0.3
Radiotherapy	0	0.0	0	0.0
Total	2389	100.0	2389	100.0

Patient Source

Fifty percent of patients lived in the local state (Akwa Ibom); the remaining 50% were largely from neighboring states, although a proportion travelled distances up to 1000 miles for treatment.

Age, Educational and Marital Status

Only 245 of the 656 patients for whom notes were retrieved in the epidemiologic part of the study (37.3%) were aware of their age at the time of presentation. This reflects their literacy, the relative under emphasis on age and birth date in this society, and also the impact of the civil war of 1967–1970, those unaware of their age stating simply that they were born before the war. Those who were aware of their age ranged between 7 and 68 years, with a median of 28 years.

The many languages used among the patient group made literacy difficult to judge, and it was rarely specifically recorded in notes; 29.0% were able to sign their name on the operation consent forms, suggesting that they had received at least a rudimentary education; the remainder indicated consent to surgery by their right thumbprint.

At the time of presentation 410 patients (62.5%) were married, 72 (11.0%) were single and 106 (16.2%) widowed; only 68 (10.4%) had been deserted by their husbands since the development of their fistula, 2.9% being separated and 7.5% divorced.

Past Obstetric History

Of the obstetric fistulae 31.4% followed first pregnancies (Fig. 1); parity ranged from 0 to 17, with a median of three pregnancies; 7.6% of the patients' previous pregnancies had ended in spontaneous miscarriage, individual patients reporting 0–6 miscarriages, with a median of 0, and mean of 0.27 miscarriages; 44.4% of previous pregnancies had ended in stillbirth, individual patients reporting 0–8 (median 0, mean 1.0) stillbirths. Although 48.1% of the previous pregnancies had resulted in a live birth, only 27.5% of patients had had one or more previous live births (range 0–10, median 1, mean 1.7).

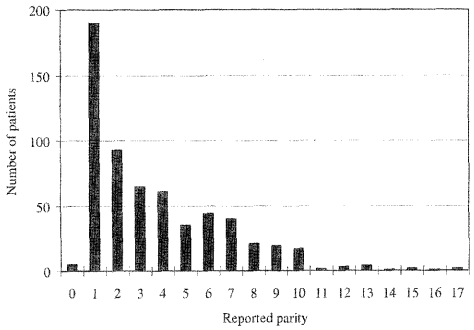

Fig. 1. Parity distribution of the 605 obstetric cases, out of 715 managed between January 1990 and December 1994, for whom notes could be retrieved.

Antecedent Labor and Delivery

The site in which the patients spent the majority of their labor and the place of delivery are shown in Table 2. Only 2.9% of women had spent the majority of their labor in hospital: most had labored at home, with a traditional birth attendant, in a peripheral maternity home or health center, or in church. By the time of delivery 73.1% had been transferred to hospital, the duration of labor prior to transfer averaging 2.5 days.

The mode of delivery in the associated pregnancies is shown in Table 3. The neonatal outcome appeared to relate to mode of delivery. The live-birth rate was only 3.4% following spontaneous vaginal deliveries, 11.1% following assisted vaginal deliveries, and 22.8% following cesarean section. The overall live-birth rate from antecedent pregnancies was only 10.3%.

Table 2. Place of labor and delivery in the 605 obstetric cases out of the 656 managed between January 1990 and December 1994, for whom notes could be retrieved

	Labor		Delivery	
	No.	Percentage	No.	Percentage
Home	330	54.6	90	14.9
Traditional birth attendant	167	27.7	57	9.5
Health center	35	5.8	5	0.8
Maternity home	30	5.0	5	0.8
Church	25	4.0	6	0.9
Hospital	18	2.9	442	73.1
Total	605	100.0	605	100.0

Table 3. Mode of delivery and live-birth rate for the 605 obstetric cases out of the 656 managed between January 1990 and December 1994, for whom notes could be retrieved

Mode of delivery	No.	Percentage	Live births	Live birth rate (%)
Spontaneous	320	52.9	11	3.4
Cesarean section	206	34.0	47	22.8
Ventouse	24	4.0	3	12.5
Forceps	12	2.0	1	8.3
Symphysiotomy or craniotomy	18	3.0	0	0
Laparotomy	18	3.0	0	0
Vaginal breech	7	1.2	0	0
Total	605	100.0	62	10.3

Duration of History

The length of history at presentation was extremely variable, ranging from a few days to 38 years; the average delay was 61.5 months.

Menstrual Status

The menstrual status of patients at the time of presentation showed an interesting pattern: 44% of patients were amenorrheic at the time of referral, and the average delay between the associated pregnancy and presentation was 23.4 months; 39% had resumed menstruation and their average delay to presentation was 51.0 months. The remaining 17% of patients were presumed postmenopausal, and had a mean delay to presentation of 183.4 months.

Fistula Types

Fistulae may be classified on the basis of site or complexity, complex cases being those with poor access for repair, significant tissue loss, ureteric involvement, or where there is a coexistent rectovaginal fistula. In this series 4.5% had ureteric involvement and 8.0% were associated with coexistent rectovaginal fistula. The site of fistulae is shown in Table 4. Over 70% were mid-vaginal, juxtacervical or large (i.e. involving the whole of the bladder base between mid-vaginal and cervical levels).

Table 4. Site of the initial fistula in the total group of 2484 patients for whom an operative record was identified

Fistula site	No.	Percentage
Urethral	70	2.8
Subsymphyseal	75	3.0
Bladder neck	132	5.3
Mid-vaginal	579	23.3
Large	432	17.4
Juxtacervical	773	31.1
Vault	5	0.2
Uterus or cervix	77	3.1
Multiple	89	3.6
Unspecified	252	10.2
Total	2484	100.0

Primary Surgical Procedures

Of primary operations 83% were carried out vaginally and 17% abdominally. Of the vaginal procedures 3% were repaired in a 'reverse lithotomy' position, with the patient prone on the operating table; these were largely bladder-neck or subsymphyseal fistulae; 4% of procedures were combined with a rectovaginal fistula repair; 0.6% of patients underwent urinary diversion.

Surgical Outcome

The assessment of surgical cure in this environment is difficult, as patients, especially those traveling long distances, rarely return for follow-up. Equally, however, they are rarely happy to leave the unit until they are dry. For the purposes of this retrospective study, therefore, cure has been defined as the point at which patients were subjectively dry at their last assessment, and subsequently underwent no further surgery within the study period.

During the study period 124 patients were not operated upon; 1954 underwent a single operation and, as far as could be established from the notes, were cured at this first operation (82.8%); 247 patients underwent a second operation, 116 a third, 32 a fourth and 11 a fifth operation during the study. In total, therefore, 2979 urogenital fistula procedures were carried out in the 2484 patients. There were in addition 32 patients who were known still to be wet after a first operation, yet underwent no further surgery; 10 still wet after a second operation, 1 after a fourth opration, and 2 after a fifth operation. These were therefore added to calculate 'corrected' cure rates (Fig. 2). Although the cumulative corrected cure rate rises progressively with succeeding operations, the cure rate by operation falls from 81.2% for first procedures to 65.0% for those requiring two or more procedures.

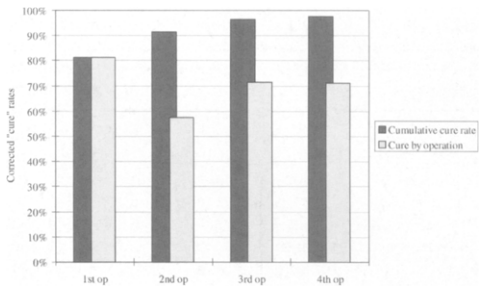

Fig. 2. Corrected cumulative cure rate and cure rate by operation number.

Discussion

The majority of patients in the study area are delivered at home, and in the absence of any effective process for the registration of births it is impossible to estimate the incidence of urogenital fistula with respect to delivery rate. Of those women attending hospital for delivery, however, the rate equates to 1.69 fistulae per 100 deliveries (based on 50% of the cases being from the local state area). The maternal mortality rate in the hospital within the period of the study varied between 0.6% and 1.6% (Itina S, personal communication). The overall fistula prevalence would therefore seem to be in keeping with previous reports [5,6,10], and in particular with the suggestion of Danso and colleagues, that the incidence of fistulae in any community might approach the maternal mortality rate [5]. It is, however, important to realize that whereas all maternal deaths, and probably most fistulae, eventually find their way to hospital, the majority of deliveries take place in the community. Although the incidence of fistulae and of maternal deaths may be related, neither figure should be taken to represent the overall incidence of the conditions in the population served.

The etiology of these cases, with 92.2% of obstetric etiology and 80.3% apparently related to neglected obstructed labor, is also very much in keeping with those of other series. The distribution of fistula types is also compatible with their largely obstetric etiology. Over 70% were mid-vaginal, juxtacervical or large in type. This distribution indicates the area of the vagina at greatest risk during obstructed labor, and therefore reflects the predominance of this factor in etiologic terms.

The association between obstetric fistulae and traditional surgical practices, e.g. circumcision and gishiri, has previously been emphasized [3,14] as an important etiologic factor in fistula, especially when they occur in relation to a first pregnancy. Such practices were not commonly recorded in the notes of patients in this series, and although probably not consistently specifically asked about, are not thought to be a significant factor in the etiology of fistulae in this population.

The importance of early marriage and childbearing in the development of obstetric fistulae has also to be emphasized (Table 5). Tahzib [3], from northern Nigeria, found 32.9% of patients to be under 16 years of age and 54.8% under 20 at the time of the development of their fistula. In the series reported from Ethiopia by Kelly and Kwast [15], 7% were under 16 and 42% under 20 at presentation. Murphy, also from northern Nigeria, reported that 88% of new referrals were under 16 at the time of their marriage, and 64% were under 18 at the time of their first pregnancy [14]. They also demonstrated, however, that the age distribution at marriage and first childbirth was not, in fact different from that of a control population of patients (with postpartum cardiac failure), early marriage and early childbearing being the norm, particularly in the Muslim culture of Hausaland. Within our present series

Table 5. Epidemiologic details from several series of fistula patients from different cultures within sub-Saharan Africa

	Northern Nigeria [14]	Northern Nigeria [3]	Ethiopia [15]	Ghana [5]	Southeast Nigeria – present study
Mean age (yrs)	20	21	22	26.6	28
% <16	45	33	7	4	13
% <20	69	55	42	21	32
Mean parity	?	1.6	2.1	2.6	3.5
% in first pregnancy	65	52	63	42.7	31
% divorced/deserted	54	?	52	?	10
% literacy	8	0.2	?	?	29
% home delivery	?	64	58	?	27

many patients were unaware of their age, although the mean age of those who did know was 28 years, and only 13.1% were under 16 years of presentation. It is likely that most of those who were unaware of their age were born prior to the civil war in Nigeria.

Murphy also found that 65% of new fistula patients had developed their fistula in relation to a first pregnancy, and 90% of their long-term patients had no living children [14]. In the current series only 31.4% arose in relation to first pregnancies; 48% of previous pregnancies to fistula patients had resulted in live births, and 27.5% of the patients had one or more living children. In respect of their previous obstetric experience our population seems more closely related to that reported from Ghana by Danso and colleagues, where the mean age of patients was 26.6, with only 21.3% being under 20 years, and the mean parity was 2.6 [5].

Others have also drawn attention to the educational background of fistula patients and their families. Murphy [14] found that the husbands of only 15% of their new patients and 8% of their long-term patients had received any form of modern education, compared to 31% of their control population [14]. Tahzib [3] found that only 0.2% of patients themselves had even the most rudimentary education, compared to 7% of all women delivering in that population [8]. Although the educational status of our patients was difficult to establish, 29% were literate to the extent of being able to sign their name at least, indicating that they had probably completed primary education.

Most previous reports have emphasized the importance of home delivery to the etiology of fistulae. Tahzib found that only 6.4% of their patients had delivered in hospital, and 64.4% at home [3]. Kelly and Kwast reported that 59.4% of women were either unattended, or attended only by family members or unqualified practitioners in labor [15]. In the present series 73% delivered in hospital, although 97% had spent the greater part of their labor away from hospital, with a substantial delay – averaging 2.5 days – before transferring to hospital. In some parts of the world this delay reflects geographic factors and problems of access. In Ethiopia Kelly and Kwast reported that 75% of the population live 2.5 days' walk from the nearest all-weather road [15]. In the present series 50% were from the local state area, and although the riverine nature of the Niger delta and Cross River area makes transportation difficult for some, for the majority this would not be the case. Of greater significance in determining delay in transfer to hospital is the local culture of mistrust or fear of hospital practices, the sense of failure in not achieving normal delivery, and the need to obtain consent from husband or elders for hospital attendance. The development of many independent neo-Christian churches in the area also appears to be of some significance in contributing to delay in some cases a number of women laboring in church for several days before ultimate transfer to hospital in extremis.

The high incidence of operative delivery is also in contrast to previous series: 34% were delivered by cesarean section, compared to 7.3% reported by Kelly and Kwast [15] and 6.7% reported by Tahzib [3]. Despite this, the perinatal outcome was not greatly improved: although those delivered by cesarean section had a live-birth rate of 22.8%, the overall live-birth rate was only 10.3% (compared to 7.3% reported by Kelly and Kwast) [15].

The length of time between development of the fistula and presentation to hospital was also considerable in many cases, averaging over 5 years. The occurrence of amenorrhea following the development of a fistula is well known, although whether this reflects the gross tissue loss within the pelvis or a hypothalamic influence as a result of the physical and emotional effects of a traumatic labor, stillbirth and fistula development, is not clear. As the live-birth rate is so low, clearly lactation is unlikely to be a significant factor. Whether the high number of postmenopausal women in this series reflects the effects of obstructed labor on the ovary, with the development of primary ovarian failure, is difficult to judge. In those deemed postmenopausal the average time from the development of the fistula to presentation was over 15 years; it was not possible to judge from the hospital records how many had been amenorrheic since their causative pregnancy. The average time to presentation in those who had resumed menstruation was 51.0 months, compared to 23.4 months in those who remained amenorrheic. This might be taken to imply that the natural history of the hypothalamic suppressive effect of the development of a fistula tends towards spontaneous ressolution after 2 years, even if the fistula remains untreated. Alternatively, however, these findings may

simply reflect the fact that the more dramatically affected patients, who are more likely to develop amenorrhea, are also more likely to present earlier for treatment than their less traumatized sisters who may have resumed menstruation at any stage.

As alluded to above, the assessment of surgical cure in this environment is difficult, as patients, especially those traveling long distances, rarely returned for follow-up. For the purposes of this study, cure has been defined as the point at which patients were subjectively dry at their last assessment, and subsequently underwent no further surgery within the study period. One has to accept that there may be some patients who had persistent fistulae but who did not return to the unit. Given the nature of the condition, and the relationships developed between patients and staff, the fact that patients were rarely happy to leave the site unless they were fully continent, and the availability of a postoperative hostel on site, this number is likely to be small. Nevertheless, cure calculated on this basis must inevitably represent an over- rather than an underestimate of the true cure rate.

The surgical outcome in this series is similar to other large series of obstetric fistulae. Kelly and Kwast reported an 88% cure rate, with 6.2% of patients having residual stress incontinence [15]. Cure at first operation has been looked on as the most appropriate outcome measure by which to judge fistula surgery. It is clear from the current series that in fistula surgery, as in other aspects of surgical practice, the first attempt at treatment gives the optimal result, with 81.2% cured at their first operation, but only 65% of those who required two or more procedures being cured by each successive attempt. We feel that this emphasizes the argument for specialist management where this is available, and for the establishment of fistula units for the provision of both service and training of indigenous doctors in fistula surgery [16–18].

Conclusions

The type and distribution of fistulae recorded in this series is consistent with previous series of largely obstetric fistulae from the developing world. Surgical cure rates are also comparable. The epidemiologic background is at variance with previous reports in several respects, notably that patients were older, of higher parity, higher literacy, and marital support, and more often delivered in hospital than previous series from other parts of Nigeria, and elsewhere in the developing world. Why patients in this area should have such a high fistula rate despite these factors remains uncertain, although this may reflect biosocial differences in the population studied.

Acknowledgements. The support of the Royal College of Obstetricians and Gynaecologists and the British Council in sponsoring the first author's visits to Nigeria is gratefully acknowledged. This paper is dedicated to the memory of the late John Bateman Lawson, who trained both authors in fistula surgery, and who died during its writing.

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EDITORIAL COMMENT: The authors present their experience with urogenital fistula repair for a large series of patients in Nigeria. It remains an unfortunate fact that the present study reveals no improvement in the incidence of urogenital fistula in this area of world compared to previous reports. Perhaps even more discouraging is the evidence that the patient population seems to be older, to have a higher degree of education and a higher incidence of operative delivery with no great improvement in the overall outcome. Greater efforts are needed to fully correct the plight of laboring women in underdeveloped countries, if the incidence of postdelivery vesicovaginal fistula is to be reduced.

Paper 3: Urogenital fistula in the UK:

a personal case series managed over 25 years.

BJUI BJU INTERNATIONAL

Urogenital fistula in the UK: a personal case series managed over 25 years

Paul Hilton

Newcastle upon Tyne Hospitals NHS Foundation Trust, Royal Victoria Infirmary, Newcastle upon Tyne, UK

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Study Type – Therapy (case series)
Level of Evidence 4

What's known on the subject? and What does the study add?
Whilst several very large series of obstetric fistulae from the developing world have been published, data on fistulae as seen in the developed world are relatively few. Most fistulae in the UK are known to follow hysterectomy, and several risk factors are recognised.

We have confirmed the common association with pelvic surgery, and in particular hysterectomy, but also show the broad range of other associated operations, including so called 'minimally invasive' procedures. High rates of both anatomical fistula closure and continence are shown, when a consistent approach to assessment, selection of surgical procedure, and postoperative care are applied. Successful closure is seen more often in women who have not undergone previous attempts at repair before referral, and as a result a pattern of surpra-regional management is proposed. Whilst overall the number of urogenital fistulae seen in the UK appears to be decreasing, there is a suggestion from these data that the rate of fistula formation following hysterectomy may be increasing; we are currently investigating this possibility through detailed interrogation of a national dataset.

OBJECTIVE

- To review demography, aetiology, surgery and outcomes of women with urogenital fistula seen in one unit over the last 25 years; to provide data for comparison with a parallel study based on Hospital Episode Statistics.

PATIENTS AND METHODS

- This is a prospective case series from a tertiary urogynaecology centre providing a *de facto* supra-regional fistula service.
- The women included had confirmed urogenital fistula referred between January 1986 and December 2010. Index cases were identified from a surgical database; data were entered prospectively and updated as appropriate; statistics are largely descriptive.
- The primary outcome is the patient's report of absence of urinary leakage.
- Secondary outcomes include operative or postoperative complications, anatomical closure of the fistula, other residual or new urinary symptoms, and the need for further intervention.

RESULTS

- In all, 348 women with urogenital fistula were referred; two-thirds were of surgical aetiology, with almost half following hysterectomy. Although 11% followed childbirth, most of these followed operative obstetric interventions.
- Spontaneous closure occurred in 6.9% of women and 291 underwent surgical treatment.
- The anatomical closure rate at first operation was 95.7%, although 2.2% reported residual urinary incontinence.
- The success rates were similar regardless of aetiology, although successful fistula closure was significantly more likely in women who had not had attempts at closure before referral (98.2 vs 88.2%; Fisher's exact test; $P = 0.003$).

CONCLUSION

- High rates of fistula closure are reported regardless of aetiology, although previous unsuccessful repair militates against successful outcome; this emphasises the appropriateness of centralisation of the management of this increasingly rare condition in UK practice.

KEYWORDS

complication, intraoperative; complication, postoperative; injuries, surgical; ionizing radiation; urinary fistula; vesico-vaginal fistula

INTRODUCTION

The prevention and management of vesico-vaginal fistula remains one of the greatest global public health challenges. It has been estimated that there are currently 2–3 million women with untreated fistula worldwide, and perhaps 30 000–130 000 new cases occur annually of which >95% are in the developing world. Most are obstetric in aetiology, resulting from prolonged neglected obstructed labour, and around 1–2 per 1000 deliveries may be affected [1,2]. Several very large case series have been published [3–5], and international aid organisations and professional groups are becoming increasingly involved in the issues of management and prevention [6,7].

In the UK, urogenital fistulae are relatively uncommon, and recent Hospital Episode Statistics suggest only 105 cases have been treated surgically per year over the last decade [8]. The literature on fistula in the

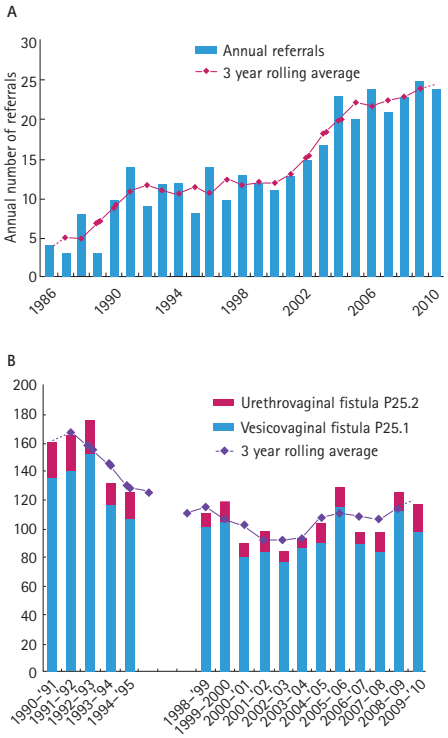

FIG. 1.
***A**, Annual number (in solid bars) and 3-year rolling average (line) of referrals to the unit over the period of the review (1986–2010). **B**, Hospital Episode Statistics during the period 1990–1991 to 2009–2010. The annual numbers of vesico-vaginal and urethrovaginal fistula repairs in England are given (in solid bars) together with a 3-year rolling average (line).*

TABLE 1 Source of referrals

Source	*N* (%)
Newcastle	53 (15)
Northern Region	177 (51)
Rest of England	61 (18)
Scotland, Wales and Northern Ireland	46 (13)
Republic of Ireland and Overseas	11 (3)
Total	**348 (100)**

developed world is also relatively sparse; ChassarMoir [9] reviewed the position in Britain in 1973, and Lee *et al.* [10] in the USA in 1988. Little has been published on the subject since that time, apart from small case series, and descriptions of surgical techniques; the largest recent UK series was of 41 cases managed in tertiary practice by Ockrim *et al.* [11] in 2009.

The aims of the present study are to review the demographic background, aetiology, surgery and outcomes of women with urogenital fistula referred to a single unit over the last 25 years, and to provide data for comparison with a parallel study based on the national Hospital Episode Statistics dataset.

PATIENTS AND METHODS

All women with confirmed urogenital fistula referred to the author between 1st January 1986 and 31st December 2010 were identified from a personally held password protected encrypted surgical database, formatted in *HanDBase*® (DDH Software, Wellington FL, USA). Only women referred for advice or treatment at the Royal Victoria Infirmary, Newcastle upon Tyne are included; those treated by the author overseas are excluded from this review. Data are entered prospectively and updated as appropriate; demographic fields are entered on referral, surgical fields are entered immediately on completion of operation, postoperative fields including complications are entered on discharge, and outcome is entered at outpatient review, and updated at any future patient contact (a copy of the dataset is included as Fig. S1: HanDBase® surgical database fields, please see Supporting Information). Anonymised data fields are regularly uploaded to a desktop computer, and converted into a Microsoft® Access™ format. Statistics presented are largely descriptive; Fisher's exact test was used for comparison of dichotomous outcomes.

The primary outcome is the patient's report of the absence of urinary leakage at follow-up 2–3 months postoperatively. Secondary outcomes include the need for surgical treatment, and the procedure(s) undertaken, operative or postoperative complications, duration of catheterisation and hospitalisation, anatomical closure of the fistula, other residual or new urinary symptoms, and the need for further intervention.

RESULTS

NUMBER AND SOURCE OF REFERRALS

In all, 348 women were referred for the assessment or treatment of urogenital fistula during the period of this review, with a median (range) age of 44 (7–89) years. The annual number of referrals has increased from about five per year in the 1980s to 25 per year currently (Fig. 1A). About one in six of the women was referred from colleagues in Newcastle, and half from elsewhere in what was previously known as the Northern Health Region (currently the North East and the northern part of the North West Strategic Health Authorities). One in six were referred from the rest of England, and a similar number from Scotland, Wales, Northern Ireland, the Republic of Ireland and elsewhere overseas combined (Table 1).

In all, 78 women (22.4%) had undergone 111 previous fistula repair procedures before referral; 55 women had one, 14 women two, eight women three, and one woman four previous unsuccessful attempts at repair.

AETIOLOGY OF FISTULAE

Two thirds of the fistulae (238 cases, 68.4%) were of surgical aetiology, and were associated with a large range of different operations (Table 2). In 172 cases (72.3% of the surgical cases and 49.4% of the series as a whole), the fistula followed excision of the uterus and or cervix; in 132 cases (55.5% of the surgical cases and 37.9% of the series as a whole), the fistula developed after simple abdominal hysterectomy. In 40 women (16.8% of the surgical cases and 11.5% of the series) the fistula followed surgery for urinary incontinence or pelvic organ prolapse, with a further 15 (4.3%) developing after excision of urethral cysts or diverticula.

In all, 38 women (10.9%) developed the fistula following childbirth (Table 2). True 'obstetric fistula' resulting from prolonged neglected obstructed labour is not seen in current obstetric practice in the developed world; two women in this series developed fistulae after obstructed labour; one had recently immigrated to the UK having developed her fistula 13 years earlier in Bangladesh; the other was referred by her medical relatives in Uganda. In most of the remaining 'obstetric' cases the fistula actually followed some form of surgical intervention, i.e. caesarean section (15, 39.5%) or caesarean hysterectomy (four, 10.5%), assisted vaginal delivery (five, 13.2%) or trial of vaginal delivery after a previous caesarean section (eight, 21.1%).

Two women (0.6%) developed their fistula from direct invasion of malignancy into the bladder; one was from ovarian cancer, the other from cancer of the rectum. In all, 34 women (9.8%) had undergone prior pelvic radiotherapy for the treatment of cancer (Table 2).

The remaining 36 cases (10.3%) were of miscellaneous aetiologies (Table 2). About half related to vaginal foreign bodies, 11 (30.6%) to the use of ring or shelf pessaries for the management of pelvic organ prolapse, and six (16.7%) to various other devices including bottles and deodorant can lids, introduced into the vagina for sexual gratification or 'by accident'.

TABLE 2 The aetiology in the present series of 348 urogenital fistulae. In addition to the cases listed there were two of malignant aetiology

Aetiology	*N*
Surgical cases	
Abdominal hysterectomy	132
Radical hysterectomy	19
Urethral diverticulectomy	15
Colporrhaphy	12
Colectomy	9
Vaginal hysterectomy	8
Mid-urethral tape procedures	7
LAVH	7
LLETZ	3
Cystoplasty and colposuspension	2
Colposuspension	2
Cervical stumpectomy	2
Nephroureterectomy	2
Subtotal hysterectomy	2
Sling procedures	2
Partial vaginectomy	2
Needle suspension	2
TAH and colporrhaphy	1
TAH and colposuspension	1
Laparoscopic oophorectomy	1
Periurethral bulking agents	1
Sub-trigonal phenol injection	1
Lithoclast	1
Colovaginoplasty	1
Ileoanal pouch	1
Sacrospinous fixation	1
Unknown surgery in childhood	1
Subtotal	238
Obstetric cases	
Caesarean section	15
Ruptured uterus	8
Forceps/ventouse	5
Caesarean hysterectomy	4
Symphsiotomy	2
Obstructed labour	2
Breech extraction	1
Placental abruption	1
Subtotal	38
Radiotherapy cases	
Cervical cancer	28
Endometrial cancer	5
Multifocal cancer	1
Subtotal	34
Miscellaneous cases	
Vaginal pessary	11
Foreign body	6
Infection	5
Congenital	6
Catheter induced	3
Trauma	2
Unexpalined	2
Coital injury	1
Subtotal	36

LAVH, laparoscopically assisted vaginal hysterectomy; LLETZ, large loop excision of the transformation zone; TAH, total abdominal hysterectomy.

TABLE 3 Fistula site using modification of Lawson's classification [11]

Fistula site	*N* (%)
Vesico-vaginal (VVF):	256 (73.6)
Vault	180 (51.7)
Midvaginal	32 (9.2)
Bladder neck	17 (4.9)
Large	13 (3.7)
Juxtacervical	11 (3.2)
Subsymphyseal	3 (0.9)
Urethro-vaginal (UVF)	38 (10.9)
Uretero-vaginal	21 (6.0)
Combined VVF + UVF	13 (3.7)
Vesico-uterine/cervical	11 (3.2)
Vesico-rectal	5 (1.4)
Uretero-rectal/pouch	4 (1.1)

SITE OF FISTULAE

In all, 256 (73.6%) of the fistulae were vesico-vaginal with a further 13 (3.7%) having combined vesico-vaginal and uretero-vaginal lesions (Table 3). Based on Lawson's anatomical fistula classification [12], 70.3% of these (51.7% of the total) opened into the vaginal vault, reflecting the preponderance of surgery, and in particular hysterectomy, as the causative factor.

In all, 38 fistulae (10.9%) were urethro-vaginal; 90% of these were of surgical aetiology, most commonly following urethral diverticulectomy (15, 39.5%), mid-urethral tape procedures (seven, 18.4%) and colporrhaphy (six, 15.8%).

In all, 21 (6.0%) of these fistulas were simple uretero-vaginal; including the combined vesico-vaginal and uretero-vaginal lesions (13), and a few ureteric fistulae involving bowel (four), in total 10.9% of women had fistulae involving the ureter.

MANAGEMENT

Immediate management

When patients were referred ≤6 weeks of the onset of leakage, assessment of the upper urinary tracts by IVU or CT was advised. If there was evidence of ureteric involvement by way of leakage or stricture, immediate referral for renography followed by stenting or re-implantation was

TABLE 4 Route and type of primary procedures undertaken

Primary procedure	*N* (%)
Abdominal procedures:	
Transperitoneal	44 (48.9) – 11 (25) included omental graft
Transperitoneal + ureteric re-implantation	7 (7.8)
Transvesical	16 (17.8)
Ureteric re-implantation	15 (16.7)
Urinary diversion	8 (8.9)
Subtotal	90 (30.9)
Vaginal procedures:	
Layer dissection	169 (84.1) – 38 (22) included Martius graft
Urethral reconstruction	15 (7.5)
Colpocleisis	16 (8.0)
Urethrocleisis and insertion of suprapubic catheter	1 (0.5)
Subtotal	201 (69.1)
Total	291 (100.0)

recommended. Where upper tract involvement was excluded, catheter drainage was recommended. If spontaneous closure of the fistula had not occurred ≤8 weeks, referral for further assessment and probably surgical treatment was offered.

In 24 (6.9%) women, the fistula healed 'spontaneously', that is either with no treatment, or with a period of continuous bladder drainage or ureteric stenting (seven). A further 33 women did not undergo surgery for various other reasons: 14 were referred for advice by telephone or by correspondence only; 12 declined treatment; four with malignant or radiation fistulae died before treatment; and three await treatment. Three patients await follow-up at the time of analysis.

Surgical treatment

When surgery was deemed appropriate, either because of failure of catheter drainage, or late presentation, it is the author's usual practice to undertake a preliminary examination under anaesthesia and cystoscopy; retrograde pyelography is also undertaken where the ureters are involved in or lie in close proximity to the fistula edge, or where prior IVU or CT indicate the possibility of ureterovaginal fistula or stricture. The choice of repair procedure is based on the need for concurrent ureteric re-implantation, the proximity to the bladder neck, the tissue mobility and access for repair vaginally. Where a vaginal approach was deemed to be both feasible and safe, this was always the route of choice. Interposition grafting by the Martius bulbocavernosus muscle and fat graft was used in urethral and bladder neck fistulae, and to fill dead space in the vagina at colpocleisis for radiotherapy induced fistulae. Omental interposition grafts were used at transperitoneal repairs depending on the size of the defect, perceived integrity of the repair, and availability of omentum.

After surgery the bladder is drained continuously for 12 days; urine output is checked hourly by ward nursing staff throughout this period. In the early years of the study, a urethral catheter was used; latterly both urethral and suprapubic 16 F Foley catheters have been used simultaneously; in this case the urethral catheter is removed on day 10, and the suprapubic catheter clamped on day 12, being finally removed when residual urine volumes are consistently <100 mL, and <50% of the voided volumes.

In all, 291 women (83.6%) underwent one or more surgical procedures, with 283 undergoing repair, and eight having primary urinary diversion (2.7%) (Table 4). One woman who had undergone surgery for a cloacal abnormality in childhood presented with a complex urethro-clitoral fistula with bilateral hydronephrosis, and underwent ileo-cystoplasty with a Mitrofanoff continent diversion. Six women with large radiotherapy induced vesico-vaginal fistulae, and one with a vesico-vaginal fistula following a repeat injection of phenol to her trigone in the treatment of intractable detrusor overactivity, underwent ileal conduit diversion.

Of the 283 undergoing primary repair, 69.1% had a vaginal procedure, and 30.9% an abdominal procedure. Ureteric re-implantation was required in 22 women, two of these being bilateral; in seven, ureteric re-implantation was combined with a transperitoneal repair of a concurrent vesico-vaginal fistula. All of these were of surgical aetiology, including 18 (81.8%) associated with hysterectomy; 12 related to total abdominal hysterectomy, five to radical hysterectomy, and one to sub-total hysterectomy.

Excluding the ureteric re-implantations and urinary diversions, 60 women underwent abdominal repair operations; 26.6% of these were transvesical, and 73.4% transperitoneal. In 25% of the transperitoneal procedures an omental interposition graft was incorporated within the repair. Of the 31 cases of obstetric aetiology undergoing repair 13 (41.9%) required an abdominal repair, compared to 43/183 of the surgical cases (23.5%), four of 19 of the radiotherapy/malignant cases (21.1%), and none of 28 of the miscellaneous cases; the distribution of abdominal to vaginal repairs in the obstetric group is significantly different from the surgical and miscellaneous groups (Fisher's exact test; $P = 0.001$), although not from the radiotherapy group ($P = 0.218$). It should be remembered that many of the obstetric cases related to caesarean section or trial of vaginal delivery after previous caesarean section; 100% of those requiring surgical repair of fistulae from other obstetric causes (Table 2) underwent vaginal repair.

Outcome of surgery

Anatomical closure vs continence Of the 283 women having repair surgery, 279 have attended for follow-up; one died from a pulmonary embolus 4 weeks after surgery, prior to her follow-up appointment, and three await follow-up at the time of analysis. In all, 261 (93.5%) women reported being fully continent, and had no clinical evidence of either urethral or extra-urethral urinary leakage. Six (2.2%) have anatomical closure of their fistula, but report some

TABLE 5 Results of fistula repair procedures

Aetiology	Patients, *n*	Healed spontaneously, *n* (%)	No surgery – other reasons*, *n* (%)	Primary diversion, *n* (%)	Primary repair procedure, *n* (%)	Closed at first operation†, *n* (%)
Surgical	238	19 (8.0)	13 (5.5)	1 (0.5)	205 (86.1)	195 (96.1)
Obstetric	38	4 (10.5)	3 (7.9)	0	31 (81.6)	28 (90.3)
Radiation/malignant	36	0	11 (30.6)	6 (24.0)	19 (52.8)	18 (94.7)
Miscellaneous	36	1 (2.8)	6 (16.7)	1 (3.4)	28 (77.8)	26 (96.3)
Total	348	24 (6.9)	33 (9.5)	8 (2.7)	283 (81.3)	267 (95.4)

**no surgery – other reasons' includes patients referred for telephone advice only, those declining surgery, those dying before treatment or follow-up, and those awaiting treatment. †patients awaiting follow-up are excluded from the calculation of closure rate.*

residual incontinence (one stress and five urgency incontinence). The primary closure rate is therefore 95.7%, with a continence rate of 93.5%.

Primary vs secondary repairs Successful fistula closure was significantly more likely in the women who had not had attempts at closure before referral (98.2%) than in those who had one or more previous unsuccessful procedures (88.2%) (Fisher's exact test; $P = 0.003$).

In all, 12 women required a second operation following unsuccessful closure after referral to our unit; one underwent secondary diversion, and 11 had second attempts at fistula repair. In nine women, the fistula was anatomically closed by the second procedure, although one woman reported some residual incontinence that was shown to be due to intrinsic sphincter deficiency. The secondary closure rate therefore is 81.8%, with a secondary continence rate of 72.7%. The differences in anatomical closure rate and continence rate between first and second procedures undertaken in our unit, whilst perhaps clinically significant, are not of statistical significance (Fisher's exact test, $P = 0.093$ and $P = 0.101$, respectively).

Two women underwent third attempts at fistula repair and both were successful. The one woman with residual urethral incontinence after a second procedure awaits a Mitrofanoff continent diversion procedure.

Outcome by aetiology The primary closure rate varied between 96% for those fistulae of surgical and miscellaneous aetiologies and 90% for those of obstetric aetiology (Table 5). These closure rates are not significantly different (Fisher's exact $P = 0.793$), although it must be recognised that the radiation related cases were less likely to undergo a repair operation, with only 52.8% undergoing repair compared to 86.1% of the surgical cases (Fisher's exact test; $P < 0.001$).

Other determinants of outcome The primary closure rate was 83.3% for those women undergoing abdominal procedures, and 96.1% for those having vaginal repairs (Fisher's exact test; $P < 0.001$), although neither closure rate nor continence rate were significantly different between vesico-vaginal (95.9%; 91.4%) and urethro-vaginal (92.1%; 80.0%) fistulae (Fisher's exact test; $P = 0.662$ and $P = 0.119$).

The primary closure rate was not significantly different between those procedures where an interposition graft (omental or labial) was (92.0%) or was not (96.1%) used in the repair (Fisher's exact test; $P = 0.264$). As noted above, the decisions about the route of repair and the use of interposition grafts are not taken at random, but are based on specific patient characteristics; these findings must therefore be interpreted with caution.

DISCUSSION

The case series described represents one of the largest recent series of urogenital fistulae reported from the UK. Although there is no current Department of Health recognition of fistula centres, nor specific funding of fistula surgery in the UK through the NHS specialised services commissioning processes, this paper describes the workload of a *de facto* supra-regional fistula service.

Hospital Episode Statistics suggest a reduction in the number of urogenital fistula cases operated on in England from ≈165 per year in the early 1990s to ≈105 per year over the last decade (Fig. 1B) [8]. Despite this downward trend in fistula cases nationally, the numbers seen in this unit continue to increase (Fig. 1A). Whilst the patterns shown in the present series cannot be said necessarily to reflect the whole of UK practice, these figures indicate that the current caseload of the unit represents >20% of the national surgical activity.

The distribution of different aetiologies of cases seen in the unit has been consistent throughout the period of this review, with two thirds being of surgical aetiology, and the remainder evenly distributed between obstetric, radiation, and miscellaneous or traumatic causes. Although fistulae were seen in patients undergoing all types of pelvic surgery, overall almost half of this series were associated with hysterectomy. ChassarMoir [9] reported 87% of fistulae in his series of patients treated in the UK to be of surgical aetiology in 1973, and Lawson [13] similarly reported 76% surgical aetiology in a small cohort of UK patients in 1978. Together with the reduction in total fistula cases cited above, these various series suggest a significant reduction in the proportion of cases associated with pelvic surgery between the periods, 1950–1970 and 1980–2010 (Fisher's exact; $P < 0.001$). Despite this finding, the number of hysterectomy procedures is also decreasing, and it is the author's impression, borne out by publicly available data [8], that the rate of fistula formation following hysterectomy may be increasing. Online tables suggest a >40% increase in the rate of fistula

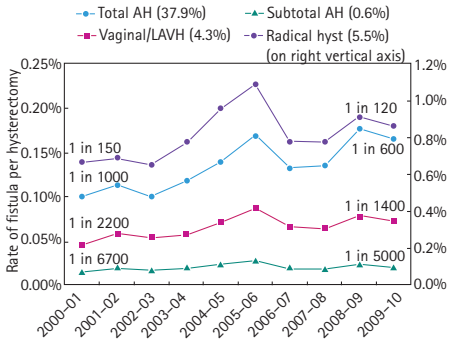

FIG. 2.

The rate of fistula formation after hysterectomy of different types, calculated from Hospital Episode Statistics, assuming that the distribution of causes of fistula in the present series reflects the national pattern, i.e. that 37.9% of all fistulae in the country follow total abdominal hysterectomy, 4.3% of all fistulae follow vaginal or laparoscopically-assisted vaginal hysterectomy etc. AH, abdominal hysterectomy; LAVH, laparoscopically-assisted vaginal hysterectomy.

following hysterectomy over the last decade, from about 1 in 1000 in 2000–2001 to 1 in 600 in 2009–2010 [8]. Assuming that the distribution of causes of fistulae in the present series reflect the national position, with 37.9% of fistulae following total abdominal hysterectomy, 5.5% following radical hysterectomy, 4.3% following vaginal or laparoscopically assisted vaginal hysterectomy, and 0.6% following subtotal hysterectomy, the same trend is apparent for all types of hysterectomy procedure (Fig. 2). A trend of this nature could be explained either by the fact that as the number of hysterectomy procedures reduces the standards of surgical training and practice in gynaecology decline, or that the cases that remain are the more complex ones, with an increased risk of operative complication. We are currently investigating these trends further in collaboration with the Royal College of Obstetricians and Gynaecologists Office of Research and Clinical Audit.

It is often supposed by patients, their lawyers, and even by 'expert' witnesses that fistula after hysterectomy results from direct injury to the lower urinary tract at the time of operation. On occasion this may be the case; intuitively, careless, hurried or rough surgical technique will make injury to the lower urinary tract more likely. However, direct operative injury is likely to be associated with immediate loss of urinary control when the patient leaves theatre or has their catheter removed; of 172 fistulae following hysterectomy in this series, only seven (4%) presented with leakage of urine on the first postoperative day. In other cases, compromise to the blood supply by suture, diathermy or crushing may result in tissue necrosis and subsequent leakage; alternatively, a pelvic haematoma at the vaginal vault may become infected and then discharge into the bladder; in each of these latter situations leakage is likely to develop later, and in the remaining 96% of women with post-hysterectomy fistulae in the present series incontinence developed between 3 days and 8 weeks after surgery. There is some evidence from animal studies that the inadvertent placement of vaginal vault sutures into the bladder wall at hysterectomy may not carry as great a risk of fistula formation as previously thought [14].

In 17 women the fistula developed in association with a vaginal foreign body. In six of these the device was known or presumed to have been introduced into the vagina by the woman herself for sexual purposes. The device was most commonly a deodorant canister, introduced with the cap in place; on removing the canister from the vagina the cap was retained. Although one woman presented within a few hours of acute bladder injury from a 'crown-capped' soft drinks bottle, others presented at periods of 1–15 months after introduction of the foreign body, the delay largely reflecting embarrassment at the nature of their condition. In three of these cases large vaginal fibro-epithelial polyps were identified; these have not been seen in other fistula types in the present series, and have not previously been reported in association with urogenital fistula; they have however been considered as a possible development from granulation tissue, and their identification in association with foreign body retention might not therefore be unexpected [15]. The three examples seen in the present series seemed to occur where there was rotation of the deodorant cap within the vagina such that the concave surface was directed laterally or cephalically, and either granulation or the vaginal tissues themselves had grown into the concavity with resultant polypoid tumour formation; in one case his had become so large that a separate operation was required to excise the polyp before an adequate view of the fistula, involving right ureter, bladder base and the whole of the urethra, could be established.

In 11 women the fistula developed in association with the use of vaginal pessaries for the treatment of vaginal prolapse; one of these was a ring pessary and 10 were shelf pessaries. This complication might perhaps be anticipated with retained, long neglected pessaries, and in one case a shelf pessary had been left in place for 6 years without review. However, in the remaining women, leakage became apparent between 2 weeks and 6 months after their last pessary change. These women had a median age of 82 years, and whilst perhaps not atypical for the group of patients likely to be managed by vaginal pessaries, the place of vaginal atrophy as a contributory factor in the development of the fistula may be relevant. Where there is no absolute contraindication to its use, topical oestriol should be considered in women with significant genital atrophy whose prolapse is managed by pessary.

Other than in the unusual circumstances where injury to the urinary tract is detected within the first few days of operation, and where extravasation of urine into the tissues is not great, it has been the author's practice to advocate delayed repair. This allows time for necrotic tissues to slough and for local inflammatory change to resolve, and spontaneous closure may occur in some cases, thereby avoiding the need for further surgery. It is worth persisting with this line of management in vesico-vaginal or urethro-vaginal fistulae for 6–8 weeks, as spontaneous closure may occur within this period [16]. Although only 6.9% of the fistulae in the present series are known to have healed with catheter drainage, this is certainly an underestimate of the value of

this approach to management. The outcome is not known in most of those women referred for telephone advice only, although in many of these, catheter drainage was recommended; many others would have been managed conservatively and not referred. It is possible that the actual rate of spontaneous healing in surgical fistulae is as high as 20%.

Spontaneous closure of radiotherapy-induced fistulae was not seen in the present series, and seems most unlikely ever to occur, in view of the impaired vascularity invariably found in association with radiation endarteritis. In the present series, 10% of the obstetric fistulae healed with catheter drainage, although it must be recognised that most of these cases were in fact not 'true' obstetric fistula resulting from ischaemic necrosis from prolonged neglected obstructed labour, but resulted from obstetric operative interventions. However, even in series of obstetric fistulae in the developing world, spontaneous healing has been reported in up to 28% of cases when bladder drainage is introduced early [17]. Although some authorities have suggested that there is no place for non-surgical management of urogenital fistula, (Mourad S, personal communication, 2010) it is the author's view that catheterisation of urethral or bladder fistulae should be considered the preferred initial management in all but exceptional cases.

The route of surgery for the repair of urogenital fistulae has perhaps been the greatest area for contention, with many urologists advocating an abdominal approach, and most gynaecologists, especially those with experience of fistula surgery in the developing world, favouring the vaginal approach. As indicated above, the author's preference has been for the vaginal approach where possible, accepting that the abdominal route has a place where access vaginally is limited (by virtue of the patient's nulliparity, or previous surgery or other pelvic pathology) or where there is concurrent ureteric involvement requiring re-implantation. Overall in the present series, almost 70% of procedures were undertaken vaginally; excluding those women requiring primary urinary diversion or ureteric re-implantation, 75% were repaired vaginally, obviating the need for an abdominal incision and the increased postoperative discomfort and morbidity associated with this, yet with comparable cure rate.

It is often suggested that vaginal vault fistulae following hysterectomy are not amenable to vaginal repair, and based on one case series of surgical fistulae it was claimed that the O'Connor (transperitoneal transabdominal) technique should be considered the 'gold standard' for supratrigonal vesico-vaginal fistula repair [18,19]. Most fistulae seen after abdominal hysterectomy are in the midline above the inter-ureteric bar, with minimal risk to the ureters, and in parous women in particular, are usually quite accessible vaginally. Of the 110 women with vaginal vault fistulae following hysterectomy who underwent a primary repair procedure in the present series, 74 (67.3%) were treated by the vaginal route, with 97% anatomical closure and 94% continence rate. Of 47 repair procedures on 37 women reported by Ockrim *et al.* [11], 49% were undertaken vaginally. Surgeons involved in fistula repair should be skilled in both abdominal and vaginal approaches, and should have experience and versatility to decide the most appropriate procedure for each individual patient.

In most previous reports of fistula surgery, particularly those relating to obstetric fistulae in the developing world, the measures of outcomes are either not stated, or are based on the patient's report of continence at the point of discharge from hospital. Longer-term follow-up is often difficult or impossible, and more objective outcome measures impractical in such healthcare settings. In the present report, cure has been defined as the patient's report of the absence of urinary leakage, combined with the absence of clinical signs of residual or recurrent fistula and the absence of clinically demonstrable urinary leakage at 2–3 months postoperatively. Where patients reported residual urinary leakage at follow-up, or presented later with symptoms of incontinence, further assessment by cystourethroscopy with or without further imaging studies and urodynamic investigation were undertaken as appropriate, to distinguish anatomical failure (with persistent or recurrent extra-urethral incontinence) from other causes of incontinence (urethral incontinence).

Primary fistula closure was apparent in 95.7% of women, with a continence rate of 93.5% in the present series. The distinction between anatomical and functional outcome is important; the persistence of stress incontinence after successful anatomical closure of obstetric fistulae has long been recognised [12], and may affect 33–50% of women [20,21]. We have previously shown a high rate of functional abnormality of the lower urinary tract in association with fistula in the UK [22], although long-term follow-up of these patients, whilst confirming many to have persistent symptoms, suggests that for most these have limited impact on health-related quality of life [23]. It is of interest that whilst stress incontinence has always been thought to be the greatest persistent problem in obstetric fistula patients, we found both stress and urge symptoms to persist in similar numbers in UK fistula patients [23], and the disparity between anatomical and functional outcome seen in the present series was similar for vesico-vaginal and urethro-vaginal fistulae.

The place of interposition grafting remains unclear. Both omental and labial grafts have been widely advocated in the past to increase local blood supply, reduce scarring and enhance the prospect for successful repair; however, neither has been subjected to randomised trial. Several authors have reported improved cure rate where grafts have been used in both obstetric [24], and surgical fistulae [11,25]. In the present series, primary closure rate was not significantly different between those procedures where an interposition graft was or was not used. However, here also it must be noted that decisions about route of repair and the use of interposition grafts were not taken at random, but based on specific patient characteristics; these findings must therefore be interpreted with caution. It is noted that there is a recent move away from the use of interposition grafting amongst obstetric fistula surgeons [6].

In women who had undergone previous unsuccessful repairs prior to referral, cure at first operation after referral was significantly less likely. Similarly, in those women whose first repair after referral was unsuccessful, the secondary closure rate was also slightly lower; whilst these latter figures were not statistically significantly different, the 15%

lower rate of closure should perhaps be seen as clinically significant. The same phenomenon has previously been reported in much larger series of obstetric fistulae [3]. It cannot be overemphasised that the best prospect for cure of a patient with a fistula is at the first operation, and this must be undertaken by a surgeon with appropriate training and experience. Optimal results are only likely to be achieved in specialist centres undertaking a 'viable' workload of cases, although exactly what constitutes such a reasonable workload has not been defined. In 1997 it was reported that an average of 84 hospitals in England and Wales carry out fistula repair surgery in any one calendar year; the average number of procedures undertaken annually in those hospitals was less than two [26]. Clearly this could not be considered as a reasonable workload for any aspect of surgical practice. It was proposed in debate at a joint meeting of the Royal College of Obstetricians and Gynaecologists, and the British Association of Urological Surgeons in 1996 that only two or three centres for urogenital fistula repair were required in the UK [26]; despite the agreement of both professional groups, such a pattern of care has never been formally established. The apparently declining number of cases since that time, makes such centralisation of management even more appropriate.

In conclusion, this case series describes the workload of a *de facto* supra-regional fistula service. Whilst the patterns cannot be said necessarily to reflect the whole of UK practice, the current caseload of the unit represents >20% of the national surgical activity. High rates of fistula closure are reported regardless of aetiology, although the appropriate selection of cases for surgery, particularly in those fistulae after ionising radiation, is crucial to this success. Previous unsuccessful repair surgery militates against successful outcome; this emphasises the appropriateness of centralisation of the management of this increasingly rare condition in UK practice.

The correlation of these data with publicly available national data suggests an increase in the rate of fistula formation associated with hysterectomy. If confirmed, such trends could have significant implications for training and practice in gynaecology; certainly they justify further evaluation and explanation and this is presently underway.

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CONFLICT OF INTERESTS

Paul Hilton has no current personal or non-personal, specific or non-specific financial interests to declare. He was previously the principal investigator for a multi-centre randomised comparative trial of TVT™ and colposuspension funded by *Gynecare* (1998–2003), and was involved in the development of implants for use in surgery for stress urinary incontinence and pelvic organ prolapse funded by *Gyne Ideas* (2001–2003). He was a member of the National Institute for Health and Clinical Excellence Interventional Procedures Advisory Committee (2002–2007), chaired the NICE development group for the clinical guideline on urinary incontinence in women (2004–2007) and is a member of the faculty of the International Consultation on Urological Diseases (ICUD)/Société Internationale d'Urologie (SIU) International Consultation on Obstetric Fistula (2010). He has also been involved in research prioritisation as a member of NIHR Evaluation, Trials and Studies Coordinating Centre(NETSCC) Health Technology Assessment (HTA)-Therapeutic Procedures Panel (2007–2008), HTA-Clinical Evaluations and Trials Prioritisation Group (2008–2010), and the James Lind Alliance Working Partnership on research priorities on urinary incontinence (2007–2009). He has current research funding from NETSCC-HTA, the Physiotherapy Research Foundation, Wellbeing of Women and from the Northumberland, Tyne and Wear Comprehensive Local Research Network.

CONTRIBUTION TO AUTHORSHIP

Paul Hilton conceived and designed the study, developed the surgical database, carried out all patient assessments and surgery, data acquisition and analysis, and wrote the article for publication. No one fulfilling criteria for authorship is excluded.

ETHICS AND CONSENT

No ethical approval was sought for this study. Following the Caldicott report and the Data Protection Act (1998), the database was registered with the Trust for data protection purposes. Since revisions to the NHS Consent Form for investigation and treatment in 2001, all patients have been asked to agree to the use of their notes for audit and research purposes.

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Correspondence: Mr Paul Hilton, Consultant Gynaecologist and Urogynaecologist, Level 5, Leazes Wing, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK.
e-mail: paul.hilton@ncl.ac.uk

SUPPORTING INFORMATION

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FIG. S1. HanDBase® surgical database fields.

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Paper 4: Urodynamic findings in patients with urogenital fistulae.

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Urodynamic findings in patients with urogenital fistulae

P. HILTON
Royal Victoria Infirmary, Newcastle upon Tyne, UK

Objective To assess the feasibility of carrying out a urodynamic investigation in patients with a urogenital fistula and to establish the incidence of abnormal lower urinary tract function in such patients.

Patients and methods Of 38 patients referred within the last 3 years with a diagnosis of lower urinary tract genital fistula, 30 were investigated by dual-channel subtracted cystometry before surgical treatment of their fistula; in addition, urethral pressure profilometry was carried out in 19 patients. Fourteen of the patients had fistulae into the vaginal vault; the urodynamic findings in this subgroup were compared with those of 12 patients with bladder neck and urethrovaginal fistulae. Twenty-six of the 30 patients underwent surgical treatment and 24 (92%) were cured anatomically by their first procedure. Ten patients complained of residual lower urinary tract symptoms and were re-investigated.

Results Of the 38 patients, 47% had genuine stress incontinence, 40% showed systolic detrusor instability and 17% impaired bladder compliance. Half had evidence of voiding dysfunction; most appeared to be of a hypotonic detrusor type, although four cases showed an obstructive pattern. Fifteen patients had more than one abnormality and only five (17%) had entirely normal urodynamic findings. The overall incidence of functional abnormality was highest in the patients with urethral or bladder neck fistulae, with only one showing entirely normal urodynamic findings. Genuine stress incontinence was found more than twice as often associated with urethral or bladder neck fistulae and detrusor instability was also more common in this group. Voiding dysfunction of both hypotonic and obstructive types was found equally in the two groups. After surgical treatment, most patients became continent and free from lower urinary tract symptoms, although one complained of residual stress incontinence and nine of urgency or urge incontinence. Of the latter, six were found to have detrusor instability, one after repair of vault fistula, three after urethral or bladder neck fistulae and the other two after mid-vaginal fistulae.

Conclusion There is a high incidence of abnormal lower urinary tract function in patients with urogenital fistulae. Patients with urethral or bladder neck fistulae had a higher incidence of both detrusor instability and genuine stress incontinence than those with fistulae into the vaginal vault. Many of these abnormalities appear to resolve after successful repair of the fistula, although detrusor instability may persist and require further treatment in some women. These findings are relevant to the counselling of patients before repair and may be of medico-legal significance.

Keywords Fistula, vesico-vaginal, urethro-vaginal, urodynamics, stress incontinence, detrusor instability

Introduction

The occurrence of stress incontinence in patients after the successful repair of obstetric vesicovaginal fistula has long been recognized, and overall has been estimated to occur in up to 10–12% of such patients [1–5]. Waaldijk documented the occurrence of stress incontinence after repair of fistulae of varying types, describing 1% where there was no sphincter involvement in the fistula, 13% where there was but with no tissue loss and 16% where there was both sphincter involvement and tissue loss [5].

The recording of detrusor pressure during cystometry depends on the ability to record intravesical pressure as distinct from intra-abdominal pressure. Conventionally, the latter is determined by rectal or vaginal pressure. The feasibility of cystometry in patients with communication between the urinary and the genital tract may therefore be questioned. Schleicher *et al.* described the application of cystometry in 18 patients after the repair of obstetric fistulae [6]; the author is unaware of previous reports of urodynamic investigation before fistula repair.

Because of concern over the possible incidence of functional abnormalities of the lower urinary tract after fistula repair and the need to counsel patients appropriately before repair, a series of urodynamic investigations in patients with urogenital fistulae was carried out. The aims of the study were to assess the feasibility of detrusor

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pressure measurement in the presence of a fistula and to describe the types and incidence of abnormality.

Patients and methods

Over the last 3 years, 38 patients (aged 27–66 years) with lower urinary tract fistula were referred to the Urogynaecology Unit, 30 of whom were investigated urodynamically before treatment. Free uroflowmetry was carried out using an air-displacement technique. Dual-channel subtracted cystometry was then carried out using 4 F fluid-filled lines connected to external transducers to measure bladder and vaginal (26 patients) or rectal (four patients) pressure. A rapid-fill (100 mL/s) method was used, filling by peristaltic pumping through a 10 F filling catheter. Urethral pressures were also measured at rest and during stress in 19 of the patients, using a dual-sensor microtransducer catheter (Gaeltec, Isle of Skye, UK) at 200 mL bladder volume or at the maximum volume tolerated without sensation [7]. Urodynamic variables between groups were compared using nonparametric statistics (Mann–Whitney *U*-test).

One patient was asymptomatic on anticholinergic medication, one healed with prolonged catheter drainage, one died from cachexia related to malignant disease and radiation effects, and one declined surgical treatment until the end of the bowling season. Twenty-six of the 30 women underwent surgical repair of their fistulae. Ten women had residual urinary symptoms after fistula repair and the urodynamic investigation was repeated in these women. The methods, definitions and units conform to the standards recommended by the ICS except where specifically noted [8].

Results

Seven of the patients had undergone a total of 11 previous unsuccessful repair procedures before referral. The aetiology of the fistulae was surgical in 23 (77%), obstetric in three (10%), related to radiotherapy in two (13%), and to a foreign body and trauma in one case each. The associated surgical procedures are shown in Table 1. One of the fistulae was vesico-uterine and six were urethrovaginal. Of the 23 vesicovaginal fistulae, 14 were situated in the vaginal vault, three were mid-vaginal and six at the bladder neck. The distribution of aetiologies is consistent with that generally seen in the UK or elsewhere in the developed world [3].

The variables from filling and voiding cystometry are shown in Table 2. Comparing the urodynamic variables among the 14 patients with vault fistulae and the 12 with fistulae at the bladder neck or urethra showed no statistically significant differences. The urodynamic diagnoses are shown in Table 3; 14 patients (47%) had genuine stress incontinence, 12 (40%) showed systolic detrusor instability, and five (17%) impaired bladder compliance. Fifteen patients (50%) showed evidence of voiding abnormality (flow rate consistently <15 mL/s); most appeared to be of a hypotonic detrusor type, although four of the patients with voiding dysfunction

Table 1 The aetiology of fistulae in the present series. Comparative values are shown for the total throughput of the unit over the last 9 years (100 cases) [3]

Associated procedure *Aetiology/pathology*	*No (%) of present*	*% of total caseload*
Surgical	23 (77)	75
Abdominal hysterectomy	11	
Vaginal hysterectomy	1	
Laparoscopic hysterectomy	1	
Radical hysterectomy	2	
Urethral diverticulectomy	4	
Colporrhaphy	1	
Colposuspension	1	
Sub-urethral sling	1	
Augmentation cystoplasty	1	
Obstetric	3 (10)	9
Forceps	1	
Vaginal delivery after previous Lower segment Caesarean section	1	
Breech delivery (30 years earlier!)	1	
Radiation	2 (7)	9
Stage 3b CC (RT alone)	1	
Stage 2a CC (pre-op RT)	1	
Miscellaneous	2 (7)	7
Foreign body	1	
Fall (no clear penetrating injury)	1	
Total	30	

CC, Carcinoma of the cervix. RT, Radiotherapy.

Table 2 Variables of filling and voiding cystometry, and resting urethral profiles in the total patient group, in the subgroups with urethral or bladder neck (UBN) fistulae and vault fistulae. There were no significant differences (Mann–Whitney *U*-test)

Cystometric variables	*Total group (n = 30)*	*UBN (n = 12)*	*Vault (n = 14)*
Free flow rate (mL/s)	13	12	15
Residual urine (mL)	2	3	1
First sensation (mL)	136	112	153
Cystometric capacity (mL)	298	319	293
Pressure rise (cmH_2O)			
At capacity	14	13	10
On provocation	20	22	17
Max voiding pressure (cmH_2O)	25	24	27
Max flow rate (mL/s)	11	14	10
Urethral			
Functional length (mm)	26.5	27.2	25.8
Total length (mm)	32.4	31.9	33.2
Max closure pressure (cmH_2O)	38.5	29.2	49.8

Table 3 Functional abnormalities in the total patient group, and in the subgroups with urethral or bladder neck (UBN) and vault fistulae.

	All patients (n = *30*) n(%)	*UBN* (n = *12*)	*Vault* (n = *14*)	*Other sites* (n = *6*)
Genuine stress incontinence	14 (47)	9	5	0
Detrusor instability	12 (40)	6	5	1
Impaired bladder compliance	5 (17)	0	3	2
Voiding dysfunction	15 (50)	7	7	1
No abnormality	5 (17)	1	2	2

(13% of the total) showed an obstructive pattern (voiding pressure > 50 cmH_2O).

The urodynamic findings in the 14 patients with vault fistulae were compared with the 12 with fistulae at the bladder neck or urethra (Table 3). The overall incidence of functional abnormality was highest in the latter group, with only one showing entirely normal urodynamic findings, compared with two in the former group. Genuine stress incontinence was found in nine of those with urethral or bladder neck fistulae, compared with five in those with vault fistulae, and detrusor instability in six and five in the same groups, respectively; voiding dysfunction of both hypotonic and obstructive types was found equally in the two groups.

After fistula repair, two patients had a persistent or recurrent fistula (92% cure at first operation). Ten patients complained of persistent urinary symptoms despite anatomical closure of their fistulae. One had stress incontinence and nine urgency or urge incontinence; all had had abnormal cystometry pre-operatively. On repeat urodynamic investigation, the former was confirmed to have persistent genuine stress incontinence and six of the latter were confirmed to have persistent detrusor instability. No women with stable bladders before surgery had persistent symptoms afterward.

Discussion

Although there are previous reports of urethral pressure measurement in patients with urethral diverticula and urethrovaginal fistulae [9] this is the first report of cystometry in patients before repair of a urogenital fistula. In four cases where fistulae were particularly large, rectal pressure was used to record intra-abdominal pressure; in the remainder, vaginal pressure was used. In all cases, the detrusor pressure was recorded satisfactorily, i.e. in the presence of small fistulae, intravesical and vaginal pressure appeared to be different throughout the filling and voiding phases of the micturition cycle. In the presence of large fistulae, whilst it could not be confirmed that the pressures recorded were what they would have been with an intact urogenital system, the intravesical pressure differed from the intra-abdominal pressure.

The present series of patients had more urethrovaginal and bladder neck fistulae than in our total fistula caseload (40% compared with 14%), although there was a similar number of vault fistulae (47% compared with 52%) [3]. However, the aetiology, patient age and parity distribution, and previous surgical history were comparable, suggesting that the slightly atypical distribution of site probably reflects no more than a clustering effect. This allowed a useful functional comparison between urethral and bladder neck fistulae and vault fistulae.

Waaldijk defined sphincter involvement in a fistula to be when the lower edge of the lesion is within 6 cm of the external urethral meatus [5]. He reported stress incontinence after fistula repair in 13% of patients where there was sphincter involvement, and in 1% without such involvement. Within the present series, the incidence of urodynamically proven genuine stress incontinence associated with fistulae before repair was nine of 12 with sphincter involvement and five of 14 without such involvement. In Waaldijk's series, the assessment was made after fistula repair and was entirely subjective, whilst in the present series the functional situation was established before repair, based on the urodynamic investigation. The definition of sphincter involvement used in these two series also differed, although probably not significantly.

It has been our standard practice to use an interposition graft of labial fat and bulbocavernosus [10]. It is likely that this limits the incidence of stress incontinence after fistula repair by adding bulk to support the bladder neck, bringing a new blood supply to the area, and limiting rigidity and scar formation between the urethra and vagina. After surgery, only one of the present patients, with a urethral fistula, complained of stress incontinence; re-investigation confirmed genuine stress incontinence. This gives an incidence of stress incontinence after repair, in this group of largely surgical fistulae, of only one of 30 or 3%, and a persistence rate of one in 14 and one of nine of the vault and urethral or bladder neck fistulae, respectively. This latter value may be directly compared with Waaldijk's value of 13% stress incontinence after repair of obstetric fistulae with sphincter involvement [5].

Of the nine patients complaining of urgency or urge incontinence after repair, six were confirmed to have persistent detrusor instability, giving an overall incidence of detrusor instability of six in 30 (20%) and a persistence rate of one of five for the vault fistulae, but three of six for the urethral or bladder neck fistulae. No patients complained of urge incontinence after surgery who had stable bladders before, i.e. there was no evidence of

so-called *de novo* detrusor instability after surgery. The occurrence of detrusor instability in patients with fistula is perhaps not surprising. The emotional impact of developing a fistula is profound, given that most of these patients were free from urinary symptoms before the causative surgery, and had entered hospital for what was anticipated to be an uneventful procedure. The psychometric background of patients with idiopathic detrusor instability has been investigated and they are consistently shown to have higher scores on anxiety scales than patients with other forms of incontinence or other chronic illnesses [11,12]. No specific steps are taken at operation to relieve detrusor instability, and indeed it is doubtful that they could. The absence of symptoms of urgency at follow-up in most of the patients, and the reversion to stability in those who were re-investigated, may therefore reflect the resolution of the psychological trauma after successful closure of the fistula, rather than any direct effect on the detrusor. Why the problems of urgency should persist in some, despite the anatomical closure of their fistula, and why this appears to happen more often in those with urethral and bladder neck than those with vault fistulae is more difficult to explain. It is possible that in these patients the mechanisms are similar to those of detrusor instability occurring after bladder-neck elevating procedures in the treatment of detrusor instability [13,14].

The persistence of these functional problems after successful repair is clearly of importance in counselling patients pre-operatively. Whilst it is undoubtedly important to give confidence to the patient that their fistula can be closed, it is equally important to give a realistic opinion as to what this may mean in symptomatic terms. Injury to the urinary tract accounts for 6–10% of medico-legal claims in gynaecology [15,16]. Proper evaluation and appropriate counselling before repair may go some way towards limiting this outcome.

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Authors

P. Hilton MD, FRCOG, Consultant Gynaecologist (Sub-specialist in Urogynaecology), Department of Gynaecology, 2nd Floor, Leazes Wing, Royal Victoria Infirmary, Newcastle upon Tyne, NE1 4LP, UK.

Paper 5: Urinary symptoms and quality of life in women following urogenital fistula repair: a long-term follow-up study.

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Short communication

Urinary symptoms and quality of life in women following urogenital fistula repair: a long-term follow-up study

LM Dolan,[a] WE Dixon,[b] P Hilton[b]

[a] Simpson Centre for Reproductive Health, Royal Infirmary of Edinburgh, Edinburgh, UK [b] Urogynaecology Unit, Directorate of Women's Services, Royal Victoria Infirmary, Newcastle upon Tyne, UK
Correspondence: Mr Paul Hilton, Directorate of Women's Services, Royal Victoria Infirmary, Newcastle upon Tyne, NE1 4LP, UK.
Email paul.hilton@ncl.ac.uk

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Using the Bristol Female Lower Urinary Tract Symptom questionnaire, we have investigated urinary and sexual symptoms and quality of life in a group of 31 women 50 months (median) after successful repair of urogenital fistula. All had undergone urodynamic investigation prior to their repair surgery, and only 36% had normal findings. Almost all women reported one or more symptoms, and for 65%, these caused at least 'a bit of a problem', although 87% said that their urinary symptoms had little or no impact on their quality of life. Symptoms were similar in urethrovaginal and vesicovaginal fistulae and were not significantly associated with prior functional abnormality.

Keywords Long-term follow up, quality of life, surgery, urodynamics, urogenital fistula.

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Introduction

Urogenital fistulae are most often acquired from obstetric, surgical, radiation, malignant and miscellaneous causes. In much of the developing world more than 90% of fistulae are of obstetric aetiology, whereas in the UK and USA more than 70% follow pelvic surgery.[1] When conservative management of a urogenital fistula fails and surgical repair is undertaken, anatomical closure and cure of extraurethral incontinence are reported between 60 and 98% of women at their first operation.[1] However, some degree of urethral incontinence may persist in up to half of women after repair of obstetric fistula, particularly where there is urethral involvement in the defect.[2] A high incidence of associated functional abnormality of the lower urinary tract has also been reported prior to repair, in a series of largely surgical fistulae from the UK, and in this study too the risk of these abnormalities was greatest in urethral and bladder neck fistulae.[3] It seems likely that a high incidence of preoperative functional abnormality will impact on outcome despite a high rate of anatomical closure. To investigate this further, we undertook a single centre study to establish the long-term incidence of lower urinary tract symptoms (LUTs) after fistula repair in women who had undergone urodynamic investigation prior to their repair procedure. We also aimed to establish the time of onset of these symptoms in relation to repair surgery, the impact of their urinary symptoms on their quality of life and any association between preoperative functional abnormality, fistula site and postoperative symptoms.

Methods

A consecutive cohort of women, referred to the senior author for treatment of urogenital fistula between January 1993 and December 2002, was identified from our surgical database. Women with a vesicovaginal or urethrovaginal fistula, who had undergone preoperative urodynamic investigation and vaginal or abdominal fistula repair with a minimum of 6 months of follow up, were eligible for inclusion. Women with fistulae that were managed conservatively and those treated by primary urinary diversion or colpocleisis were excluded.

All eligible women had undergone dual channel subtracted filling and voiding cystometry performed using intravesical and either vaginal or rectal catheters attached to external pressure transducers. Filling cystometry was performed at a rate of 50 ml/minutes using normal saline at room

temperature, with the patient supine. Provocation tests were performed supine and erect on completion of filling. All methods, definitions and units conform to the standards recommended by of the International Continence Society, except where specifically noted. A voiding dysfunction was defined when two of the following three criteria were present at voiding cystometry: voiding pressure >50 cm H_2O, maximum urine flow rate of <15 ml/second and residual urine volume >100 ml.

Eligible women were contacted by post and invited to participate by completing the Bristol Female Lower Urinary Tract Symptom (BFLUTS) questionnaire,[4] together with a further self-administered questionnaire that provided information on parity, body mass index (BMI), interim surgery, current medical problems and regular medication. A stamped addressed envelope for return was enclosed, and nonresponders were contacted again 4 weeks later. Additional information was obtained from case records and those held on the unit surgical database.

Statistical analysis

All questionnaires were coded for identification. Statistical analysis was undertaken using Mann–Whitney *U* test and Fisher's exact test for continuous and categorical data, respectively.

Results

Questionnaire response rate

A consecutive series of 84 women with urogenital fistulae were identified. Forty women were not eligible for inclusion for various reasons: preoperative cystometry not performed (20); declined surgery or healed without surgery (8); surgical treatment by urinary diversion (3) or colpocleisis (2); other fistula types: ureterovaginal (2) colovesical (1), vesicouterine (1), rectovaginal (1), peritoneovaginal (1); and 1 woman was known to be deceased. In nine women, case information was missing or inadequate to allow contact. Therefore, there were 35 contactable women with vesicovaginal or urethrovaginal fistulae who fulfilled all eligibility criteria for inclusion, and they were sent postal questionnaires.

Completed questionnaires were returned by 31 women (89%); 1 was returned unanswered as the woman was deceased. The median age of respondents was 46 years (range 16–85 years), median parity 2 (range 0–5) and mean BMI 26.9 kg/m^2 (SD 4.9). The median length of time between the surgery and the survey was 50 months (range 7–115 months).

Preoperative findings

Twenty-one of the fistulae were into the vaginal vault (68%) and 9 were bladder neck or urethral fistulae (29%); 1 was juxtacervical in position. The aetiology was surgical in 25 women (81%), obstetric in 3 (10%), congenital in 1 (3%), following pessary use in 1 (3%) and radiation in 1 woman (3%). The antecedent procedures in the surgical cases were total abdominal hysterectomy (15), vaginal hysterectomy (2), laparoscopically assisted vaginal hysterectomy (2), urethral diverticulectomy (3), colposuspension (2) and colporrhaphy (1). This distribution of cases is comparable to the total fistula workload referred to the unit.[1]

On the basis of preoperative urodynamic investigation, functional abnormality of the lower urinary tract was present in 20 women overall (65%) (Table 1); the rate of abnormality was not significantly different between those with vault fistulae (62%) and bladder neck or urethral fistulae (78%) (Fisher's exact test $P = 0.74$). Five women (16%) demonstrated mixed urodynamic diagnoses; the breakdown of the main diagnoses in pure and mixed forms is shown in Table 2.

Fistula repair was performed vaginally in 27 women (87%) by a transvesical approach in 2 and a transperitoneal

Table 1. Distribution of urodynamic abnormalities found in association with urogenital fistula and the rate of symptoms and significantly problematic symptoms at later follow up

	n (%)	Number with at least one symptom graded as at least 'a bit of a problem', *n* (%)	Number with at least one symptom graded as 'quite a problem' or 'a serious problem', *n* (%)
Preoperative urodynamic diagnosis			
No abnormality	11 (35.5)	6 (54.5)	3 (27.3)
Voiding dysfunction	6 (19.4)	4 (66.7)	0
USI	5 (16.1)	4 (80.0)	0
Detrusor overactivity	4 (12.9)	2 (50.0)	1 (25.0)
Mixed urodynamics	5 (16.1)	4 (80.0)	0
Total	31	20 (64.5)	4 (12.9)
Fistula type			
Bladder neck or urethral	9 (29.0)	7 (77.8)	1 (11.1)
Vaginal vault	21 (67.7)	13 (61.9)	3 (14.3)

Table 2. Distribution of urodynamic abnormalities in pure and mixed forms

Preoperative urodynamic diagnosis	Pure diagnoses, *n* (%)	Mixed diagnoses, *n* (%)	Pure or mixed, *n* (%)
No abnormality	11 (35.5)	—	—
Voiding dysfunction	6 (19.4)	4 (12.9)	10 (32.3)
USI	5 (16.1)	5 (16.1)	10 (32.3)
Detrusor overactivity	4 (12.9)	1 (3.2)	5 (16.1)
Mixed urodynamics	—	5 (16.1)	—

approach in 2. Successful anatomical closure of the fistula was achieved with a single operation in all women. A continence procedure was combined with fistula repair in three women with preoperative urodynamic stress incontinence (USI).

Lower urinary tract symptoms

The BFLUTS questionnaire asks respondents to describe symptoms in terms of their frequency of occurrence as 'never', 'occasionally', 'sometimes', 'most of the time' or 'all of the time'; in a second stem, they are then asked to grade the impact of symptoms as 'not a problem', 'a bit of a problem', 'quite a problem' or 'a serious problem'. Thirty of the 31 women (97%) reported having one or more urinary symptoms at a median of 50 months after fistula repair, with urgency (71%), nocturia (68%), stress incontinence (68%) and urge incontinence (65%) being the most commonly reported symptoms.

Table 1 shows the proportion of women in each of the preoperative cystometric diagnostic groups who reported bothersome LUTs postoperatively and the frequency of occurrence of symptoms. Overall, 20 women (65%) had at least one bothersome symptom (i.e. one that they graded as being at least 'a bit of a problem'). Fifty-five percent of women without functional abnormality preoperatively reported symptoms that were bothersome after surgery compared with 80% of those with mixed urodynamic findings or USI; however, these differences were not statistically significant. There was no significant difference in the rate of bothersome symptoms between those women with urethral or bladder neck fistulae (78%) and those with fistulae into the vaginal vault (62%) (Fisher's exact test $P = 0.34$).

Urinary incontinence was the most commonly bothersome symptom (35%), with stress and urge incontinence being similarly represented. Despite the apparently high incidence of urinary symptoms, only four women (13%) described symptoms that were either 'quite a problem' or 'a serious problem' to them. One woman with detrusor overactivity described nocturia in this way; the other three, all in fact with normal urodynamic findings prior to repair, reported a number of symptoms in this way: one reported stress incontinence and nocturnal enuresis; one frequency, bladder pain and unexplained leakage and one urgency and both stress and unexplained leakage as significantly problematic.

Of those women with bothersome symptoms, nine (43%) reported the onset of symptoms as being 'before the repair' and nine (43%) felt their symptoms as starting 'shortly after the repair'; one described symptoms of recent onset and others did not specify the onset.

Impact on quality of life

The BFLUTS questionnaire asks respondents to grade how they would feel if they had to spend the rest of their life with their current urinary symptoms as 'perfectly happy', 'pleased', 'mostly satisfied', 'mixed feelings', 'mostly dissatisfied', 'very unhappy' or 'desperate'. Ten women (32%) had at least mixed feelings, although only two women described feeling dissatisfied or unhappy at the prospect. Twenty-seven women (87%) said that their urinary symptoms caused little (12) or no (15) interference with their lives.

Sexual function

Twenty-two women were sexually active at the time they responded to the questionnaires and 15 (68%) described one or more symptoms in relation to intercourse. Vaginal dryness (46%), sex life spoilt by urinary symptoms (41%) and dyspareunia (36%) were the most commonly reported symptoms. In nine women (41%), the sexual symptoms were described as being at least 'a bit of a problem', and for six (27%), these were either 'quite a problem' or 'a serious problem'. Three women described leaking urine during intercourse, although only one found this 'a bit of a problem'.

Discussion

We have demonstrated that the majority of women report one or more urinary or sexual symptoms in the long term following successful anatomical closure of urogenital fistula. For approximately two-thirds of women, these symptoms cause at least some degree of bother, although only one in eight found them to be significantly problematic. Nocturia, urgency and urinary incontinence were the most frequently reported symptoms, with incontinence the most commonly bothersome, and stress and urge incontinence occurring with equal frequency. Recent epidemiological studies undertaken in Newcastle on a cohort of 3000 women 20 years after their first delivery (and hence of similar age and parity distribution to the women reported in this study) also found a high prevalence of all symptoms of pelvic floor dysfunction, albeit using a different questionnaire.[5] For example, nocturia, urgency and stress incontinence were reported by 63, 48 and 30% of women, with 18, 21 and 14%, respectively, describing the symptom as causing at least 'a bit of a problem'.[5] For each of

the urinary symptoms examined, however, the prevalence was 1.5 to 2 times higher in our population of women following fistula repair than it was in the general population.

Hysterectomy has often been looked on as a cause of urinary symptoms, although longitudinal studies suggest that they are more likely to improve than they are to deteriorate or to present for the first time following hysterectomy. It should be noted, however, that 23 (74%) of our women had undergone prior hysterectomy, and in 19 (61%), it was an immediate antecedent to their fistula.

Of those women who were able to specify the time of onset of their symptoms, approximately half felt symptoms had developed at or around the time of their fistula and or repair, although half recalled having symptoms before the development of their fistula. We cannot exclude the possibility of recall bias in defining the onset of symptoms, although it seems likely that only a proportion of the symptomatology demonstrated in this study can be appropriately ascribed to the fistula or its repair.

Few studies have reported urodynamic investigation in women with urogenital fistulae. In a study of women with obstetric fistulae in Ethiopia where urodynamic investigation was undertaken after repair, 55% of women were incontinent despite successful closure of their fistula; USI was most common abnormality identified.[6] We have previously demonstrated USI in 47% of women prior to repair in a series of largely surgical fistulae in the UK, although in only 3% did this persist after repair. Detrusor overactivity was found in 40% at presentation and persisted in half of these at follow up.[3] It is noteworthy, however, that although symptoms were somewhat more common in the long term after fistula repair in women with urodynamic abnormalities defined prior to repair, the majority of the most bothersome symptoms were actually found in women without such abnormalities. One might therefore question the value of urodynamics in this group of women. It should, however, be noted that it has always been our practice to undertake labial fat/muscle interposition grafts (Martius graft) in women with urethral or bladder neck fistulae. Later, we have also offered concurrent fascial sling (with urethrovaginal fistulae) or tension-free vaginal tape (with vesicovaginal fistulae) in those women with problematic stress urinary incontinence confirmed urodynamically. In that sense, the use of bladder function testing has certainly influenced our practice.

Our previous studies of urodynamic investigation in women with fistulae suggested that functional abnormalities were more likely to be found in women with urethrovaginal or bladder neck fistulae than in those with vault fistulae and that symptoms were also more likely to persist after repair in this group.[3] In the current series, however, the incidence of abnormality overall and the distribution of urodynamic diagnoses were similar in these different fistula types; the overall prevalence of symptoms and of clinically significant symptoms at later follow up was also similar. It is difficult to explain the difference in findings in our two series, and it may simply reflect the small sample size and limited power to draw firm conclusions from either. The findings of the current series are in keeping with those of the only previous series of women with obstetric fistulae in which urodynamic investigation was undertaken.[6]

Although the causes, types, size and social impact of fistulae seen in the developing world are very different from those seen in the UK,[1] the follow-up study from Browning and Menber[2] makes an interesting comparison. They found that the urinary incontinence persisting after anatomically successful repair of obstetric fistulae tended to improve over time (6 months after repair); together with that improvement, there was evidence of improvement in several aspects of quality of life, with reintegration into society. Although our women were assessed over a longer time scale (median 4 years), we did not see a tendency for symptoms to resolve completely. The patients' responses to an incontinence-specific quality-of-life questionnaire, however, show that in the majority, residual urinary symptoms have limited impact on their quality of life.

Conclusions

We have demonstrated that LUTs are common after successful anatomical closure of urogenital fistulae of largely surgical aetiology, and in approximately half of these women, the symptoms develop at or shortly after the onset of the fistula. There is no significant difference in urodynamic abnormalities found in association with different fistula types or in the symptoms found subsequently. Normal cystometry prior to fistula repair did not appear to be associated with a lower incidence of bothersome symptoms 4 years postoperatively. Even where a good prognosis for fistula closure can be given, women undergoing fistula repair should be counselled about the possibility of persisting urinary symptoms afterwards; they can be reassured that in most cases, these will be mild, with limited impact on their quality of life.

Disclosure of interests

The authors have no current financial or other interests to declare.

Contribution to authorship

P.H. conceived and designed the study, contributed to investigations and undertook all surgery; he also contributed to acquisition and analysis of data and in drafting and revision of the paper and approved the final version for publication. L.M.D. contributed to the study design, acquisition and

analysis of data, drafting and revision of the paper and approved the final version for publication. W.E.D. contributed to patient investigations and approved the final version for publication.

Details of ethics approval

Approval for the study was obtained from the Newcastle and North Tyneside Local Research Ethics Committee (ref: 2002/350) and from the Newcastle upon Tyne Hospitals NHS Trust Research and Development Department.

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Paper 6: The risk of vesicovaginal and urethrovaginal fistula after hysterectomy performed in the English National Health Service - a retrospective cohort study examining patterns of care between 2000 and 2008.

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The risk of vesicovaginal and urethrovaginal fistula after hysterectomy performed in the English National Health Service—a retrospective cohort study examining patterns of care between 2000 and 2008

P Hilton,[a] DA Cromwell[b,c]

[a] Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK [b] Office of Research and Clinical Audit, Royal College of Obstetricians and Gynaecologists, London, UK [c] Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, London, UK
Correspondence: P Hilton, Consultant Gynaecologist & Urogynaecologist, Directorate of Women's Services, Level 5, Leazes Wing, Royal Victoria Infirmary, Newcastle upon Tyne, NE1 4LP, UK. Email paul.hilton@ncl.ac.uk

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Objective To estimate rates of vesicovaginal and urethrovaginal fistula among women undergoing hysterectomy by indication and type of procedure, and to assess trends in risk over time.

Design Retrospective cohort using data from Hospital Episode Statistics.

Setting English National Health Service (NHS) hospitals.

Population Women undergoing hysterectomy for selected common conditions in English NHS hospitals between January 2000 and December 2008.

Methods Unadjusted rates of urogenital fistula were calculated by type of procedure and indication. Logistic regression was used to assess whether the risk of fistula was associated with age, or had changed over time.

Main outcome measure Rate of urogenital fistula (vesicovaginal and urethrovaginal fistula) within 1 year of hysterectomy.

Results Among 343 771 women undergoing hysterectomy, the overall rate of fistula was 1 in 788. The rate varied by indication and procedure, being highest following radical hysterectomy for cervical cancer (1 in 87; 95% CI 61–128) and lowest following vaginal hysterectomy for prolapse (1 in 3861; 95% CI 2550–6161). After total abdominal hysterectomy for endometriosis, menstrual problems or fibroids, the risk of fistula was lower in women aged 50 years or over than in women under 40 years (adjusted odds ratio 0.61; 95% CI 0.38–0.98). The overall rate of fistula increased by 46% during the study period.

Conclusions The risk of urogenital fistula was associated with type of hysterectomy and indication; the risk increased during the study period, and was lower after hysterectomy for benign conditions in women aged 50 years or over.

Keywords Hysterectomy, intraoperative complications, postoperative complications, surgical injuries, urinary fistula, vesicovaginal fistula.

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Introduction

The prevention and management of vesicovaginal fistula remains a major global public health challenge.[1] It has been estimated that there are currently 2 000 000–3 000 000 women with untreated fistula worldwide, although over 95% of these are of obstetric aetiology and are in the developing world.[2] In the developed world, urogenital fistulae are relatively uncommon, and publically available Hospital Episode Statistics (HES) for England suggest that approximately 105 cases have been repaired surgically each year over the last decade.[3]

Chassar Moir[4] reviewed the position of vesicovaginal fistula in Britain in 1973, and Lee et al.[5] did the same in the USA in 1988. The largest recent UK case series are those reflecting tertiary-care practices, published by Ockrim

et al.[6] in 2009 (41 cases), and Hilton[7] in 2011 (348 cases). In the latter series, two-thirds of cases were of surgical aetiology, and the remainder were evenly distributed between obstetric, radiation and miscellaneous or traumatic causes. Overall, almost half of this series were associated with hysterectomy.[7]

The number of hysterectomy procedures undertaken in the UK has been falling over the last decade, with the increasing availability and acceptability of nonsurgical treatments for menorrhagia in particular.[8] However, with the number of surgically treated urogenital fistulae remaining fairly constant over the same period, this suggests that the risk of urogenital fistula following hysterectomy may be increasing.[7] In this study, we describe rates of vesicovaginal fistula and urethrovaginal fistula within 1 year of hysterectomy among women treated in English NHS Trusts between January 2000 and December 2008, and examine whether the risk of a urogenital fistula is affected by the indication, the type of procedure carried out, and the age at surgery. We also investigate whether the risk of fistula has changed over time.

Methods

The study used data from the HES database, which contains records of all patient admissions to NHS hospitals in England. Its records capture patient demographics, hospital administrative information, diagnostic information using the International Classification of Diseases (ICD), 10th revision,[9] and operative procedures using the UK Office for Population Censuses and Surveys classification (OPCS), 4th revision.[10]

Patient selection

This study included adult women (18 years and over) who underwent hysterectomy for selected common indications in English NHS hospitals between 1 January 2000 and 31 December 2008. The study was restricted to elective procedures and distinguished between four types of hysterectomy: total abdominal hysterectomy (TAH) (OPCS code: Q07.4), subtotal abdominal (STH) (Q07.5), vaginal (VH) (Q08.9), and radical abdominal hysterectomy (RAH) (Q07.1-07.3). The selected benign conditions were endometriosis (ICD10 code: N80), uterine fibroids (D25), genital prolapse (N81) and menstrual disorders (N92–N94). Four 'malignant' conditions were also selected, namely, cervical carcinoma *in situ* (D06), cervical cancer (C53), uterine cancer (C54, C55) and ovarian cancer (C56). The analysis was restricted to women under 55 years of age if their primary diagnosis was endometriosis or menstrual irregularities. Further, the analysis also excluded radical hysterectomies coded to women with benign diagnoses, and combinations of conditions and procedures for which there were fewer than 500 cases.

Women were defined as having a postoperative fistula if the ICD10 codes N82.0 (vesicovaginal fistula) or N82.1 (other urinary-genital tract fistula) were found in the diagnostic fields of the index procedure episode or any subsequent episode that occurred within 1 year of the index procedure. The majority of fistulae occurred within 6 months of the index procedure. Surgical repair of fistulae was examined using the most pertinent OPCS codes, namely, repair of vesicovaginal fistula (OPCS P25.1), repair of urethrovaginal fistula (P25.2) and construction of an ileal conduit (M19.1).

Statistical analysis

The unadjusted incidence rate of urogenital fistula was expressed as the percentage of fistulae within 1 year of hysterectomy; rates were stratified by type of procedure and indication. We estimated the 95% confidence intervals (CI) assuming that the number of events followed a Poisson distribution. Fisher's exact test was used to judge the statistical significance of differences between unadjusted rates.

We also examined whether the risk of urogenital fistula had changed over time and was related to patient age at the time of procedure. The primary analysis was restricted to TAH procedures for endometriosis, fibroids or menstrual conditions because of the small number of fistulae recorded for other procedure–indication combinations. Two additional analyses were performed. One extended the first analysis by including both VH and TAH procedures for these three benign indications. The other examined the associations among women undergoing TAH for a malignant indication. Logistic regression was used to calculate adjusted odds ratios (OR) and 95% CI. All P values were two-sided, and those <0.05 were judged to be statistically significant. All analyses were performed using STATA version 11 (StataCorp LP, College Station, TX, USA). The formulation of this report has followed the STROBE Statement.[11]

Results

Between 1 January 2000 and 31 December 2008, there were 351 505 hysterectomies performed in English NHS hospitals for the selected indications (Figure 1). Of the 292 250 operations performed for benign conditions, 3262 (1.1%) were excluded because the procedure was coded as a radical hysterectomy (abdominal or vaginal) and 290 (0.1%) were excluded because of the small number criterion. A further 2645 (2.5%) of the 106 440 women with endometriosis or menstrual conditions were excluded for being 55 years or older. Of the 59 255 procedures performed for malignant conditions, 1537 (2.6%) were excluded because of the small number criterion. The characteristics of the remaining 343 771 women are summarised in Table 1.

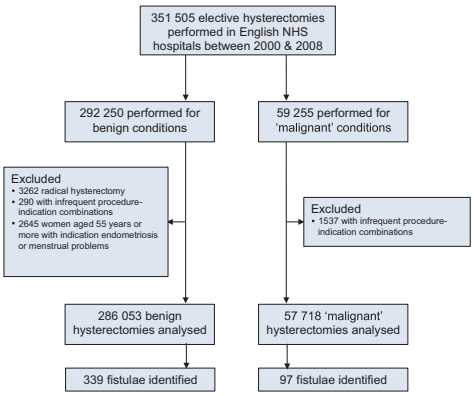

Figure 1. Flow chart of included and excluded patients and procedures.

Number of hysterectomy procedures by indication

The number of hysterectomies performed for the different indications varied over the 9-year period (Figure 2). For women with menstrual conditions, endometriosis, or fibroids, the number of procedures fell by 37%, 30% and 15%, respectively. The number of procedures for cervical cancer and carcinoma *in situ* fell by 13% and 39%. In contrast, the number of hysterectomies for uterine cancer, ovarian cancer and prolapse rose by 37%, 18% and 11%, respectively. Overall, the annual number of hysterectomies declined by 16% from 43 014 in 2000 to 36 189 in 2005, before increasing by 5% to 37 923 in 2008. Between 2000 and 2008, the proportion of TAH procedures decreased from 60% to 53%, whereas VH increased from 34% to 39%. The relative frequency of STH and RAH remained comparatively static.

Rates of urogenital fistula by procedure and condition

There were 436 women who had a diagnosis of vesicovaginal fistula or urethrovaginal fistula recorded within a year of their hysterectomy, giving an overall rate of 1 in 788 (95% CI 718–868). However, the risk posed to women differed across the various combinations of procedure and indication (Table 2). For women undergoing VH for prolapse, the estimated rate was 1 in 3861 (95% CI 2550–6161). Among women undergoing a TAH for the other three benign conditions, the overall rate was 1 in 540 (272/146 841; 95% CI 479–540), whereas for women who underwent STH, the rate was 1 in 2279 (9/20 511; 95% CI 1205–5000). For both these abdominal procedures, the differences in the fistula rates across the three benign conditions were not statistically significant (Fisher's Exact; $P = 0.9$ for TAH and $P = 0.17$ for STH). In contrast, the absolute risk for women undergoing VH differed slightly across the three conditions (Fisher's Exact, $P = 0.04$), the rate ranging from 1 in 486 for endometriosis to 1 in 1922 for fibroids.

The risk of vesicovaginal fistula or urethrovaginal fistula was greatest among those women who had cervical cancer, with TAH and RAH both having estimated rates of around 1 in 100 (Table 2). Among women undergoing TAH, the rate was roughly five times greater than the rates for

Table 1. Patient characteristics of women undergoing hysterectomy in NHS hospitals for selected conditions between 2000 and 2008 (after exclusions as described in text)

	Prolapse N81	Endometriosis N80	Menstrual N92 to N94	Fibroids D25
Benign conditions				
All patients	87 329	24 947	78 848	94 929
Average age				
Mean	61.1	41.1	41.0	47.4
SD	11.9	5.7	5.8	7.5
Age group				
Under 40	5%	45%	45%	14%
40–50	14%	50%	50%	60%
50–60	28%	5%	5%	20%
60–70	30%	–	–	4%
70 and over	23%	–	–	2%
Type of hysterectomy				
Abdominal subtotal	–	2331	6634	11 546
Abdominal total	2386	19 216	53 851	73 774
Vaginal	84 943	3400	18 363	9609

	Cervical cancer *in situ* D06	Cervical cancer C53	Uterine cancer C54, C55	Ovarian cancer C56
Malignant conditions				
All patients	3886	5327	34 261	14 244
Average age				
Mean	46.0	45.1	65.7	60.6
SD	11.4	13.1	10.9	12.5
Age group				
Under 40	38%	44%	1%	6%
40–50	31%	27%	6%	16%
50–60	18%	16%	26%	27%
60–70	10%	8%	33%	27%
70 and over	3%	6%	34%	24%
Type of hysterectomy				
Abdominal subtotal	–	–	–	1080
Abdominal total	2890	2627	31 032	13 164
Abdominal radical	–	2700	538	–
Vaginal	996	–	2691	–

women with cervical carcinoma *in situ* (relative risk 4.6; 95% CI 1.7–12.2; $P < 0.001$). Among the other uterine cancers, RAH also posed an increased risk of urogenital fistula, but overall the rates of fistula were of the same order of magnitude as the rates for the benign conditions.

Effect of age and year of surgery

For the benign conditions of endometriosis, fibroids and menstrual disorders, there were noticeable changes in the number of fistulae after TAH across the age categories and by year of surgery (Table 3). In terms of age, the rate of fistula was stable until women passed 50 years of age, after which it fell by around 40%. The rate of fistula increased from 0.15% in 2000–02 to 0.22% in 2006–08, a rise of 46%. Adjustment for possible confounding by indication and time period did not alter these patterns. Extending the model to include both VH and TAH for these benign conditions produced comparable results for the estimated relationship between rate of fistula and age categories and year of surgery. For patients with malignant conditions, there was no association between the adjusted OR for fistula by year of surgery ($P = 0.97$) nor by age category ($P = 0.86$).

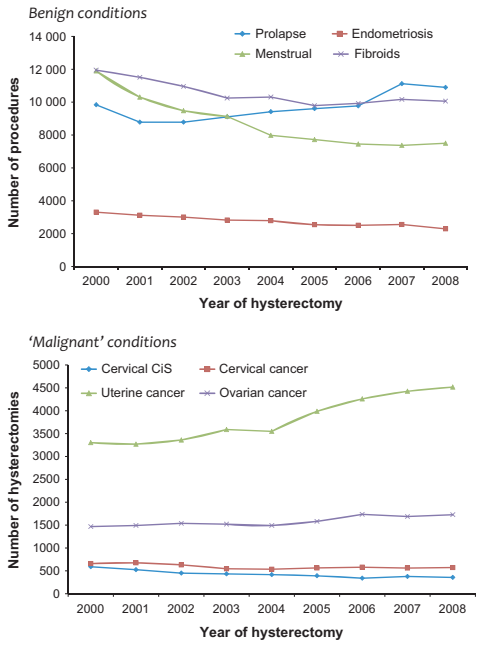

Figure 2. Number of hysterectomy procedures in English NHS hospitals for selected conditions between 2000 and 2008.

Surgical repair

The majority of women with fistula underwent one of the repair operations. Urogenital fistula repair procedures (P25.1, P25.2) were found for 71% of fistulae among women with benign conditions (241/339). None of these women had a urinary diversion. For women with malignant conditions, fistula repair was identified for 41% (41/97) of women. Another three women (all of whom had RAH for cervical cancer) had a urinary diversion.

Discussion

This study of elective hysterectomies in English NHS hospitals has established the overall rate of lower urinary–genital tract fistulae within 1 year of surgery, of 0.13% or 1 in 788. The rate was highest among women who had either an RAH or TAH for cervical cancer, with approximately 1 in 100 experiencing a fistula. The most common type of hysterectomy undertaken for fibroids, endometriosis and menstrual disorders was TAH, and resulted in an estimated fistula rate of 1 in 540. For the same diagnostic groups, the rate was 1 in 2279 for STH. The lowest rate of fistula following hysterectomy was observed for VH for prolapse (1 in 3861).

The Cochrane review of approaches to hysterectomy for benign disease found no difference in the rate of fistula following abdominal, vaginal and laparoscopic routes;[12] and the VALUE study, a non-randomised cohort study of hysterectomy from the UK, although not reporting on the development of fistula, found no difference in the rate of operative bladder injury between abdominal, vaginal and laparoscopic routes.[13] The national cohort study from Finland on the other hand reported a higher rate of both bladder injury (relative risk 11.4) and subsequent fistula formation (relative risk 2.2) following laparoscopic procedures.[14] Unfortunately, the OPCS-4 coding used in HES does not allow easy separation between open and laparoscopic hysterectomies. There is an option to use an additional code for 'laparoscopic approach' alongside the codes for hysterectomy, although an evaluation of OPCS coding completeness in other situations has shown that laparoscopic procedures are under-reported.[15] Given the range of surgical techniques and coding systems used during our study period, we do not feel that much of use can be stated about the risks of fistulae associated with laparoscopic hysterectomy procedures.

It is often stated that distorted anatomy (e.g. from fibroids or malignancy), abnormal tissue adhesion (e.g. from previous caesarean section or endometriosis) or previous radiation therapy increase the risk of urinary tract injury and fistula formation following hysterectomy.[16] The HES database does not include radiotherapy treatments, and given the average age of these women (51 years) does not

Table 2. Rates of fistula within 1-year of undergoing hysterectomy, by condition and type of procedure

Conditions	Type of hysterectomy	No. of procedures	No. of Fistulae	Fistula rate (%)	95% confidence interval (%)	
Benign conditions						
Prolapse	Abdominal total	2386	1	0.04	0.00	0.23
	Vaginal	84 943	22	0.03	0.02	0.04
Endometriosis	Abdominal subtotal	2331	0	0.00	0.00	0.16*
	Abdominal total	19 216	36	0.19	0.13	0.26
	Vaginal	3400	7	0.21	0.08	0.42
Menstrual	Abdominal subtotal	6634	1	0.02	0.00	0.08
	Abdominal total	53 851	103	0.19	0.16	0.24
	Vaginal	18 363	23	0.13	0.08	0.19
Fibroids	Abdominal subtotal	11 546	8	0.07	0.03	0.14
	Abdominal total	73 774	133	0.18	0.15	0.21
	Vaginal	9609	5	0.05	0.02	0.12
'Malignant' condition						
Cervical carcinoma *in situ*	Abdominal total	2890	5	0.17	0.06	0.40
	Vaginal	996	1	0.10	0.00	0.56
Cervical cancer	Abdominal total	2627	21	0.80	0.49	1.22
	Abdominal radical	2700	31	1.15	0.78	1.63
Uterine cancer	Abdominal total	31 032	28	0.09	0.06	0.13
	Abdominal radical	538	3	0.56	0.11	1.63
	Vaginal	2691	0	0.00	0.00	0.14*
Ovarian cancer	Abdominal subtotal	1080	1	0.09	0.00	0.52
	Abdominal total	13 164	7	0.05	0.02	0.11

*One-sided confidence interval.

Table 3. Estimated association between rates of fistula and various risk factors for women undergoing total abdominal hysterectomy for fibroids, endometriosis and menstrual disorders

	No. of procedures	No. of fistulae	Rate (%)	Adjusted odds ratio	95% confidence interval		*P* value
Condition							
Fibroids	73 774	133	0.18	1			0.99
Endometriosis	19 216	36	0.19	0.98	0.67	1.43	
Menstrual disorders	53 851	103	0.19	1.01	0.76	1.32	
Age group (years)							
Under 40	42 873	77	0.18	1			0.037
40–44	43 957	92	0.21	1.14	0.83	1.55	
45–49	37 312	78	0.21	1.14	0.82	1.58	
50 plus	22 699	25	0.11	0.61	0.38	0.98	
Year of surgery							
2000–02	56 561	83	0.15	1			0.033
2003–05	47 535	97	0.20	1.38	1.03	1.85	
2006–08	42 745	92	0.22	1.44	1.07	1.94	

have sufficient historical information to capture obstetric history. We did not find the rate of fistula to be increased in women undergoing abdominal hysterectomies for fibroids or endometriosis compared with women with menstrual problems (although there was variation in risk for women having vaginal procedures for these benign

indications). The HES database gives no information on the stage of endometriosis or the size of fibroids, making it difficult to comment on their significance as risk factors.

Calculating precise rates of post-hysterectomy fistula requires a large sample size and a complete data set. Both of these criteria were met in this study, with the data extracted from the HES database containing 343 771 procedures in total, and over 10 000 patients for many of the indication–procedure combinations analysed. However, in any study using routine data, there are potential limitations arising from coding omissions and inaccuracy. The quality of the clinical coding in HES has been shown to vary between NHS trusts,[17] although the overall quality is considered to be high in relation to operations and procedures.[18]

Coding accuracy could have influenced the identification of hysterectomy procedures, and the classification by type. However, studies that have compared medical notes to routine data for hysterectomy have found very good agreement.[19] In addition, to remove records affected by coding errors, we restricted our analysis to patient records with (a) expected combinations of diagnosis and procedure, and (b) age ranges consistent with the diagnosis.

Coding accuracy and completeness could have also affected our estimated incidence of fistula. In series of fistulae from the developed world, between 50% and 90% follow hysterectomy,[7,20] and postoperative fistula rates between 0.1% and 4.0% are reported.[16,21] The overall rate described in our study (1 in 788) lies within this range of estimates, and is consistent with other large-scale national studies.[14,21] There is no reason to suspect that the coding of fistula would be more complete for some procedures than for others, so the estimated relative rates among the different patient groups are likely to be robust.

Comparison with other studies

Our study is the first to report a significantly lower risk of urogenital fistula for women over 50 years of age. This is at odds with a study by Forsgren et al.,[21] who reported the rate of 'fistula disease' to be higher in women over 50 years of age. However, their study did not separate intestinal from urinary fistulae, and almost 60% did not involve the urinary tract. The same group recently examined the extent of association between 'fistula disease' in women with diverticulitis undergoing hysterectomy and reported the main associations being with intestino-genital and uro-intestinal fistulae.[22] It is conceivable therefore that the increase in fistulae reported in older women in these studies relates more to bowel than urinary fistulae, and to the prevalence of inflammatory bowel disease than to hysterectomy. The VALUE study found a reduction in overall serious morbidity with increasing age at operation, although this was limited to women with fibroids and to women undergoing vaginal hysterectomy.[13]

Our analysis provides no insight into the reasons for lower risk of urogenital fistula for women over 50 years of age. We can speculate that the reduced vascularity and uterine size in the estrogen-deficient postmenopausal pelvis might reduce the risk of operative injury or postoperative haematoma formation. The finding is unlikely to reflect confounding because of the exclusion of women over 55 years old coded as having hysterectomy for endometriosis and menstrual problems from the analysis because indication was an explanatory factor in the multiple logistic regression. Moreover, a lower risk of urogenital fistula for women over 50 years of age was still apparent if the analysis was restricted to women with uterine fibroids whose age range was not restricted. A quarter of the women were aged over 50 years.

The national cohort studies from Sweden,[21] and Finland,[14] both showed lower overall rates of fistula following hysterectomy for benign indications, most notably for TAH (1 in 1019 and 1 in 959, respectively, compared with one in 540 in this series). One possible explanation for the difference is that the Swedish study covered the period 1973–2003 and the Finnish study 1990–95 whereas our study covered a later period (2000–08). We also observed a 46% increase in risk of fistula following hysterectomy for benign conditions over the study period. One explanation for this could be an increase in the proportion of more difficult procedures among all hysterectomies. Between 2000 and 2008, the total number of hysterectomy procedures fell by 12% and those for the main benign indications (excluding prolapse) fell by 27%. This was mainly a result of the fall in the number of hysterectomies for menorrhagia, a trend that has been ongoing since the mid-1990s.[23]

Another potential contributory factor is the changes in surgical training and practice in gynaecology. A consequence of the reduced number of hysterectomy procedures is that trainees, in the UK at least, obtain less surgical experience during their training. It was calculated in 2001 that even if every hysterectomy carried out in the NHS were carried out by a trainee (and the majority are not), each would undertake only 27 procedures per year during their training.[24] The reduction of the length of the working week resulting from the 'New Deal' and the European Working Time Directive,[25,26] and reduced years in training implemented following the Report of the Working Group on Specialist Medical Training and 'Modernising Medical Careers',[27,28] both add to this problem. Trainees themselves perceive this to be an issue. Although the quality of supervision of surgical training is reported to be of a good standard, trainees' satisfaction with operative teaching declined consistently between 1995 and 2008, and operating volume was seen as a significant factor in this.[29]

Conclusions

This is the largest reported cohort study on the risk of urogenital fistula following hysterectomy. Overall, 1 in 788 hysterectomies in the NHS in England is followed by vesicovaginal fistula or urethrovaginal fistula. The rate is highest following RAH for cervical cancer (1 in 87), and lowest following VH for prolapse (1 in 3861). The most common procedure–indication combination is TAH for benign indications, which carries a risk of fistula formation of 1 in 540. Whereas urogenital fistula remains an uncommon complication of hysterectomy,[30] our study also identified a trend of increasing surgical morbidity within the NHS, of which all concerned in the provision of service and training should be aware.

Disclosure of interests

PH has no financial interests to declare. He is a faculty member on ICUD-SIU 1st International Consultation on Obstetric Vesicovaginal Fistula—complications committee (2010/11) and on the ICUD-EUA 5th International Consultation on Incontinence—fistula committee (2011/12). DC has no interests to declare.

Contribution to authorship

PH conceived the study and contributed to its design, contributed to analysis and writing of the paper, and approved the final version for publication. DC contributed to study design, data extraction and analysis, writing of the paper, and approved the final version for publication.

Details of ethics approval

The study is exempt from UK NREC approval because it involved analysis of an existing data set of anonymised data for service evaluation. Approvals for the use of HES data were obtained as part of the standard Hospitals Episode Statistics approval process.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. Powerpoint slides summarising the study.

Please note: Wiley-Blackwell is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author. ■

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Journal club

Discussion points

1. Background: Describe the risks of hysterectomy.[1] Discuss the implications of vesicovaginal and urethrovaginal fistula following hysterectomy and their clinical presentation in practice.
2. Methods: Discuss the possible benefits and pitfalls of using the Hospital Episode Statistics (HES) database as a source to investigate outcomes of surgery in the NHS. Compare HES with central and local clinical databases, with particular reference to provision of demographic data, case ascertainment, completeness of data, availability of clinical detail (endometriosis stage, clinical history). [2,3]
   Discuss coding issues including provision or not of codes for recent and novel procedures (e.g. laparoscopic hysterectomy).
   (Optional advanced task): Regression analysis was conducted at patient-level data and not hospital-level aggregated data. Compare the two approaches. Which one would account for variation in rates per individual surgeon? Can the two approaches be combined?
3. Results and implications: The authors describe an increase in the overall rate of fistula of 46% during the study period. A possible contributory factor to this increase proposed by the authors is the change in surgical training and practice in gynaecology and the reduced number of hysterectomies performed by trainees—discuss.

Would the findings of this paper affect your counselling of women for hysterectomy depending on their indication for surgery? (Data S1) ■

Further reading

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Disclosure of interest

Rebecca Simms has been conducting research on maternity databases.

D Siassakos & R Simms
RiSQ, School of Clinical Sciences, University of Bristol, UK
Email jsiasakos@gmail.com

Paper 7: The risk of ureteric injury associated with hysterectomy: a 10-year retrospective cohort study.

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Gynaecological surgery

The risk of ureteric injury associated with hysterectomy: a 10-year retrospective cohort study

A Kiran,[a,b] P Hilton,[c] DA Cromwell[a,b]

[a] Department of Health Services Research and Policy, London School of Hygiene & Tropical Medicine, London, UK [b] Lindsay Stewart Centre for Audit and Clinical Informatics, Royal College of Obstetricians and Gynaecologists, London, UK [c] Directorate of Women's Services, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK
Correspondence: P Hilton, Directorate of Women's Services, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK.
Email paul.hilton@ncl.ac.uk

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Objective To evaluate the rates of ureteric injury among women undergoing hysterectomy.

Design Retrospective cohort.

Setting English National Health Service hospitals.

Population Women undergoing hysterectomy in 2001–2010.

Methods Unadjusted rates of ureteric injury, within 1 year of hysterectomy, calculated by indication and type of procedure. Multivariable logistic regression used to assess the risk of ureteric injury with year of surgery.

Main outcome measures Ureteric injury within a year of the hysterectomy.

Results In 2001–2010, 377 073 women underwent hysterectomy, of whom 1792 (0.5%) experienced a ureteric injury. In both benign and malignant groups the rate of injury was higher in 2006–2010 than 2001–2005. After 2006, ureteric injuries were most common for abdominal radical hysterectomy for uterine cancer (10.7%; 95% CI 7.3–15.1%). The proportion of women having a ureteric injury was similar for ovarian and cervical cancer (1.9–4.0% depending on type of procedure). For benign conditions, the rate of injury tended to be lower, typically <1%. Women with endometriosis had the highest risk among this group (1.7% following total abdominal hysterectomy; 95% CI 1.4–2.0%).

Conclusion The risk of ureteric injury within 1 year of hysterectomy varied by type of hysterectomy for benign and malignant conditions. The rates of injury have increased between 2001 and 2010.

Tweetable abstract Ten-year study shows ureteric injury rates have increased.

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Introduction

Ureteric injury is an uncommon but serious complication of gynaecological surgery.[1] Iatrogenic trauma is the commonest cause of ureteric injury. Recent systematic reviews have reported that gynaecological and colorectal surgery may be associated with ureteric injury in up to 6% of cases.[1–3]

It is often stated that the majority of iatrogenic ureteric injuries follow what was thought at the time to have been straightforward operations.[1] Presumed risk factors include those contributing to abnormal anatomy, abnormal tissue adhesion or major intraoperative haemorrhage.[1,3] Risks are higher in surgery for pelvic malignancies, and this may reflect one or more of these factors.

Injury to the ureter at hysterectomy most typically occurs in the lower third, the most common mechanisms being, in descending order of frequency, ligation, kinking by suture, transection/avulsion, partial transection, crush, and devascularization.[1] It is perhaps because of these mechanisms that the diagnosis of iatrogenic ureteric injury may be delayed, identified after the index procedure, in 65–80% of cases. The delay in diagnosis results in more common and serious complications including renal unit loss.[1]

The objectives of this study were to: (1) evaluate the risk of ureteric injury, including the later consequences of

injury, ureterovaginal fistula or ureteric stricture, associated with hysterectomy; (2) determine whether the risk of ureteric injury was affected by the type of hysterectomy or the indication for surgery; and (3) establish whether the rates of ureteric injury have changed over time.

Methods

We used data extracted from the Hospital Episode Statistics (HES) database.[4] HES holds records for patients admitted to English NHS hospitals, with each record containing data on patient demographics, hospital administrative information, diagnostic information using the International Classification of Diseases (ICD), 10th revision,[5] and operative procedures using the UK Office for Population Censuses and Surveys classification (OPCS), 4th revision.[6] Records relating to the same individual are linked using a unique patient identifier (HESID).

Patient selection

The study cohort contained adult women with selected benign and malignant indications who had an elective hysterectomy in the 10-year period between 1 January 2001 and 31 December 2010. The study was separated into women with benign conditions and women with malignant conditions. The group of benign conditions included endometriosis (ICD10 code: N80), uterine fibroids (D25), genital prolapse (N81), and menstrual disorders (N92–N94). The group of malignant conditions were limited to cervical carcinoma-*in-situ* (D06), cervical cancer (C53), uterine cancer (C54, C55) and ovarian cancer (C56). Women who had a primary diagnosis of endometriosis or menstrual disorders were restricted to age below 55 years, assuming that older women were likely to be postmenopausal, and therefore probable coding errors; no age restriction was applied to women in other diagnostic groups.

The study distinguished between four types of open procedures: total abdominal hysterectomy (TAH; OPCS code: Q07.4), subtotal abdominal (STH; Q07.5), vaginal (VH; Q08.9), and radical abdominal hysterectomy (RAH; Q07.1–07.3). We excluded radical hysterectomies coded to women with benign diagnoses, and combinations of conditions and procedures for which there were fewer than 500 cases. We also identified laparoscopic procedures as follows: total laparoscopic hysterectomy (TLH; Q56.8), laparoscopically-assisted vaginal hysterectomy (LAVH; Q08.9), laparoscopically assisted subtotal hysterectomy [LASH; code as for subtotal hysterectomy (Q07.5) with additional laparoscopic approach qualifier (Y50.8)].

Ureteric injuries within a year of hysterectomy were identified using codes for relevant diagnoses and related surgical treatment. A woman was identified as having an injury if the diagnostic fields of the index procedure episode, or a subsequent episode within 1 year of the index procedure contained: ureteric injury (S37.1), hydronephrosis with ureteric stricture (N13.1) or other urinary-genital tract fistula (N82.1). Ureteric injury was also identified if surgical treatments for ureteric fistula or obstruction were identified within the same timeframe. These included: insertion of stent; insertion of nephrostomy tube; ureteroscopic dilatation; removal of suture from ureter; ureteric repair; closure of ureteric fistula; and re-implantation of ureter (see Supporting Information Appendix S1 for OPCS codes).

Statistical analysis

Rates of ureteric injury were estimated for women by the indication and type of hysterectomy, and were expressed as the percentage of injuries within 1 year of hysterectomy. We also investigated whether the rate of injury varied over time by indication. Inspection of the time-series did not reveal linear/incremental changes but, for several conditions, the series were stable before increases after 2006. We therefore grouped events into 2001–2005 and 2006–2010 time periods. Finally, we derived overall injury rates associated with laparoscopic procedures. We calculated 95% confidence intervals (CI) for the estimated rates assuming that the number of events followed a Poisson distribution. The statistical significance of differences in injury rates between patient groups were tested using the chi-square test (tabulation of injury/non-injury and patient group).

Multivariable logistic regression was used to assess whether the risk of injury was associated with age, indication, and time. This analysis was restricted to women who underwent total abdominal hysterectomy and vaginal hysterectomy, due to the limited number of events for other procedures. All statistical tests were two-sided, and *P*-values lower than 0.05 were judged to be statistically significant. All analyses were performed using STATA SE version 11 (StataCorp LP, College Station, TX, USA). The formulation of this report has followed the STROBE Statement.[7]

Results

There were 380 351 hysterectomies for the selected conditions in English NHS hospitals between 1 January 2001 and 31 December 2010. Removing records that did not meet the inclusion criteria left 377 073 hysterectomies in the analysis (Supporting Information Figure S1). The number of procedures for benign and malignant conditions was 310 105 and 66 968, respectively. The characteristics of these women are shown in Supporting Information Table S1.

Number of hysterectomy procedures by indication

In the benign group, the number of hysterectomies per year demonstrated a decrease from 33 713 in 2001 to 30 480 in 2010 (test for trend, $P = 0.058$). The number of

hysterectomies varied by year across the various conditions (Supporting Information Figure S2). In women with prolapse, the number of hysterectomies increased from 8781 in 2001 to 10 687 in 2010 (test for trend, $P < 0.001$) and those with menstrual conditions showed a decrease from 10 300 in 2001 to 6710 in 2010 (test for trend, $P < 0.001$).

In the malignant group, the number of hysterectomies per year increased from 5963 in 2001 to 7778 in 2010 (test for trend, $P < 0.001$). The most notable differences were for uterine cancer, which increased from 3270 in 2001 to 4999 in 2010 (test for trend, $P < 0.001$) and for carcinoma-*in-situ*, which decreased from 525 in 2001 to 361 in 2010 (test for trend, $P = 0.004$) (Supporting Information Figure S2).

Rates of ureteric injuries by indication and procedure

Among the 377 073 women in the study, 1792 (0.5%) had a ureteric injury recorded within a year of their hysterectomy. The annual number of injuries increased from 90 in 2001 to 259 in 2010 (test for trend, $P < 0.001$).

Of the 1792 women identified as having ureteric injury, 66% (1184) were identified by surgical treatment codes only (i.e. they had no related diagnostic code in any treatment episode), 25% (447) were identified by diagnostic code only (i.e. they had no related surgical code in any treatment episode) and 9% (161) were identified by both. All ureteric injuries were recorded within 2 months of the index procedure; 42% of those identified by a diagnostic code and 38% of those identified by a surgical code were found within the same admission as the index procedure.

The rate of ureteric injury was higher from 2006 onwards for six of the eight conditions (Figure 1). The change was greatest for women with ovarian cancer, increasing from 1.06 to 3.86%. In the majority of subgroups, the change in the injury rate corresponded to an increase in the number of surgical treatments for injury.

Tables 1 and 2 give the rates of ureteric injury for the benign and malignant conditions for the various types of hysterectomy. For benign conditions, the 2006–2010 injury rates did not vary greatly by type of procedure in absolute terms, except for women with endometriosis, where the rate was as high as 1 in 100. The risk of injury associated with vaginal hysterectomy tended to be less than with other types of hysterectomy, being four times less than abdominal total procedures for prolapse (chi-square, $P < 0.001$) and about half the rate of abdominal hysterectomy for fibroids (chi-square, $P < 0.001$). For malignant conditions, the pattern was more varied (Table 2). The 2006–2010 injury rate was not associated with type of hysterectomy among women with cervical cancer. In contrast, there was

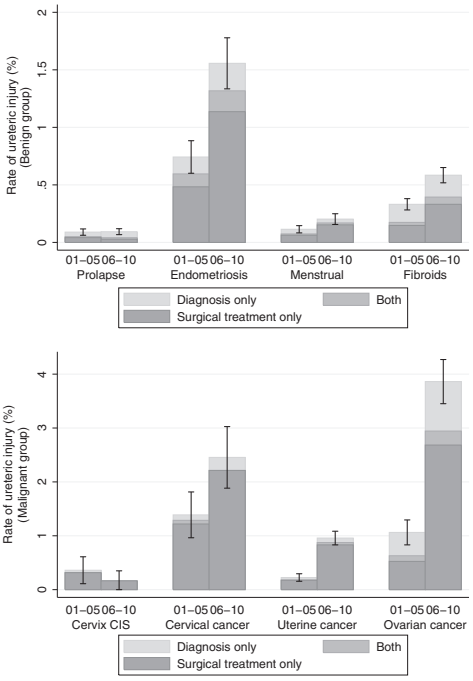

Figure 1. Rate of ureteric injury (95% CI) following hysterectomy for benign (above) and malignant conditions (below), for 2001–2005 and 2006–2010.

a two-fold difference between subtotal and total abdominal hysterectomy for women with ovarian cancer (chi-square, $P = 0.028$). The greatest variation by type of procedure exists for women with uterine cancer, ranging from 0.17 to 10.67%. All 2006–2010 injury rates had increased compared with those from 2001–2005, but the increase in the injury rate for abdominal radical hysterectomy stands out, changing from around 1 in 300 women to 1 in 10.

Effect of age and period of surgery

A feature of the patient populations analysed in this paper is the different age structures of women across the conditions. It was therefore possible that some of the variation in the rates across the conditions and procedures was due to the different age structures. Consequently, we performed a multivariable logistic regression to examine the patterns of ureteric injury rate in more detail.

The only groups with sufficient events for this analysis were total abdominal hysterectomies (benign and malignant conditions) and vaginal (benign only). For total abdominal

Table 1. Rate of ureteric injury by benign conditions and type of procedure, for 2001–2005 and 2006–2010

Conditions	Type of hysterectomy	2001–2005			2006–2010		
		No. of procedures	No. of ureteric injuries	Rate of ureteric injuries % (95% CI)	No. of procedures	No. of ureteric injuries	Rate of ureteric injuries % (95% CI)
Prolapse	Abdominal total	1374	3	0.22 (0.05, 0.64)	1142	4	0.35 (0.10, 0.90)
	Vaginal	44 315	39	0.09 (0.06, 0.12)	52 432	46	0.09 (0.06, 0.12)
Endometriosis	Abdominal subtotal	1 265	14	1.11 (0.61, 1.86)	1325	21	1.58 (0.98, 2.42)
	Abdominal total	11 187	81	0.72 (0.58, 0.90)	8899	150	1.69 (1.43, 1.98)
	Vaginal	1823	11	0.60 (0.30, 1.08)	1918	18	0.94 (0.56, 1.48)
Menstrual	Abdominal subtotal	3294	4	0.12 (0.03, 0.31)	4186	4	0.10 (0.03, 0.24)
	Abdominal total	31 325	41	0.13 (0.09, 0.18)	22 861	49	0.21 (0.16, 0.28)
	Vaginal	9987	7	0.07 (0.03, 0.14)	8963	20	0.22 (0.14, 0.34)
Fibroids	Abdominal subtotal	6020	24	0.40 (0.26, 0.59)	7573	41	0.54 (0.39, 0.73)
	Abdominal total	41 741	149	0.36 (0.30, 0.42)	37 734	242	0.64 (0.56, 0.73)
	Vaginal	5057	2	0.04 (0.00, 0.14)	5684	16	0.28 (0.16, 0.46)

Table 2. Rate of ureteric injury by malignant conditions and type of procedure, for 2001–2005 and 2006–2010

Conditions	Type of hysterectomy	2001–2005			2006–2010		
		No. of procedures	No. of ureteric injuries	Rate of ureteric injuries % (95% CI)	No. of procedures	No. of ureteric injuries	Rate of ureteric injuries % (95% CI)
Cervical cancer-*in-situ*	Abdominal total	1689	7	0.41 (0.17, 0.85)	1282	3	0.23 (0.05, 0.68)
	Vaginal	531	1	0.19 (0.00, 1.05)	550	0	0.00 (0.00, 0.67)
Cervical cancer	Abdominal total	1458	20	1.37 (0.84, 2.11)	1480	36	2.43 (1.70, 3.37)
	Abdominal radical	1495	22	1.47 (0.92, 2.23)	1412	35	2.48 (1.73, 3.45)
Uterine cancer	Abdominal total	16 355	38	0.23 (0.16, 0.32)	19 548	183	0.94 (0.81, 1.08)
	Abdominal radical	309	1	0.32 (0.01, 1.80)	300	32	10.67 (7.30, 15.06)
	Vaginal	1092	1	0.09 (0.00, 0.51)	3013	5	0.17 (0.05, 0.39)
Ovarian cancer	Abdominal subtotal	656	8	1.22 (0.53, 2.40)	463	9	1.94 (0.89, 3.69)
	Abdominal total	6967	73	1.05 (0.82, 1.32)	8368	332	3.97 (3.55, 4.42)

hysterectomies in the benign group, the regression model did not find an association between risk of injury and age, and confirmed the different relative risks by condition and over time (see Table 3). We further examined whether the relative risks across the benign conditions had changed between 2001–2005 and 2006–2010 by introducing an interaction term for condition and year, but we found no evidence that the relative risks had changed. For the malignant conditions, there was a weak relation between age and risk, being highest among women under 40 years. As before, we explored whether the relative risks across the conditions changed over time, and again found no significant interaction between condition and time.

For vaginal hysterectomies in the benign group, the regression model revealed a potential association between risk of injury and age, but this had a minimal effect on the adjusted odd ratios describing the risk of injury by condition and time (Table 3). As before, we found no evidence that the relative risks across the conditions changed over time (interaction term was non-significant).

Laparoscopic hysterectomies

Of 310 105 hysterectomies in the benign group, 4.7% (14 692) were laparoscopic. Women undergoing laparoscopic hysterectomies had a rate of ureteric injury of 0.6% (94/14 692), which was higher than for other types

Table 3. Association between ureteric injury and condition, age and period of surgery, for total abdominal and vaginal procedures

	n	Abdominal total		*n*	Vaginal	
		Ureteric injury OR (95% CI)	*P*-value		Ureteric injury OR (95% CI)	*P*-value
Benign condition						
Prolapse	99 263	1.48 (0.67 3.26)		96 747	0.75 (0.43, 1.31)	
Endometriosis	26 417	6.89 (5.40 8.80)	<0.001	3741	5.46 (3.23, 9.24)	<0.001
Menstrual	80 616	1		18 950	1	
Fibroids	103 809	2.84 (2.24 3.60)		10 741	1.36 (0.73, 2.51)	
Age group (years)						
Under 40	53 136	1		14 088	1	
40–49	136 413	0.91 (0.75 1.10)	0.534	30 650	0.83 (0.53, 1.30)	0.004
50–59	57 249	1.01 (0.79 1.30)		28 054	0.35 (0.17, 0.71)	
60–69	35 562	1.16 (0.72 1.87)		31 481	0.58 (0.30, 1.12)	
70 and above	27 745	1.24 (0.64 2.40)		25 906	1.06 (0.57, 1.96)	
Year of surgery						
2001–2005	157 388	1		61 182	1	
2006–2010	152 717	1.95 (1.67 2.26)	<0.001	68 997	1.56 (1.13, 2.16)	0.007
Malignant condition						
Cervical cancer-*in-situ*	4052	1				
Cervical cancer	5845	5.11 (2.60, 10.05)	<0.001			
Uterine cancer	40 617	1.72 (0.89, 3.29)				
Ovarian cancer	16 454	7.60 (4.01, 14.41)				
Age group (years)						
Under 40	4975	1			Insufficient events	
40–49	7577	0.59 (0.42, 0.84)	0.027			
50–59	15 316	0.66 (0.47, 0.91)				
60–69	19 352	0.67 (0.48, 0.92)				
70 and above	19 748	0.75 (0.54, 1.03)				
Year of surgery						
2001–2005	30 552	1				
2006–2010	36 416	3.49 (2.90, 4.22)	<0.001			

of hysterectomy [0.3% (889/295 413), laparascopic versus open procedures, chi-square $P < 0.001$]. Among the various indications, the highest rate was observed among women who had endometriosis, 2.2% (50/2363) for laparoscopic procedures and 1.0% (245/24 054) for open procedures.

Of the 66 968 hysterectomies in the malignant group, 8.0% (5321) were laparoscopic. Women who had laparoscopic hysterectomies had a rate of ureteric injury of 0.2% (8/5321), which was lower than the rate for open procedures [1.3% (798/61 647), laparascopic versus open procedures, chi-square $P < 0.001$). There were insufficient events for further stratification by condition.

Discussion

Main findings

This 10-year study of elective hysterectomies in English NHS hospitals examined the rates of ureteric injury within 1 year of the procedure among women with selected conditions. The overall rate of injury is low but has more than doubled over time, from 0.29% in 2001–2005 to 0.66% in 2006–2010. An increase in the rates of injury was observed in six of the eight selected conditions, and was associated with a greater number of women having a surgical treatment for ureteric injury. Only two-fifths of ureteric injuries identified in this study were recorded during the admission of the index procedure.

In the group of benign conditions, the injury rate was highest in women with endometriosis who had abdominal hysterectomy (total or subtotal), affecting 1 in 60 during 2006–2010. The rate was lowest in women with prolapse who had a vaginal hysterectomy, affecting 1 in 1140 in 2006–2010. The risk of ureteric injury was typically greater among women with a malignant condition, being greatest among those with ovarian or uterine cancer. The most unexpected finding was an increase in the injury rate for abdominal radical hysterectomy in women with uterine cancer, changing from around 1 in 300 women during 2001–2005 to 1 in 10 during 2006–2010.

Strengths and limitations

This study is the first from England to report rates of ureteric injury using a large national database. Ureteric injury is an uncommon condition, for which a large sample is required to capture the events; one of the main strengths of this study is therefore its sample size. By using the HES database, we were able to identify a sufficient number of ureteric injuries and extend the analysis to provide rates of ureteric injury by condition and type of hysterectomy.

A limitation of using routinely collected patient information like HES is the potential for coding omissions and inaccuracies. Although the quality of HES coding has been widely accepted,[8] it has been shown to vary by NHS trusts.[9] In our study, for example, the coding recorded by hospitals in the North West region indicated a notable increase in the number of ureteric injuries for uterine cancer and ovarian cancer in the second half of the study (2006–2010) (regional results not shown). In a sensitivity analysis, we excluded the North West region to assess how this altered our results. The rate (95% CI) for uterine cancer fell to 0.46 (0.37–0.56) from 0.96 (0.84–1.10) and the rate for ovarian cancer fell to 2.46 (2.14–2.82) from 3.86 (3.46–4.29). Other results did not change substantially. The study did not have the ability to explore the reasons for the change in the North West region, but it is important to note that the number of cases remained small.

We had expected ureteric injuries to be identified with both diagnostic and treatment codes. However, only 9% of records had both codes present. Surgical codes were identified in 75% of women, the proportion increasing by approximately 10% in the latter years of the study.

There is a possibility that our results are affected by 'susceptibility bias'. Endometriosis or gynaecological cancers give an increased risk of ureteric obstruction; surgery undertaken for these conditions, which results in ureteric injury, might therefore be erroneously assigned causality. However, the risk of bias is likely to be small because the majority (60%) of ureteric injuries were not recorded concurrently with the hysterectomy.

Finally, while we presented ureteric injury rates for laparoscopic hysterectomies, we caution against comparing these with the rates for open procedures. It is possible for coders to distinguish between open and laparoscopic hysterectomies in HES by entering allowing an additional OPCS code for 'laparoscopic approach' alongside the codes for hysterectomy. However, these codes have been shown to be under-reported,[10] and we suspect that a minority of patients in the open procedure groups will have had laparoscopic procedures.

Interpretation

The reduction in the use of hysterectomy for the treatment of heavy menstrual bleeding (HMB) has previously been reported,[11,12] and our data show a continuance of this trend. In contrast, an increasing trend in surgery for pelvic organ prolapse (POP) has also been highlighted,[13] and we have shown that this is associated with an increase in the use of hysterectomy for POP. Although there appears to have been an increase in demand for uterine-preserving surgery for prolapse in some areas, the lack of data on long-term outcomes and need for subsequent hysterectomy[14,15] may have limited its application to date. Khan et al.[16] have recently reported a reduced use of hysterectomy at prolapse surgery among Medicare beneficiaries in the USA, although on-going research may better define the place of these procedures in future.[17] The risk of ureteric injury associated with vaginal hysterectomy for POP, however, seems to be low, and was unchanging over time during our study period. The risks associated with hysterectomy for other benign indications, most notably endometriosis, are significantly higher than for HMB and POP; despite, or perhaps because of, decreasing application, the risk of ureteric injury in this group has doubled over our study period. This is in contrast to our earlier findings in relation to lower urinary tract fistula following abdominal hysterectomy, where we found no difference in risk for different benign indications.[18]

The trend seen in relation to hysterectomy for endometriosis during the study period (23% reduction in procedures; doubling in risk of ureteric injury) is similar to that seen in cervical cancer (16% reduction in procedures, near doubling in risk). This perhaps reflects the surgical complexity of these cases and argues in favour of centralised surgical management of advanced endometriosis by a multidisciplinary team.

The finding of an increasing rate of ureteric injury at hysterectomy in malignant conditions again contrasts with earlier findings in relation to vesicovaginal fistula, where we found no change in risk over time.[18] The prevalence of uterine cancer has been increasing over the last four decades, most notably since the 1990s;[19] our data confirm a continuing upward trend in the number of hysterectomies undertaken in England for this diagnosis. While the prevalence of ovarian cancer may be decreasing in some age groups, as a result of oral contraceptive use,[20] hysterectomy for the treatment of the condition also continues to increase in England. For both uterine and ovarian cancers, the increase in use of hysterectomy during our study period has happened alongside an increase in the risk of ureteric injury. There are, of course, issues of disease staging that ICD-10 diagnosis codes do not include, and the extent of surgery may not be fully captured by the OPCS codes.

Changes in management, e.g. the use of pelvic or para-aortic lymph node sampling/dissection in uterine cancer or stripping of peritoneal disease in ovarian cancer, which may carry an increased risk of complications, may therefore easily be overlooked within HES data. Nevertheless, the increasingly high rates of ureteric injury seen within a year of hysterectomy for uterine and ovarian cancers (four-fold increase between 2001–2005 and 2006–2010) do demand re-appraisal by those providing or commissioning cancer services.

As in our study, an analysis of severe complications following hysterectomy in the VALUE study (n = 37 512) found ureteric damage to be associated with the presence of endometriosis.[21] The Cochrane review of surgical approaches to hysterectomy for benign indications found no difference in the rate of fistula following hysterectomy by abdominal, vaginal, and laparoscopic routes from 34 included studies with 4495 women. When bladder and ureter injuries were pooled under a single category 'urinary tract injury' (n = 2090), a significant increase in urinary tract injury was detected for laparoscopic compared with both abdominal (OR 2.4, 95% CI 1.2–4.8) and vaginal routes (OR 3.7, 95% CI 1.1–12.2).[22] Although our data are consistent with these findings, the limitations of coding for laparoscopic procedures in HES referred to earlier, means that we cannot confidently confirm this trend.

Although all ureteric injuries identified in the study were recorded within 2 months of the index procedure, approximately 60% of injuries were not recorded during the admission of the index procedure but at a later admission, i.e. they might be looked on as having a delayed diagnosis. This is in keeping with recent reviews of iatrogenic injury to the urinary tract and urogenital fistula,[1–3] and indicates a need for awareness of risk factors prior to operation, meticulous surgical technique, alertness to symptoms and signs postoperatively, and early recourse to further imaging investigation where there is any suspicion of ureteric injury.

Conclusion

Using a large national database, this study has identified the number of ureteric injuries found within 1 year of elective hysterectomy, and showed these to vary by condition, indication, and procedure. The overall rate of ureteric injury was 0.66% in recent years (2006–2010), an increase from 0.29% in the 5 years previously. This could be attributable in part to improvements in coding of injuries in later years, and, as the events are rare, small increases in the number of ureteric injuries can significantly increase the observed rate. Further research is also needed to look at the patient populations now being considered for surgery in order to understand more definitively the causal pathways linking surgery and outcomes.

Nevertheless, although ureteric injury remains an uncommon complication of hysterectomy, its potential significance is such that any adverse trend must be taken seriously. The demonstration of increasing surgical morbidity within the NHS, and the particular changes seen in association with hysterectomy in advanced endometriosis, as well as uterine and ovarian cancers, are issues of which all involved in the procurement and provision of service and training should be aware.

Disclosure of interests

Full disclosure of interests available to view online as supporting information.

Contribution to authorship

Study design PH and DC. Data extraction and analysis AK, PH and DC. Writing of the paper AK, PH and DC. All authors have approved the final version of the manuscript.

Details of ethics approval

The study is exempt from UK NREC approval because it involved analysis of an existing data set of anonymised data for service evaluation. Approvals for the use of HES data were obtained as part of the standard Hospitals Episode Statistics approval process.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Flow chart of patients included in this study and the number of ureteric injuries identified.

Figure S2. Number of hysterectomy procedures for benign (above) and malignant conditions (below) between 2001 and 2010.

Table S1. Characteristics of women undergoing hysterectomy for benign and malignant conditions between 2001 and 2010.

Appendix S1. Diagnostic (ICD-10) and operative (OPCS-4) codes associated with ureteric injury. ■

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Table S1. Characteristics of women undergoing hysterectomy for benign and malignant conditions between 2001 and 2010

	Benign conditions (n=310,105)			
	Prolapse N81 (n=99,263)	Endometriosis N80 (n=26,417)	Menstrual N92 to N94 (n=80,616)	Fibroids D25 (n=103,809)
Age (years), mean (sd)	61.2 (11.8)	41.3 (5.8)	41.3 (5.7)	47.4 (7.5)
Age group, % (n)				
under 40	4.1 (4,095)	36.5 (9,654)	36.3 (29,247)	9.8 (10,140)
40 to 49	13.2 (13,072)	56.3 (14,876)	57.0 (45,968)	60.2 (62,497)
50 to 59	25.5 (25,313)	7.1 (1,887)	6.7 (5,401)	23.7 (24,648)
60 to 69	31.3 (31,073)	-	-	4.3 (4,489)
70 and above	25.9 (25,710)	-	-	2.0 (2,035)
Type of hysterectomy, % (n)				
Abdominal subtotal	-	9.8 (2,590)	9.3 (7,480)	13.1 (13,593)
Abdominal total	2.5 (2,516)	76.0 (20,086)	67.2 (54,186)	76.6 (79,475)
Vaginal	97.5 (96,747)	14.2 (3,741)	23.5 (18,950)	10.4 (10,741)
	Malignant conditions (n=66,968)			
	Cervical cancer in situ D06 (n=4,052)	Cervical cancer C53 (n=5,845)	Uterine cancer C54, C55 (n=40,617)	Ovarian cancer C56 (16,454)
Age (years), mean (sd)	46.2 (11.4)	44.8 (13.1)	65.7 (10.9)	60.7 (12.5)
Age group (years), % (n)				
under 40	32.7 (1,326)	41.1 (2,402)	1.2 (468)	4.7 (779)
40 to 49	33.9 (1,372)	29.0 (1,695)	5.0 (2,029)	15.1 (2,481)
50 to 59	18.6 (753)	15.1 (884)	23.1 (9,379)	26.1 (4,300)
60 to 69	11.6 (468)	8.9 (519)	33.8 (13,714)	28.3 (4,651)
70 and above	3.3 (133)	5.9 (345)	37.0 (15,027)	25.8 (4,243)
Type of hysterectomy, % (n)				
Abdominal subtotal	-	-	-	6.8 (1,119)
Abdominal total	73.3 (2,971)	50.3 (2,938)	88.4 (35,903)	93.2 (15,335)
Abdominal radical	-	49.7 (2,907)	1.5 (609)	-
Vaginal	26.7 (1,081)	-	10.1 (4,105)	-

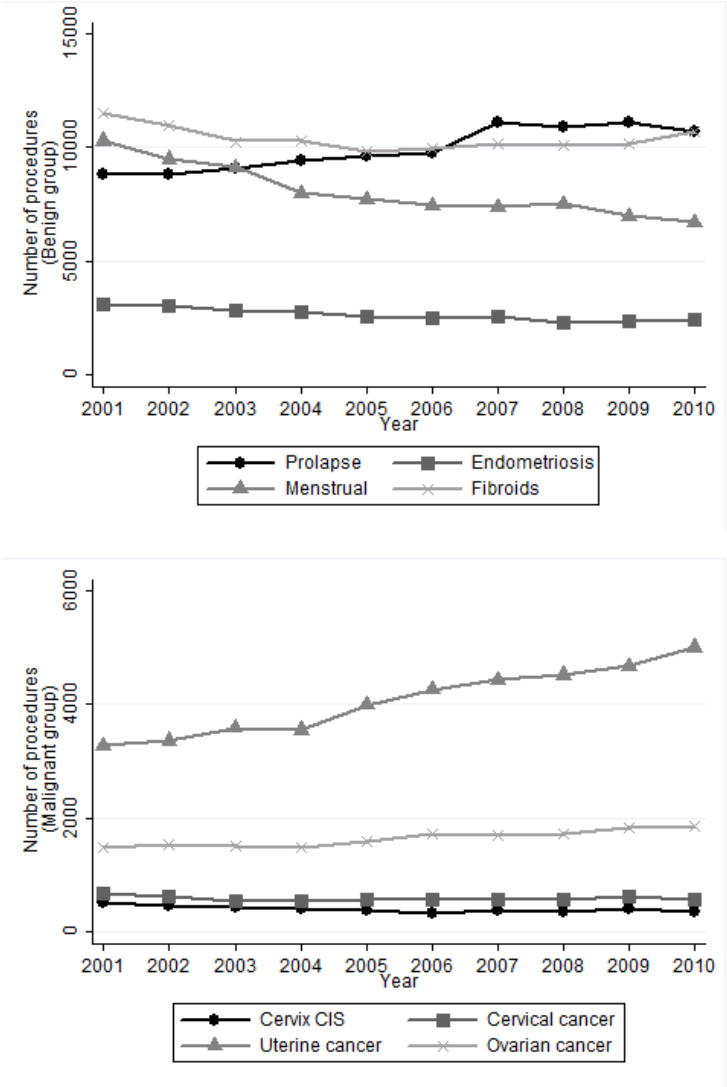

Figure S2. Number of hysterectomy procedures for benign (above) and malignant conditions (below) between 2001 and 2010.

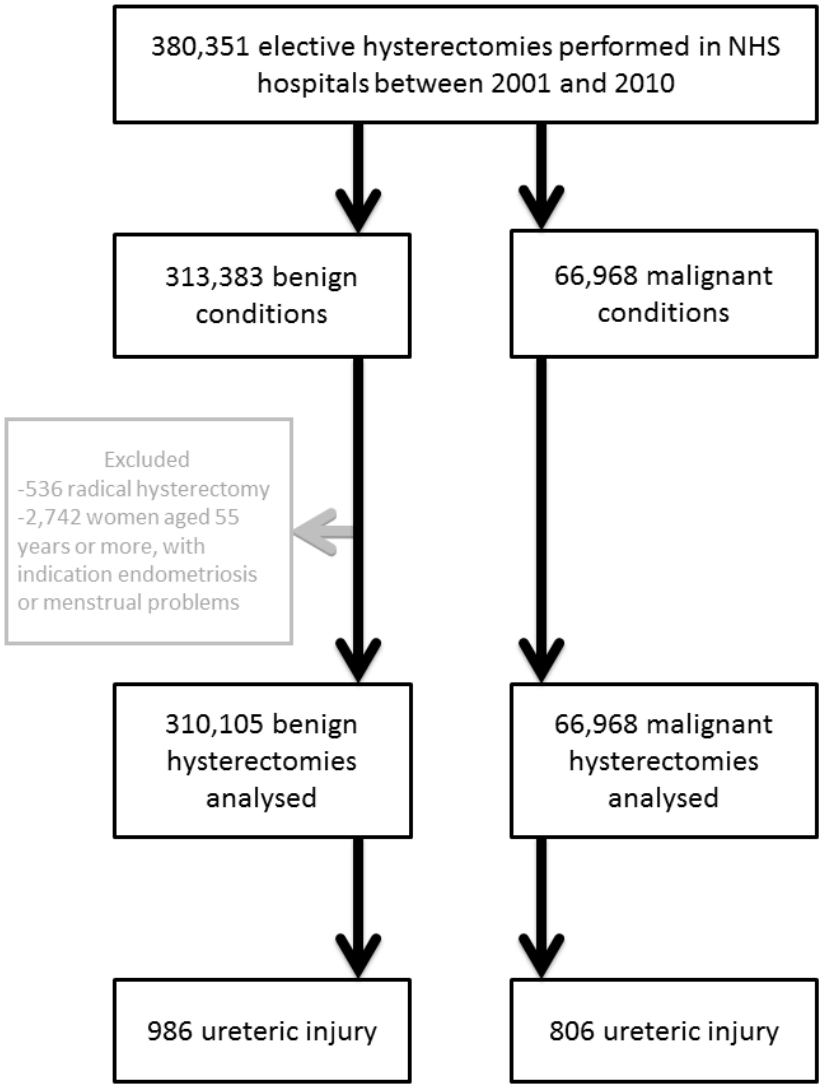

Figure S1. Flow chart of patients included in this study and the number of ureteric injuries identified.

Appendix S1. Diagnostic (ICD-10) and operative (OPCS-4) codes associated with ureteric injury

Ureteric injury ICD-10 codes

ureteric injury (S37.1)

hydronephrosis with ureteric stricture (N13.1)

other urinary-genital tract fistula (N82.1).

Surgical treatment for ureteric fistula or obstruction OPCS codes

ureteroscopic insertion of stent (M27.4, M27.8 + Y02.2)

endoscopic insertion of stent (M29.2)

percutaneous insertion of stent (M13.8 + Y02.2, M33.1, M33.2)

percutaneous insertion of nephrostomy tube (M13.6)

ureteroscopic dilatation (M27.8, M29.4)

removal of suture from ureter (M22.2)

ureteric repair (M22.1)

closure of ureteric fistula (M22.3, M22.8, M22.9)

re-implantation of ureter (M20.1 to M21.9)

Paper 8: Retrospective cohort study on patterns of care and outcomes of surgical treatment for lower urinary–genital tract fistula among English National Health Service hospitals between 2000 and 2009.

BJUI
BJU INTERNATIONAL

Retrospective cohort study on patterns of care and outcomes of surgical treatment for lower urinary–genital tract fistula among English National Health Service hospitals between 2000 and 2009

David Cromwell and Paul Hilton*

*Office of Research and Clinical Audit, Royal College of Obstetricians & Gynaecologists and London School of Hygiene and Tropical Medicine, London, UK, and *Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK*

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Study Type – Therapy (retrospective cohort)
Level of Evidence 3a

What's known on the subject? and What does the study add?
Many case series of lower urinary tract fistula have been reported, usually reporting the results from individual surgeons using their preferred techniques. Definitions of cure and the case-mix or complexity of reported cases vary widely, and a wide range of outcome results are reported in the literature, with primary closure rates between 53% and 95%.

Using the Hospital Episode Statistics database we have demonstrated for the first time the pattern of care provided nationally. A large number of surgeons (490) are currently involved in providing this care in a large number of units (138), with individual workloads varying between 1 and 90 procedures in 10 years; only three undertook >3 operations per year. We have demonstrated an overall operative failure rate (re-operation rate) of 12%, and a high rate of urinary diversion (24%). Cure rates varied between 50 and 100% and were higher in units undertaking >3 operations per year.

OBJECTIVES

- To examine patterns of care among women with urogenital fistula treated in the English National Health Service (NHS) between 2000 and 2009.
- To assess whether failure of repair was associated with hospital or surgeon workload.

PATIENTS AND METHODS

- We conducted a retrospective cohort study using data from Hospital Episode Statistics on women undergoing vesicovaginal or urethrovaginal fistula repair between January 2000 and December 2009 in English NHS hospitals.
- The main outcome measure was the number of fistula repairs and the incidence of re-repair; re-repair rates were stratified by age, NHS trust and consultant team volume.

RESULTS

- Between 2000 and 2009, 1194 women underwent surgical repair ($n = 905$) or ileal conduit ($n = 289$) for urogenital fistula under the care of 490 consultant teams.
- A total of 281 teams performed only a single index procedure, and only three consultant teams performed a mean of >3 per year.
- The rate of unsuccessful repair was 11.9% (108/905).
- The rate of re-operation at NHS trusts who performed over 30 procedures over the 10-year study period was 7.4% compared with 13.2% at those undertaking fewer ($P = 0.02$).
- A similar difference in re-operations between consultant teams performing > or <30 procedures did not reach significance (8.4% v 12.7%, $P = 0.13$).

CONCLUSIONS

- One in nine women required re-operation after surgical repair of a urogenital fistula.
- Our results lend weight to the argument for a 'minimum workload' for fistula management; given the number of fistulae occurring in England currently, this would best be provided by a network of supra-regional centres.

KEYWORDS

national health programmes, treatment outcome, urinary fistula, vesicovaginal fistula, workload

INTRODUCTION

Over the last decade there has been increasing awareness of the global public health issues of obstetric vesicovaginal fistula (VF), with many professional, charitable and non-governmental organizations becoming increasingly concerned about its management and prevention. Training programmes have been developed [1], and through the WHO's guiding principles for management and

programme development [2], increasing numbers of treatment centres have been established [3]. Urogenital fistula in the developed world is usually of non-obstetric cause, and is numerically a much smaller problem. Nonetheless, it can be devastating to those women affected and, as it is commonly iatrogenic, is a major cause of complaint or medico-legal claim [4]. It was proposed in debate at a joint meeting of the Royal College of Obstetricians and Gynaecologists (RCOG), and the BAUS in 1996 that only two or three centres for urogenital fistula repair were required in the UK [5]. Despite the agreement of both professional groups [6], such a pattern of care has never been formally established.

Evidence of the outcomes of fistula repair surgery in developed countries typically describe the results achieved by individual surgeons using preferred procedures. They tend to be small in sample size, and this limits their generalizability and their application to service planning, particularly in relation to understanding any volume–outcome effect. In the present study, we aimed to describe patterns of surgical repair among women with urogenital fistula treated in English NHS trusts between 2000 and 2009 using a national dataset. We also examined whether the rate of repeat surgical repair was associated with volume of activity within NHS trusts and with consultant team.

PATIENTS AND METHODS

DATA SOURCE

We used data from the Hospital Episode Statistics (HES) database, which contains records of all patient admissions to NHS hospitals in England. Its core fields contain patient demographics, and hospital administrative information. Diagnostic information is coded using the International Classification of Diseases (ICD), 10th revision [7], and operating procedures are described using the UK Office for Population Censuses and Surveys classification (OPCS), 4th revision [8].

DESIGN

The study included all women aged ≥18 years who underwent surgery for a urogenital fistula in an English NHS hospital between 1 January 2000 and 31 December 2009. Women were selected if they had an ICD-10 code N82.0 (VVF) or N82.1 (other urinary-genital tract fistula) in a diagnostic field and an OPCS-4 procedure code for repair of VVF (P25.1), repair of urethrovaginal fistula (UVF) (P25.2) or ileal conduit/urinary diversion (M19.1). We only included procedures that were performed during or after the first episode containing a diagnosis of urogenital fistula. For 91% of women, surgery was within 6 months of the first fistula diagnosis. Women were allocated to the NHS trust that performed the index procedure, and to account for mergers among NHS acute trusts after January 2000, we took the NHS trusts that existed in December 2009 as our reference. The consultant team was identified from a pseudonymized consultant code in the HES database.

Hospital admissions in the year before the index procedure were examined to identify historical patterns of care that could be possible causative factors. We identified previous hysterectomy procedures (OPCS codes: Q07 and Q08) and caesarean sections (R17, R18 and R25.1). We also identified three broad groups of conditions: malignant gynaecological (ICD10: C52-C56, D04), benign gynaecological (D25, N80, N81, N92-N94), and malignant bladder/bowel (C18-C20, C67).

A woman was defined as having a repeat repair, and therefore failure of an initial repair, if a subsequent episode of care contained in any procedure field one of the three OPCS codes (P25.1, P25.2 or M19.1) after an index procedure of fistula repair (P25.1, P25.2).

STATISTICAL METHODS

The unadjusted incidence of repeat repair was expressed as the percentage of women who had further repair surgery after an index procedure of fistula repair. Rates were stratified by age, NHS trust volume and consultant team volume. We estimated the 95% CIs, assuming that the number of events followed a binomial distribution. The chi-squared test was used to assess the statistical significance of differences between categorical groups. A trend across ordered categories was tested using Cuzick's extension of the Wilcoxon rank-sum test [9]. All *P* values were two-sided, and a *P* value <0.05 was considered to indicate statistical significance.

Funnel plots were used to examine variation in the rates of repeat repair between NHS trusts and between consultant teams [10]. The plots contain two funnel limits. The inner and outer funnels would be expected to contain 95 or 99.8% of providers, respectively, if the variation from the rate for England was only attributable to random fluctuations. All analyses were performed using STATA version 11 (StataCorp LP, Texas, USA). This report was prepared with reference to the STROBE Statement [11].

RESULTS

Between 2000 and 2009, there were 1194 women who had a surgical repair or an ileal conduit constructed for a urogenital fistula. This corresponds to approximately 120 procedures per year, although there has been a slight increase over time (Fig. 1). Of the index procedures, 76% (905/1194) were fistula repair operations (P25.1, P25.2), while 24% (289/1194) were ileal conduit formation.

The mean (SD) age of the women undergoing surgical repair was 52.4 (15.6) years. There were 177 women (15%) with a malignant gynaecological condition, while a further 328 women (27%) had a benign gynaecological condition. There were 171 women (14%) with a diagnosis of bowel or bladder cancer, but there were no frequently occurring conditions among the remaining 518 women (43%). A previous diagnosis of a malignant condition was much more common among patients undergoing urinary diversion than a fistula repair procedure (51.9% v 9.6%; chi-squared test, $P < 0.001$). A total of 426 women (36%) had undergone hysterectomy in the previous year, and 33 women (3%) had undergone a caesarean section.

CONSULTANT AND HOSPITAL VOLUME

The index procedures were allocated to 490 consultant teams, of which 127 (26%) were in the main specialty of gynaecology, and 306 (62%) were in urology. In terms of the volume of women treated by individual consultant teams, 281 teams performed only one index procedure. Only 10 teams performed ≥10 index procedures during the 10-year study period, and only three had

FIG. 1. Number of index surgical repair procedures over time for women diagnosed with a urogenital fistula in English NHS hospitals between 2000 and 2009.

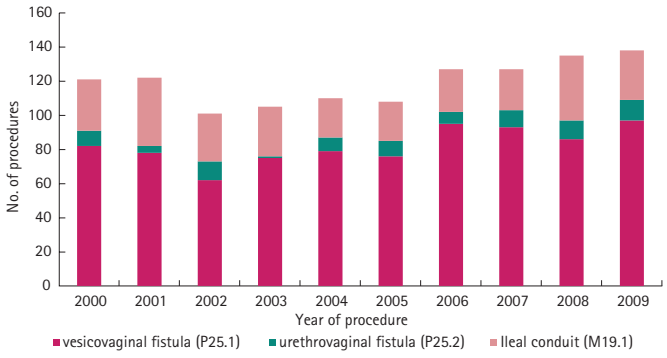


TABLE 1 Rate of repeat repair among index procedures performed between 2000 and 2009 in the English NHS, stratified by selected risk factors

Risk factor	Index Procedures, *n* (%)	Repeat repairs, *n*	Rate % (95% CI)	*P* for trend
Age at surgery, years				
<40	250 (28)	33	13.2 (9.3, 18.0)	0.24
40–49	300 (33)	36	12.0 (8.5, 16.2)	
50–59	149 (16)	19	12.8 (7.9, 20.8)	
60–69	97 (11)	11	11.3 (5.8, 19.4)	
≥70	109 (12)	9	8.3 (3.8, 15.1)	
NHS trust volume				
1–5	202 (22)	27	13.4 (9.0, 18.8)	0.10
6–10	318 (35)	40	12.6 (9.1, 16.7)	
11–30	183 (20)	26	14.2 (9.5, 18.7)	
Over 30	202 (22)	15	7.4 (4.2, 12.0)	
Consultant volume				
1–3	435 (48)	57	13.1 (10.1, 16.6)	0.15
4–6	182 (20)	22	12.1 (7.7, 17.7)	
7–30	133 (15)	16	12.0 (7.0, 17.6)	
>30	155 (17)	13	8.4 (4.5, 13.9)	

carried out a mean of >3 procedures per year. A similar pattern was observed among the repair procedures (P25.1, P25.2; i.e. excluding urinary diversions). Among the 376 consultant teams that performed repair surgery, only five teams performed ≥10 procedures. The number of index procedures performed within each NHS trust was also low. Among the 129 NHS trusts that performed surgery for urogenital fistula, only 20 trusts undertook ≥10 index procedures during the 10-year study period.

REPEAT SURGICAL REPAIRS

There were 108 women (11.9%) among the 905 women undergoing surgical fistula repair who required a repeat operation; their progress through re-repair or diversion procedures is shown in Fig. 2. The 'cure' rate from one operation was 88.1% (797/905), from a re-operation was 81.9% (77/94), and from a second re-operation was 68.9% (11/16). If the need for secondary urinary diversion is considered to indicate failure of a previous repair, these figures become 88.1, 71.3 (77/108) and 64.7% (11/17), respectively. The relative risk of needing a further procedure after a second repair compared with after a first operation was 1.52 (95% CI 0.95–2.41; $P = 0.086$). The annual rate of re-operation fluctuated between 4 and 20% per year (Fig. 3) but there was no significant evidence for the rate of repeat surgery having changed over time (test for trend, $P = 0.17$).

Table 1 describes the strength of association between the rate of repeat repair and other factors. There was no association between rate of repeat repair and age at surgery, and there was no linear relationship between the rate of repeat repair and volume at NHS trusts, nor between the volume of activity and outcome among the consultant teams; however, there was a noticeable step change between NHS trusts who performed >30 procedures over the 10-year study period and those that did not (7.4 v 13.2%, $P = 0.02$). A similar step change was apparent among the consultant teams but the difference was not significant (8.4 vs 12.7%, $P = 0.13$). There were 10 trusts and seven consultant teams with re-operation rates over twice the national average. However, the variation in the rates of repeat repair across NHS trusts (Fig. 4) and consultant teams (Fig. 5) was consistent with that expected from random variation alone. The rate of repeat repair was not significantly different between main specialities of treatment (chi-squared, $P = 0.24$).

DISCUSSION

We have described the patterns of care and outcomes for women undergoing surgical treatment of urogenital fistula in the English NHS over the last decade. Approximately 120 operations per year were undertaken, of which a quarter were urinary diversions. A large number of surgeons have contributed to this surgical workload, although the majority performed only one index procedure in 10 years. Just three consultants performed a mean of >2 index procedures per year during the study period. The rate of unsuccessful repair was lower among NHS trusts that had a surgical workload of ≥3 procedures per year. It was not possible to comment on the influence of aetiology on outcome, since this cannot be defined from the HES dataset for the majority of cases. In other studies, we have examined outcomes

FIG. 2. Progress of patients through operation and re-operation during the study period.

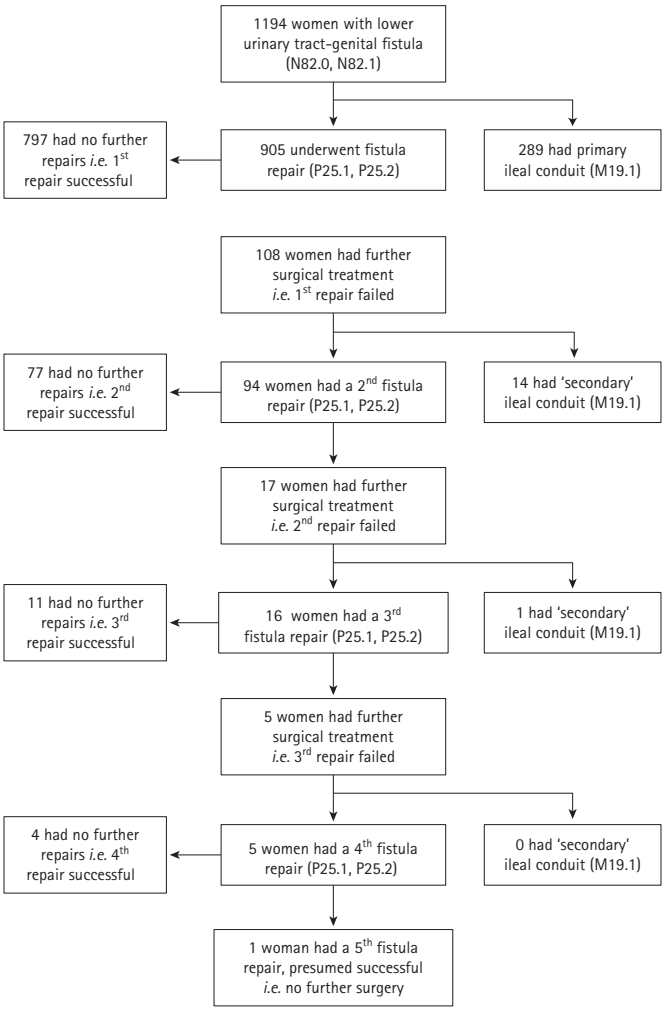
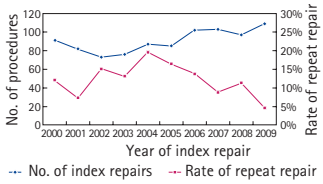


FIG. 3. Annual number of surgical fistula repairs (OPCS: P25.1, P25.2) between 2000 and 2009, together with the proportion of women who had another repair procedure.



in a single centre by aetiology [12], and have examined the risk associated with hysterectomy specifically on a national basis [13].

This is the largest cohort study of urogenital fistula of all aetiologies reported using data from the developed world [14]. But, as with any study using routine data, there are potential limitations that arise from coding inaccuracies and completeness. The quality of the clinical coding in HES has been shown to vary between NHS trusts [15], although the overall quality is considered to be high, particularly in relation to surgical procedures [16]. We restricted our patient sample to records with the expected combinations of diagnosis and procedure to reduce the risk of including poor quality records. More detailed quality assurance of the data is difficult, although the number of procedures identified for one of the larger units included within this study lies within 6% of their recently published data [12].

The overall cure rate after first operations found in the present study (defined as patients not requiring further surgery or diversion during the study period) was 88%. Definitions of cure and the case-mix or complexity of reported cases vary widely between studies, and a wide range of outcome results are reported in the literature, with primary closure rates between 53 and 95% [14].

The surgical volume required to achieve or maintain competence for any particular operation is inadequately defined. The volume–outcome relationship has been considered in several clinical areas, including cardiology, gastroenterology, orthopaedics, ophthalmology and breast cancer surgery [17]. It is little studied in relation to continence surgery, and not at all in relation to fistula surgery.

Several studies have examined the learning curve for the tension-free vaginal tape (TVT) procedure and found that the complication rate was relatively higher during the surgeon's early cases [18–21]. A Finnish study on TVT reported the incidence of complications was 40% in hospitals performing ≤15 operations, but reduced to 14% once this number was exceeded [22]. In the UK TVT/colposuspension trial [23], objective cure rates were found to be higher for centres recruiting >30 patients compared with those recruiting <20 [24].

Surveys on the volume of procedures required to maintain good surgical results also tend to support the definition of a

FIG. 4.
Unadjusted rates of repeat operations among NHS trusts performing surgical repair for urogenital fistula between 2000 and 2009 (minimum of four procedures performed [P25.1, P25.2]).

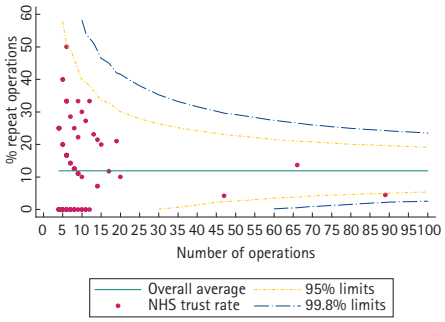
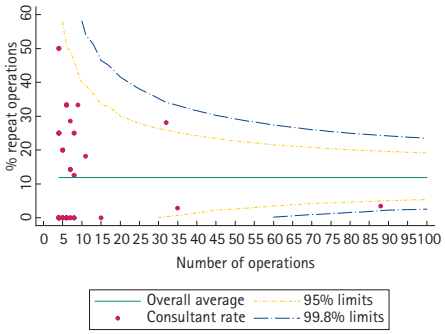


FIG. 5.
Unadjusted rates of repeat operations among consultants performing surgical repair for urogenital fistula between 2000 and 2009 in English NHS trusts (minimum of four procedures performed [P25.1, P25.2]).



minimum threshold [25]. In a survey of UK consultants performing mid-urethral tape procedures, the majority view was that performing 10–20 or 20–50 cases of TVT under supervision was required to gain competence [25]. The National Institute for Health and Clinical Excellence recommends that surgery for urinary incontinence in women should be undertaken only by surgeons who carry out a sufficient case load to maintain their skills [26]. An annual workload of at least 20 cases of each primary procedure was recommended.

It is difficult to extrapolate from these recommendations to the much more heterogeneous and often highly complex nature of fistula surgery. One consideration is that success rates appear to be higher for first operations than repeat repairs [12,27]. We found a similar increased risk but did not have sufficient statistical power to confirm this result.

The present study found some evidence of a volume–outcome relationship at the level of a NHS trust, although we did not have sufficient power to detect one at surgeon level. Nonetheless, there are strong arguments for the centralization of services in the case of fistula management [5]. The overall numbers are relatively small (120 cases per year in England), and the number of surgeons with specific training and reasonable workload is in single figures. In addition to the development of urogynaecological and urological surgical expertise, support from colo-rectal and plastic surgery colleagues is important, and the requirement for skilled and experienced postoperative nursing, physiotherapy and social work input are seen as pivotal to optimum care. A small number of supra-regional centres would allow fistula repair surgery to be undertaken by surgeons with appropriate training, a 'minimum viable workload', and who work within a multidisciplinary team. One argument against centralization is that this may limit access to care for patients who cannot or will not travel greater distances for treatment; however, a recent review of a single fistula centre showed that patients will travel long distances if they feel they can obtain better outcome [12].

The pattern of supra-regional management for urogenital fistula was agreed by members of the RCOG and BAUS around 16 years ago [6]. Despite subsequent application for national specialist funding, centres have never been formally recognized, nor this pattern of care established. The concept of 'any willing provider' as originally proposed in the Health and Social Care Bill was inherently at odds with this proposal, and 'any qualified provider' still leaves local commissioners with considerable ambiguity. The Advisory Group for National Specialised Services may provide an appropriate channel to facilitate such arrangements.

In conclusion, in the English NHS, around 120 women per year have surgical treatment of urogenital fistula and around 12% of women will require another procedure after an unsuccessful repair. Outcomes appear to be better in NHS trusts with fistula repair workloads >3 procedures per year over a period of time, but the majority of women had their surgery performed by surgeons who rarely undertake this surgery. The results of the present study lend weight to the argument for the greater centralization of fistula management.

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CONFLICT OF INTERESTS

The authors have no financial interests to declare. Paul Hilton was a faculty member on ICUD-SIU 1st International Consultation on Obstetric Vesicovaginal Fistula – complications committee (2010–2011) and on the ICUD-EAU 5th International Consultation on Incontinence – fistula committee (2011–2012).

CONTRIBUTION TO AUTHORSHIP

Paul Hilton conceived the study and contributed to its design and analysis, and writing of the paper; he approved the final version for publication. David Cromwell contributed to the study design, undertook the data extraction and analysis, writing of

the paper, and approved the final version for publication; he had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

DETAILS OF ETHICS APPROVAL

The study is exempt from UK NREC approval as it involved analysis of an existing dataset of anonymized data for service evaluation. Approvals for the use of HES data were obtained as part of the standard HES approval process.

FUNDING

None.

PROVENANCE

This study was not commissioned.

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Correspondence: Paul Hilton, Directorate of Women's Services, Level 5, Leazes Wing, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK.
e-mail: paul.hilton@ncl.ac.uk

Abbreviations: **RCOG**, Royal College of Obstetricians and Gynaecologists; **HES**, Hospital Episode Statistics; **ICD**, International Classification of Diseases; **OPCS**, Office for Population Censuses and Surveys; **VVF**, vesicovaginal fistula; **UVF**, urethrovaginal fistula; **TVT**, tension-free vaginal tape.

Chapter 3: Summary of main findings from included papers

The methodology and main findings of each of the included papers are documented below; the findings are then set in the context of existing literature in chapter 4.

Paper 1: Hillary C, Osman N, Chapple CR, Hilton P. The aetiology, treatment and outcome of urogenital fistulae managed in well- and low-resourced countries: a systematic review. **Eur Urol** 2016; 70(3): 478-492.

Methods:

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement, a prospective search protocol was developed and registered with the PROSPERO database. Evidence was identified through a search of the PubMed and Scopus databases using the following search terms: "obstetric fistula", "vaginal fistula", "bladder fistula", "urethral fistula", "urinary fistula", "vesicovaginal fistula", "genital fistula", and "fistula"; this yielded 12,626 articles. After limiting to studies involving women published between January 1980 and March 2015, and excluding various male and child specific terms, and duplicate publications, 654 articles remained. Abstract screening followed by full text screening was performed. The primary objective was to report fistula aetiology; secondary objectives included reporting surgical techniques applied and outcomes achieved. Each article was rated following the Oxford Centre for Evidence-Based Medicine levels of evidence scale.

Main findings:

Of the 654 articles screened, 49 were identified for inclusion in evidence synthesis, 15 reporting on fistula repair in HICs and 34 on fistula management in LMICs; only two randomised controlled trials were identified, the majority of studies (43/49) being grade 4 evidence level.

The 15 included articles reporting data from HICs included 2,055 fistulas, of which 83.2% were of a surgical aetiology, and 13.0% followed radiotherapy. In contrast, the 34 included articles reporting data from LMICs included 10,398 fistulas, of which only 4.4% were of a surgical aetiology, and 0.2% followed radiotherapy.

Of 10,398 fistulas reported from LMICs, 95.2% were of an obstetric aetiology. Of the so-called '*obstetric fistulas*', 9.5% were associated with caesarean section and 13.5% were associated with some surgical intervention.

There was limited information regarding conservative management, and only a proportion of studies reported on specific approaches to surgical management. Where a specific approach was described, in HICs 70.7% of procedures were performed vaginally, compared to 84.4% of those reported from LMICs. Although a variety of interposition grafts were used in reported studies, we found no high-quality evidence to support the use of graft interposition in any context.

The definition of surgical success varied between studies, generally in the range '*anatomical closure*', '*anatomical closure but residual leakage*', and '*failed repair*', while others use the '*need for a repeat repair procedure*' as the definition of failure. The timing of determining outcome also varied, most commonly being at the time of catheter removal or discharge (typical in LMICs) or at clinic follow-up (more common in HICs). No studies reporting follow-up beyond 3 months were included in this review.

Of patients undergoing surgical closure in HICs, the median overall closure rate was 94.6% (range, 75.8–98.6%). Studies included with the lowest overall success had a high proportion of radiation-induced fistulas. Of patients undergoing surgical repair in LMICs, the median overall closure rate was 87.0% (range, 58.0–100%). The median rate of postoperative SUI for patients with a closed fistula was 10.0% (range, 3.8–30.0%), across all surgical approaches and fistula characteristics.

There are no randomised studies available that directly compare the outcomes of abdominal and vaginal approaches to repair, given that each surgeon has a particular preference for a certain indication and clearly there would be ethical issues with the conduct of such a study. Of the included studies, three reported the outcomes of non-randomised comparisons; amongst these, the overall success rates were 90.8% of 286 vaginal repairs and 83.9% of 250 abdominal repairs; whilst statistically significant,

it must be emphasised that the particular approach used in individual cases is likely to have been selected on the basis of pre-operative evaluation and dependent on individual surgical bias and direct comparison of outcomes is not valid.

These findings are set in the context of existing literature on page 127 in chapter 4 - paper 1.

Paper 2: Hilton P, Ward A. Epidemiological and surgical aspects of urogenital fistulae: a review of 25 years' experience in southeast Nigeria. **Int Urogynecol J & Pelvic Floor Dysfunct** 1998; 9: 189-194.

Methods:

This retrospective, individual surgeon, cohort study was undertaken during the course of two visits made by the candidate to St Luke's Hospital, Uyo, and the associated VVF Unit at Mbribit Itam, Akwa Ibom State, Nigeria, in 1989 and 1995. Cases were identified from operating theatre record books, and notes were subsequently retrieved from the hospital records department; 2979 operative procedures were initially identified, undertaken in 2484 patients between January 1970 and December 1994; 2389 case notes were subsequently retrieved (96%). Details of the causative processes, fistula site, surgical procedure(s) undertaken, and outcome were well recorded in notes throughout the study period.

Epidemiological data were less well recorded in the early part of the study, and the protocol was changed to limit analysis of these aspects to the period between the two visits, *i.e.* between January 1990 and December 1994. A total of 715 patients were identified during this period, from whom 656 case records (92%) were available for review.

Main findings:

The length of history at presentation was extremely variable, ranging from a few days to 38 years; the average delay in presentation was 5 years. Overall, 44% of patients experienced amenorrhoea at the time of referral, and their average delay between the index pregnancy and presentation was 2 years; 39% had resumed menstruation and their average delay to presentation was just over 4 years. The remaining 17% were presumed postmenopausal and had a mean delay to presentation of around 15 years.

Amongst the total cohort, 92.2% of fistulas were of obstetric aetiology, with 80.3% following obstructed labour, 6.9% following caesarean section, and 5% following rupture of the uterus.

The impact of civil war in Nigeria (1967-1970) meant that barely a third of patients were aware of their age, and a similar proportion literate. At the time of presentation with their fistula, 62.5% were married, 11.0% were single and 16.2% widowed; 10.4% had been deserted by their husbands since the development of their fistula. Of the obstetric fistulas 31.4% followed first pregnancies; parity ranged from 0 to 17 (median 3). Although 48.1% of the previous pregnancies had resulted in a live birth, only 27.5% of patients had had previous live births (range 0-10, median 1).

In the index pregnancy, 82.3% of women had laboured at home with or without the support of a traditional birth attendant. Despite this, 73% ultimately delivered in hospital, with 47.1% undergoing operative delivery. Only 10.3% had a livebirth resulting from the index pregnancy, 22.8% following caesarean section, 12.5% following ventouse delivery, 8.3% following forceps, and 3.4% following normal vaginal delivery.

In this series, 4.5% of fistulas had ureteric involvement and 8.0% were associated with coexistent rectovaginal fistula; over 70% were mid-vaginal, juxtacervical or large (*i.e.* involving the whole of the bladder base between mid-vaginal and cervical levels). Of the total, 0.6% of patients underwent urinary diversion, and 99.4% a primary repair procedure; of the latter, 83% were carried out vaginally and 17% abdominally.

For the purposes of this study, '*cure*' was defined as a patient being subjectively dry at their last assessment, and subsequently undergoing no further surgery in the unit within the study period. Overall, 1954 underwent a single operation and, as far as could be established from the notes, were cured at this first operation (82.8%); 247 patients underwent a second operation, 116 a third, 32 a fourth and 11 a fifth operation during the study. In total, therefore, 2979 urogenital fistula procedures were carried out in the 2484 patients. There were in addition 32 patients who were known still to be wet after a first operation yet underwent no further surgery; 10 still wet after a second operation, one after a fourth operation, and two after a fifth operation. These were added to calculate '*corrected*' cure rates - 81.2% for first procedures and 65.0% for those requiring two or more procedures.

These findings are set in the context of existing literature on page 129 in Chapter 4 – paper 2.

Paper 3: Hilton P. Urogenital fistula in the UK – a personal case series managed over 25 years. **BJU Int** 2012; 110(1): 102-110.[2]

Methods:

This is a retrospective, individual surgeon, cohort from a tertiary urogynaecology centre providing a *de facto* supra-regional service for urogenital fistula repair in the UK. The women included had confirmed urogenital fistula referred between January 1986 and December 2010. Index cases were identified from the unit surgical database; data were entered prospectively for all fistula referrals (regardless of whether they underwent surgical repair) and updated with operative, postoperative and follow-up information as appropriate; statistics are largely descriptive. The primary outcome was the patient's report of absence of urinary leakage; secondary outcomes included operative or postoperative complications, anatomical closure of the fistula, other residual or new urinary symptoms, and the need for further surgical intervention.

Main findings:

During the period of this review 348 women were referred for the assessment or treatment of urogenital fistula, aged between 7 years and 89 years (median 44 years). The annual number of referrals increased from approximately 5 per year in the 1980's to 25 per year in the 2000's. Approximately one in six was referred from colleagues in Newcastle, and half from elsewhere in what was previously known as the Northern Health Region. One in six were referred from the rest of England, and a similar number from Scotland, Wales, Northern Ireland, the Republic of Ireland and elsewhere overseas combined.

[2] An update of these data, including the total cohort of 498 patients with urogenital fistulae referred to and managed by the candidate in the UK, covering the period 1985-2015, is included as *Appendix 3*.

Seventy-eight women (22.4%) had undergone 111 previous fistula repair procedures before referral; 55 women had one, 14 women two, eight women three, and one woman four prior unsuccessful attempts at repair.

Two thirds of the fistulas (238 cases, 68.4%) were of surgical aetiology, and were associated with a large range of different operations. In 172 cases (72.3% of the surgical cases and 49.4% of the series as a whole) the fistula followed excision of the uterus and or cervix, with 132 cases (55.5% of the surgical cases and 37.9% of the series as a whole) occurring after simple abdominal hysterectomy.

Thirty-eight women (10.9%) developed the fistula following childbirth; in most this followed some form of surgical intervention, *i.e.* caesarean section (15, 39.5%) or caesarean hysterectomy (4, 10.5%), assisted vaginal delivery (5, 13.2%) or trial of vaginal delivery following a previous caesarean section (8, 21.1%).

Two women (0.6%) developed their fistula from direct invasion of malignancy into the bladder; 34 women (9.8%) had undergone prior pelvic radiotherapy for the treatment of cancer. The remaining 36 cases (10.3%) were of miscellaneous aetiologies, approximately half of which related to vaginal foreign bodies, and a third to the use of ring or shelf pessaries for the management of POP.

256 (73.6%) of the fistulas were VVF with a further 13 (3.7%) having combined VVF and ureterovaginal fistula; 70.3% of these (51.7% of the total) opened into the vaginal vault, reflecting the preponderance of surgery, and in particular hysterectomy, as the causative factor.

In 24 women (6.9%) the fistula healed '*spontaneously*', that is either with no treatment, or with a period of continuous bladder drainage or ureteric stenting. A further 33 women did not undergo surgery for a variety of other reasons.

In total, 291 women (83.6%) underwent one or more surgical procedures, with 283 undergoing repair and eight having primary urinary diversion (2.7%). Of those undergoing primary repair, 69.1% had a vaginal procedure, and 30.9% an abdominal procedure. Ureteric re-implantation was required in 22 women, two of these being bilateral; in seven, ureteric re-implantation was combined with a transperitoneal repair of a concurrent VVF.

Excluding the ureteric re-implantations and urinary diversions, 60 women underwent abdominal repair operations; 26.6% of these were transvesical, and 73.4% transperitoneal. Of the 31 cases of obstetric aetiology undergoing repair 13 (41.9%) required an abdominal repair, compared to 43/183 of the surgical cases (23.5%), 4/19 of the radiotherapy/malignant cases (21.1%), and 0/28 of the miscellaneous cases.

Of the 283 women having repair surgery 279 had attended for follow-up; 261 (93.5%) women report being fully continent and had no clinical evidence of either urethral or extra-urethral urinary leakage. A further six (2.2%) had anatomical closure of their fistula but reported some residual incontinence (1 SUI and 5 urgency urinary incontinence (UUI)). The primary closure rate was therefore 95.7%, with a continence rate of 93.5%.

Successful fistula closure was significantly more likely in the women who had not had attempts at closure prior to referral (98.2%) than in those who had one or more previous unsuccessful procedures (88.2%).

Twelve women required a second operation following unsuccessful closure after referral to our unit; one underwent secondary diversion, and 11 had second attempts at fistula repair. The secondary closure rate therefore was 81.8%, with a secondary continence rate of 72.7%.

The primary closure rate varied between 96% for those fistulas of surgical and miscellaneous aetiologies and 90% for those of obstetric aetiology. These closure rates were not significantly different although it must be recognised that the radiation related cases were less likely to undergo a repair operation.

The primary closure rate was 83.3% for those women undergoing abdominal procedures, and 96.1% for those having vaginal repairs, although neither closure rate nor continence rate were significantly different between VVF (95.9%; 91.4%) and UVF (92.1%; 80.0%). The primary closure rate was not significantly different between those procedures where an interposition graft was or was not employed in the repair.

These findings are set in the context of existing literature on page 132 in Chapter 4 – paper 3.

Paper 4: Hilton P. The urodynamic findings in patients with urogenital fistulae. **BJU Int** 1998; 81: 539-542.

Methods:

During the period 1995-1997, 30 of the 38 patients referred to a tertiary urogynaecology unit with urogenital fistula underwent urodynamic investigation prior to treatment. Investigation included free uroflowmetry, dual-channel subtracted cystometry (in all), and urethral pressure measurement (in 19 patients).

Main findings:

The distribution of fistula types and aetiologies was consistent with that reported elsewhere from this unit (*paper* 3) and in other HICs (*paper* 1). One of the fistulas was vesico-uterine, and six were UVF. Of the 23 VVFs,14 were situated in the vaginal vault, three were mid-vaginal, and six at the bladder neck.

Following investigation 14 patients (47%) were shown to have USI (then described as '*genuine stress incontinence*'), 12 (40%) showed DOA (then described as '*detrusor instability*'), and 5 (17%) impaired bladder compliance. Fifteen patients (50%) showed evidence of voiding dysfunction (flow rate consistently less than 15ml/sec).

The urodynamic findings in the 14 patients with vault fistulas were compared with the 12 whose fistulas were at the bladder neck or urethral. USI was found in 75% of those with urethral or bladder neck fistulas, compared to 36% in those with vault fistulas; DOA was present in 50% and 35% in the same groups respectively; however, these differences were not of statistical significance.

Following fistula repair two patients had a persistent or recurrent fistula (92.3% cure at first operation). Ten patients complained of persistent urinary symptoms despite anatomical closure of their fistulas; one reported SUI, and nine urgency or UUI; all these women had abnormal cystometry pre-operatively. On repeat urodynamic investigation the former was confirmed to have persistent USI; this suggests an incidence of post-fistula repair USI in this group of largely surgical fistulas, of only 3%, and a persistence rate of 11% in women with UVF or bladder neck fistulas. Of the nine women with overactive bladder (OAB) symptoms following repair, six were confirmed

to have persistent DOA on repeat urodynamic testing; one followed repair of a vault fistula, and 3 followed repair of urethral or bladder neck fistulas. This indicates an overall incidence of post-fistula repair DOA of 20%, and a persistence rate of 20% for the vault fistulas, and 50% for the urethral or bladder neck fistulas. No women with stable bladders pre-operatively had persistent symptoms postoperatively, and no patients complained of UUI postoperatively who had not had OAB pre-operatively, *i.e.* there was no evidence of so-called '*de novo*' DOA post-operatively.

These findings are set in the context of existing literature on page 135 in Chapter 4 – paper 4.

Paper 5: Dolan LM, Dixon WE, Hilton P. Urinary symptoms and quality of life in women following urogenital fistula repair: a long-term follow-up study. **BJOG** 2008; 115(12): 1570-1574.

Methods:

A consecutive cohort of women, referred for treatment of urogenital fistula between January 1993 and December 2002, was identified from our surgical database. Women with a VVF or UVF, who had undergone preoperative urodynamic investigation and vaginal or abdominal fistula repair with a minimum of 6 months of follow up, were eligible for inclusion.

Eligible women were contacted by post and invited to participate by completing the Bristol Female Lower Urinary Tract Symptom (BFLUTS) questionnaire, together with a further self-administered questionnaire that provided information on parity, body mass index, interim surgery, current medical problems and regular medication. Non-responders were contacted again 4 weeks later. Additional information was obtained from case records and those held on the unit surgical database.

Main findings:

A consecutive series of 84 women with urogenital fistulas were identified from the unit surgical database within the study period; 40 women were not eligible for inclusion for various reasons; in 9 women, case information was missing or inadequate to allow contact. There were 35 contactable women with VVF or UVF who fulfilled all eligibility criteria for inclusion, and they were sent postal questionnaires. Completed questionnaires were returned by 31 women (89%); 1 was returned unanswered as the woman was deceased.

The median age of respondents was 46 years (range 16–85 years); the median length of time between the surgery and the survey was 50 months (range 7–115 months).

Twenty-one of the fistulas were into the vaginal vault (68%) and 9 were bladder neck or UVF (29%). The aetiology was surgical in 25 women (81%), the antecedent procedure being hysterectomy in 19 (76%) of these. This distribution of fistula types

and aetiology was comparable to the total workload referred to the unit (*see also included papers 3 & 4*).

On the basis of preoperative urodynamic investigation, one or more functional abnormalities were present in 20 women (65%); the rate of abnormality was not significantly different between those with vault fistulas (62%) and bladder neck or UVF (78%).

Fistula repair was performed vaginally in 27 women (87%) by a transvesical approach in two and a transperitoneal approach in two. Successful anatomical closure of the fistula was achieved with a single operation in all women. A continence procedure was combined with fistula repair in three women with preoperative USI.

Thirty of the 31 women (97%) reported having one or more urinary symptoms at a median of 50 months after fistula repair, with urgency (71%), nocturia (68%), SUI (68%) and UUI (65%) being the most commonly reported symptoms. There was no significant difference in urodynamic abnormalities found in association with different fistula types or in the symptoms found subsequently. Normal cystometry prior to fistula repair did not appear to be associated with a lower incidence of bothersome symptoms at a median of 4 years postoperatively.

The BFLUTS questionnaire asks respondents to grade how they would feel if they had to spend the rest of their life with their current urinary symptoms as '*perfectly happy*', '*pleased*', '*mostly satisfied*', '*mixed feelings*', '*mostly dissatisfied*', 'very unhappy' or 'desperate'. Ten women (32%) had at least mixed feelings, although only two women described feeling dissatisfied or unhappy at the prospect. Twenty-seven women (87%) said that their current urinary symptoms caused little (12) or no (15) interference with their lives.

These findings are set in the context of existing literature on page 137 in Chapter 4 – paper 5.

Paper 6: Hilton P, Cromwell D. The risk of vesicovaginal and urethrovaginal fistula after hysterectomy performed in the English National Health Service – a retrospective cohort study examining patterns of care between 2000 and 2008. **BJOG** 2012; 119(12): 1447-1454.

Methods:

The study used data from the HES database, which contains records of all patient admissions to National Health Service (NHS) hospitals in England, capturing patient demographics, hospital administrative information, diagnostic information using the International Classification of Diseases (ICD), 10th revision, and operative procedures using the UK Office for Population Censuses and Surveys classification (OPCS), 4th revision.

This study included adult women who underwent elective hysterectomy for selected common indications in English NHS hospitals between 1st January 2000 and 31st December 2008.

We distinguished between four types of hysterectomy: total abdominal hysterectomy (TAH) (OPCS code: Q07.4), subtotal abdominal (STH) (Q07.5), vaginal (VH) (Q08.9), and radical abdominal hysterectomy (RAH) (Q07.1-07.3). The selected benign conditions were endometriosis (ICD10 code: N80), uterine fibroids (D25), POP (N81) and menstrual disorders (N92–N94). Four '*malignant*' conditions were also selected, namely, cervical carcinoma *in situ* (D06), cervical cancer (C53), uterine cancer (C54, C55) and ovarian cancer (C56).

Women were defined as having a postoperative fistula if the ICD10 codes N82.0 (VVF) or N82.1 (other urinary-genital tract fistula) were found in the diagnostic fields of the index procedure episode or any subsequent episode that occurred within 1 year of the index procedure. Surgical repair of fistulas was examined using the most pertinent OPCS codes, namely, repair of VVF (OPCS P25.1), repair of UVF (P25.2) and construction of an ileal conduit (M19.1).

Main findings:

There were 351,505 hysterectomies performed for the selected indications, and after exclusions as defined in the paper, there were 286,053 operations performed for benign conditions, and 57,718 for '*malignant'* indications. In the former group, 339 fistulas were identified (0.12%), and amongst the latter 97 fistulas were identified (0.17%).

The risk posed to women differed across the various combinations of procedure and indication. For women undergoing VH for POP, the estimated rate was 1 in 3861 (95% CI 2550–6161). Among women undergoing a TAH for the other benign conditions, the overall rate was 1 in 540 (272/146 841; 95% CI 479–540), whereas for women who underwent STH the rate was 1 in 2279 (9/20 511; 95% CI 1205–5000).

The risk of VVF or UVF was greatest among those women who had cervical cancer, with TAH and RAH both having estimated rates of around 1 in 100. Among women undergoing TAH, the rate was roughly five times greater for women with invasive cervical cancer than cervical carcinoma *in situ* (relative risk 4.6; 95% CI 1.7–12.2; $p < 0.001$).

For the benign conditions of endometriosis, fibroids and menstrual disorders, there were noticeable changes in the number of fistulas after TAH across the age categories and by year of surgery. In terms of age, the rate of fistula was stable until women passed 50 years of age, after which it fell by around 40%. The rate of fistula increased from 0.15% in 2000–2002 to 0.22% in 2006–2008, a rise of 46%. Extending the model to include both VH and TAH for these benign conditions produced comparable results for the estimated relationship between rate of fistula and age categories and year of surgery, although the relationship was not seen for malignant conditions.

These findings are set in the context of existing literature on page 139 in chapter 4 – paper 6.

Paper 7: Kiran A, Hilton P, Cromwell DA. The risk of ureteric injury associated with hysterectomy: a 10-year retrospective cohort study. **BJOG** 2016: 123(7); 1184-1191.

Methods:

This study employed a similar methodology to that described in the previous included paper (*paper 6*) to investigate the risk of ureteric injury after hysterectomy, between 1st January 2001 and 31st December 2010.

The indications explored were defined as in the former study, as were the types of hysterectomy, with the exception that we also sought to identify laparoscopic procedures as follows: total laparoscopic hysterectomy (TLH; Q56.8), laparoscopically-assisted vaginal hysterectomy (LAVH; Q08.9), laparoscopically-assisted subtotal hysterectomy [LASH; code as for subtotal hysterectomy (Q07.5) with the additional laparoscopic approach qualifier (Y50.8)].

Ureteric injuries within a year of hysterectomy were identified using codes for relevant diagnoses and related surgical treatment. A woman was identified as having an injury if the diagnostic fields of the index procedure episode, or a subsequent episode within 1 year of the index procedure contained: ureteric injury (S37.1), hydronephrosis with ureteric stricture (N13.1) or other urinary-genital tract fistula (N82.1). Ureteric injury was also identified if surgical treatments for ureterovaginal fistula or obstruction, *e.g.* insertion of stent; insertion of nephrostomy tube; ureteroscopic dilatation; removal of suture from ureter; ureteric repair; closure of ureterovaginal fistula; or re-implantation of ureter, were identified within the same timeframe.

Main findings:

After exclusions, 377,073 hysterectomies were identified for analysis, 310,105 for benign indications and 66,968 for malignant indications. In total, 1792 ureteric injuries were identified (0.5%) within a year of the index procedures.

The annual number of injuries showed a significant trend, increasing from 90 in 2001 to 259 in 2010. The rate of ureteric injury was higher from 2006 onwards for six of the eight conditions, the change being greatest for women with ovarian cancer, increasing over three-fold from 1.06% to 3.86%.

Women undergoing laparoscopic hysterectomies had a rate of ureteric injury of 0.6% (94/14,692), which was higher than the overall rate for other types of hysterectomy [0.3% (889/295 413).

Among the various indications, the highest rate was observed among women who had endometriosis, 2.2% (50/2363) for laparoscopic procedures and 1.0% (245/24 054) for open procedures. Of the 66,968 hysterectomies in the malignant group, 8.0% (5321) were laparoscopic. Women who had laparoscopic hysterectomies had a rate of ureteric injury of 0.2% (8/5321), which was lower than the rate for open procedures [1.3% (798/61 647), laparoscopic versus open procedures, chi-square $p < 0.001$).

These findings are set in the context of existing literature on page 141 in chapter 4 – paper 7.

Paper 8: Cromwell D, Hilton P. Retrospective cohort study on patterns of care and outcomes of surgical treatment for lower urinary – genital tract fistula among English National Health Service hospitals between 2000 and 2009. **BJU Int** 2013; 111(4b): E257-E262.

Methods:

This was a retrospective cohort study using data from HES on women undergoing VVF or UVF repair between January 2000 and December 2009 in English NHS hospitals. Women were selected if they had an ICD-10 code N82.0 (VVF) or N82.1 (other urinary-genital tract fistula) in a diagnostic field and an OPCS-4 procedure code for repair of VVF (P25.1), repair of UVF (P25.2) or ileal conduit/urinary diversion (M19.1). We only included procedures that were performed during or after the first episode containing a diagnosis of urogenital fistula. A woman was defined as having a repeat repair, and therefore failure of an initial repair, if a subsequent episode of care contained in any procedure field one of the three OPCS codes (P25.1, P25.2 or M19.1) after an index procedure of fistula repair (P25.1, P25.2).

The main outcome measure was the number of fistula repairs and the incidence of re-repair; re-repair rates were stratified by age, NHS trust and consultant team volume.

Main findings:

We found a 37% increase in the number of repair or diversion operations carried out for lower urinary-genital tract fistulas between 2002 and 2009. Considering only primary fistula repair procedures, we found a 68% increase over the same period (from 62 primary repairs in 2002 to 104 in 2009).

The index procedures were allocated to 490 consultant teams, of which 127 (26%) were in the main specialty of gynaecology, and 306 (62%) were in urology. Overall, 281 consultant teams performed only one index procedure during the 10-year period studied, and only ten teams performed ten or more procedures in the same period. Only three consultant teams had carried out over 3 procedures per year consistently throughout the 10-year period studied. 114 consultant teams (23%) carried out no repair procedures, and only undertook urinary diversion in women with a diagnosis of

urinary fistula. Among the 376 consultant teams that performed repair surgery only five teams performed ten or more repairs in the period studied.

There were 108 women (11.9%) among the 905 women undergoing surgical fistula repair who required a repeat operation. The '*cure*' rate from one operation was 88.1% (797/905), from a first re-operation was 81.9% (77/94), and from a second re-operation was 68.9% (11/16). If one assumes that the need for secondary urinary diversion after a repair represents failure of the previous repair, these figures become 88.1% (797/905), 71.3% (77/108) and 64.7% (11/17), respectively. The relative risk of needing a further procedure after a second repair compared with after a first operation was 1.52 (95% CI 0.95 – 2.41; $p = 0.086$). The annual rate of re-operation fluctuated between 4 and 20% per year, but there was no significant evidence for the rate of repeat surgery having changed over time (test for trend, $p = 0.17$).

Whilst there was no association between rate of repeat repair and workload of NHS trusts or consultant teams, there was a noticeable step change between NHS trusts who performed over 30 procedures over the 10-year study period and those that did not (7.4 v 13.2%, $p = 0.02$). A similar step change was apparent among the consultant teams but this difference was not significant (8.4 vs 12.7%, $p = 0.13$). There were ten trusts and seven consultant teams with re-operation rates over twice the national average, and two Trusts and consultant teams with re-operation rates less than half the national average. However, the variation in the rates of repeat repair across NHS trusts and consultant teams was consistent with that expected from random variation alone (using the 99.8% limits of certainty).

These findings are set in the context of existing literature on page 143 in chapter 4 – paper 8.

Chapter 4: Findings from the included studies set in context

Paper 1: Hillary C, Osman N, Chapple CR, Hilton P. The aetiology, treatment and outcome of urogenital fistulae managed in well- and low-resourced countries: a systematic review. **Eur Urol** 2016; 70(3): 478-492.

Although the candidate has undertaken a number of systematic reviews relating to aspects of urogenital fistula, covering epidemiology (of oncological fistulas, and those involving the gastro-intestinal tract (GIT)), management (of surgical and radiotherapy-associated fistula and those involving the GIT) (de Ridder *et al.*, 2013), and complications of fistula and repair surgery (including urinary tract infection, vaginal stenosis, dyspareunia and sexual dysfunction) (Mourad *et al.*, 2012), this particular review is included in view the commonality of its themes those of other included papers.

In common with other systematic reviews in the area of urogenital fistula (Mourad *et al.*, 2012; Adler *et al.*, 2013; de Ridder *et al.*, 2013; Bodner-Adler *et al.*, 2017; World Health Organization, 2018), we found the published evidence to be of poor quality, based largely on retrospective case series. Of 12,626 publications identified in our initial search, only 49 were appropriate for inclusion, and only two were RCTs, comparing variations in operative technique in obstetric fistulas in LMICs (Safan *et al.*, 2009; Shaker *et al.*, 2011).

The distribution of aetiologies seen in our review was in keeping with other literature (*see page 6: Chapter 1: Background literature – Epidemiology of urogenital fistulas – Aetiology*). In women reported from HICs, 83% of fistulas were of surgical aetiology, and in those reported from LMICs, 95% were of obstetric aetiology. This is also in keeping with our findings in the submitted papers 2 & 3.

Despite the reported, albeit modest, success rate from conservative management (*see page 18: Chapter 1: Background literature – Treatment outcomes – Conservative management*), we found little evidence of the consistent application of this management strategy in the included papers.

Similarly, despite enthusiastic reports of the use of interposition grafting, especially in women with large, multiple, recurrent, radiotherapy-associated or urethral fistulas

(Rangnekar *et al.*, 2000; Pushkar *et al.*, 2009; Malde *et al.*, 2017), we found no high-quality evidence to support their use in any of these situations. It is certainly the case that many colleagues working in LMICs describe a decreasing place for interposition grafting in their practices.

The variation in definition of outcome across the included studies was emphasised, and again this is in keeping with other reviews (*see page 12: Chapter 1: Background literature – Outcomes of treatment for lower urinary tract fistula – Definition of cure*). With that limitation, we did find a statistically significant difference in outcome between vaginal procedures (91% cures) and abdominal procedures (84% cures). We do concede however that there is no high-level evidence to support this finding, which is based on comparison of cohort studies only, and not randomised controlled trials. It is also discordant with the findings of the ICI review, which found no significant differences between 'early' and 'late' repairs, vaginal and abdominal repairs, transvesical and transperitoneal repairs, and repairs with and without the use of interposition grafting (*candidates own searches and analyses*) (de Ridder *et al.*, 2013).

Paper 2: Hilton P, Ward A. Epidemiological and surgical aspects of urogenital fistulae: a review of 25 years' experience in southeast Nigeria.
Int Urogynecol J & Pelvic Floor Dysfunct 1998; 9: 189-194.

Although larger well-documented case series of obstetric fistula patients managed in LMICs have since been published (Muleta *et al.*, 2010a; Waaldijk, 2018), in paper 2 we presented what was at the time the largest single surgeon cohort study (Hilton and Ward, 1998). We highlighted the considerable delays from the onset of symptoms to presentation, and in keeping with other reports (Muleta *et al.*, 2010a; Bangser *et al.*, 2011) found an average delay of 5 years. Additionally, the women in our series often travelled distances of up to 1000 miles, to obtain treatment, consistent with the concept of Maine's first and second delays (Thaddeus and Maine, 1991).

We also reported, for the first time, the association between menstrual status and time of presentation. Although the occurrence of amenorrhea following the development of a fistula is well known(Aimakhu, 1974), whether this reflects gross tissue destruction within the pelvis or a hypothalamic influence as a result of the physical and emotional effects of a traumatic labour, stillbirth and fistula development, has not been clear. As the live-birth rate is so low in obstetric fistula patients (10% in our series), lactation is unlikely to be a significant factor in causing amenorrhoea. The average time to presentation in those who had resumed menstruation was just over 4 years, compared to 2 years in those who remained amenorrhoeic. We opined that the natural history of the hypothalamic suppressive effect of the development of a fistula tends towards spontaneous resolution after 2 years, even if the fistula remains untreated. Alternatively, these findings may simply reflect the fact that the more dramatically affected patients, who are more likely to develop amenorrhea, are also more likely to present earlier for treatment than their less traumatized sisters who may have resumed menstruation at an earlier stage. The latter suggestion would however not be in keeping with the findings that that women who have difficulties obtaining care in labour also tend to have difficulties securing treatment for their fistulas (Tahzib, 1983).

Amongst the cohort reviewed, 92% of fistulas were of obstetric aetiology, 80% following obstructed labour, 7% following caesarean section, and 5% following uterine

ruptured; only 4% followed non-obstetric pelvic surgery. These findings being entirely consistent with earlier reports from LMICs (Waaldijk, 1989; Danso *et al.*, 1996; Hilton, 2003).

Female genital mutilation (FGM), poor educational attainment, early age at marriage, lack of contraception, early pregnancy, and childbearing before growth and maturation of the pelvis, have commonly been seen as important factors in accentuating the risks of obstruction in labour, and high rates of separation and divorce, a common consequence (Murphy, 1981; Tahzib, 1983; Kelly and Kwast, 1993a; Ibrahim *et al.*, 2000). Despite the high proportion of fistulas of obstetric aetiology, and the common association with obstructed labour in our cohort, we did not find the same distribution of social attributes, and FGM in particular was rarely seen. The mean age was 28 years (*compared to 16 - 22 years in the latter cited studies*), mean parity was 3.5 (*compared to 1.2 - 2.1*), with less than a third of the fistulas resulting from their first pregnancy (*compared to 52% - 81%*); almost a third had completed at least primary education (*compared to 0.2% - 8%*), and less than a third delivered at home (although in many cases they attended hospital after several days at home) (*compared to 58% - 77%*). Why our patients in south-east Nigeria should have such a high fistula rate despite these factors remains uncertain, although this may reflect biosocial differences in the population studied. It is of interest that in the only case-controlled study exploring this issue, although fistula patients were of shorter stature, poorer nutritional status, lower educational level, and lower socioeconomic status, the control women actually married at a younger age than index cases, and there was no difference in age at first pregnancy or utilization of conventional health and maternity care (Onolemhemhen and Ekwempu, 1999). Abhorrent as it is, how far FGM should be seen as a risk factor for fistula, and how far simply an associated feature of some populations in which fistula is common, also remains unclear.

Although '*cure*' could be determined only from the patient's report of being dry at the time of discharge, and subsequently undergoing no further surgery in the unit during the study period, this did allow the calculation of '*cure rates*' for both primary and secondary surgery, in a way that had rarely been reported previously. We found 81.2% '*cure rate*' from first operations, and 65.0% in women undergoing second or subsequent procedures. A closure rate of 88% for primary procedures(Kelly and

Kwast, 1993a), and 57.8% from secondary procedures has been reported from the Addis Ababa Fistula Hospital (Kelly and Kwast, 1993b) (*candidate's calculation from published raw data*). In a more recent personal communication from the same unit, Browning reports 92% closure from first operations, 73% from second operations and 52% from third operations (Mourad *et al.*, 2012). In the same communication it was indicated that 33% of women reported SUI after a first repair procedure, 50% following a second repair, and 75% following a third repair. Although we identified a small number of women with residual incontinence who did not undergo further fistula repair, these were included as '*failures*' in our calculation of outcome, which was therefore quoted as '*cure rate*' rather than '*closure rate*'. It was unfortunately not possible to make reliable estimates of post-repair SUI in our cohort.

Paper 3: Hilton P. Urogenital fistula in the UK – a personal case series managed over 25 years. **BJU Int** 2012; 110(1): 102-110.

This is one of the largest published cohort studies of urogenital fistula from an HIC - the largest with the unpublished re-analysis following the candidate's retirement, when the total number had increased to 498 cases (see A*ppendix 3*). More importantly, it is the first study to show the referral pattern of patients with urogenital fistulas. Although arguments have been made for the general concept of '*treatment near to home*' (NHS England, 2014b), it is clear that, given the option, patients will travel the length of the country, and indeed cross national boundaries, to obtain effective care. A document describing the commissioning of centralised services for urogenital fistulas in the UK has been in draft since 2013 (NHS England, 2013), but remains to be implemented.

The distribution of aetiology amongst the included cases was broadly in line with earlier reports, with 68% of surgical aetiology. A further 11% followed childbirth, although most of these followed some obstetric surgical intervention, and it would be more appropriate to look on 80% of urogenital fistulas being iatrogenic in aetiology in current surgical practice in HICs.

We described 'spontaneous' healing (*i.e.* associated with prolonged catheterisation) in only 24 of our referred cases (6.9%). Recent, largely overlapping, systematic and non-systematic reviews found closure with catheter drainage alone in 13% and 31% of included surgical fistulas, respectively (Bazi, 2007; de Ridder *et al.*, 2013). It must be noted however, that the number of cases in the included reports varied from 1 to 238, with spontaneous closure in 0% to 100%, giving a very large CI around the estimate of 13% (95% CI 0%, 36%). Two thirds of the included cases and almost one half of the spontaneous closures came from the candidate's cohort. It should also be noted that many of the referred cases in our cohort attended after epithelialisation had occurred, and a consistent approach to conservative management was not appropriate. Where a consistent approach to conservative management has been applied, spontaneous healing has been reported in 15-28% of obstetric fistulas (Waaldijk, 1997; Waaldijk, 2004); one would therefore anticipate that this would be the minimum estimate of spontaneous healing in iatrogenic fistulas. Certainly a case can be made for more

widespread use of catheterisation in the early days after fistula recognition, and the recommendation of the ICI (*the candidate's own wording*) is (de Ridder *et al.*, 2013):

> "Spontaneous closure of surgical fistulae does occur, although it is not possible to establish the rate with any certainty; if a vesicovaginal fistula is diagnosed within (*3 to*) 6 weeks of surgery, indwelling catheterisation can be considered for a period of up to (*6 to*) 9 weeks (*i.e.* up to 12 weeks after the causative event)."

As noted previously, the candidate's preference has always been for the vaginal approach to fistula repair surgery where possible, accepting that the abdominal route has a place where access vaginally is limited (by virtue of the patient's nulliparity, or previous surgery or other pelvic pathology) or where there is concurrent ureteric involvement requiring re-implantation. Within this cohort the primary closure rate was 83.3% for those women undergoing abdominal procedures, and 96.1% for those having vaginal repairs (Fisher's exact test; $p < 0.001$). This is consistent with the findings in the meta-analysis reported in paper 1, although it must be acknowledged that our cohort represented a large proportion (80%) of those in whom this analysis was feasible (Hillary *et al.*, 2016). Given that the decisions about the route of repair are not taken at random but are based on specific patient characteristics; these findings must be interpreted with caution. We would simply urge that those involved in fistula surgery should have appropriate training, skills and experience to select the most appropriate procedure for each patient (de Ridder *et al.*, 2013).

The fistula closure rate at first operation (that is, the first operation in the referral centre) varied by aetiology, 96.3% for miscellaneous fistulas, 96.1% for surgical fistulas, 94.7% for radiation-associated fistulas, and 90.3% for obstetric (largely obstetric surgery) fistulas. These differences were not significantly different. It has been suggested that urinary diversion may be the procedure of choice in radiotherapy-associated fistulas (Langkilde *et al.*, 1999). In keeping with that approach, our review of national outcomes from fistula surgery from England (*vide infra* - paper 8) showed that 24% of all patients with a diagnosis of urogenital fistula underwent diversion. Nonetheless, in this personal cohort study only 2.7% overall required diversion (albeit 17.6% for radiotherapy-induced fistulae, compared with 0.6% for other aetiologies). These data would suggest that urinary diversion should not be seen as the automatic

response to radiotherapy-associated fistulas, and at least some consideration should be given to the option of repair.

Fistula closure was achieved significantly more often in women who had not undergone attempts at repair prior to referral (98.2%) than in those with previous unsuccessful procedures (88.2%). Similarly, the primary closure rate after referral (95.4%) was higher than the closure rate in those women who needed 2 or more repairs after referral (81.8%) – a clinically if not statistically significant difference. This is in keeping with our earlier larger cohort of obstetric fistulas (paper 2) (Hilton and Ward, 1998). These findings indicate that the best time to close a fistula, both from the patient's and surgeon's perspectives, is at the first operation, and again, this strengthens the arguments for centralised management of fistulas.

Paper 4: Hilton P. The urodynamic findings in patients with urogenital fistulae. **BJU Int** 1998; 81: 539-542.

Although prior to this publication there had been one small series of patients undergoing urodynamics after fistula repair (Schleicher *et al.*, 1993), this was the first, and indeed remains the only, report of urodynamics carried out prior to repair in women known to have urogenital fistula. Whether it is possible to undertake conventional dual-channel cystometry when there is direct communication between the bladder and the genital tract has been questioned (Abrams and Hilton, 2002). We were, nevertheless, able to demonstrate that the intra-vesical pressure was different from the intra-abdominal pressure (recorded either vaginally or rectally), and that detrusor contractions could be identified during both filling and voiding phases of the procedure. It is acknowledged that this was a cohort of women recruited in the UK, with aetiologies typical of fistula patients in an HIC; most were surgical fistulas of only a few millimetres in diameter, although there were also radiotherapy-associated fistulas up to 3cm. diameter. Intuitively, there must be a maximum fistula size above which it is not possible to record detrusor pressures reliably, and this may have implication for the value of pre-repair investigation in LMICs.

We found a high incidence of both USI (47%) and DOA (40%) in this cohort of women with largely surgical fistulas, prior to repair. Whilst there are no directly comparable data, these findings can be seen in context with:

- the reports of post-fistula repair SUI in up to 50% of women (Kelly and Kwast, 1993b; Waaldijk, 2009; de Ridder *et al.*, 2012);
- the symptomatic report of bladder spasms in 45% of women immediately after obstetric fistula repair (Ekwedigwe *et al.*, 2017); and
- the urodynamic findings in women with persistent UI **after** obstetric fistula repair, where USI was identified in 31% - 49%, DOA in 3% - 6%, and mixed USI and DOA in 20% - 43% ((Schleicher *et al.*, 1993; Murray *et al.*, 2002; Goh *et al.*, 2013).

This would suggest that whatever mechanisms account for the high incidence of functional abnormalities of the urinary tract after repair surgery in fistula patients, be

that USI, DOA or both, they are likely to be effective prior to the fistula repair procedure.

By repeating urodynamic investigation after fistula repair (in those women with persistent symptoms) we were able to determine both incidence and persistence rates (*i.e.* the number who had the finding prior to repair in whom it was also found after repair) for USI and DOA. This was the first time (and, as far as we are aware, the only time) that sequential studies have been carried out in this patient group. The incidence of post-fistula repair SUI was 1/30 or 3%; the persistence rate 1/14 or 7%. Post-fistula repair DOA was found in 6/30 or 20% and persisted in 6/12 or 50%. Perhaps most notably, we found no women who had had stable bladders prior to their fistula repair who reported symptoms of OAB postoperatively, and no women who complained of UUI postoperatively who did not report OAB symptoms pre-operatively, *i.e.* there was no evidence of so-called '*de novo*' DOA postoperatively. Clearly these findings are of major significance in terms of counselling women prior to fistula repair in HICs; their concordance with the postoperative findings in obstetric fistula patients implies relevance also in LMICs.

Paper 5: Dolan LM, Dixon WE, Hilton P. Urinary symptoms and quality of life in women following urogenital fistula repair: a long-term follow-up study. **BJOG** 2008; 115(12): 1570-1574.

The limited availability of long-term follow-up studies in the area of surgery for pelvic floor dysfunction is well recognised (Hilton, 2008). In view of the high incidence of symptoms of SUI and OAB, and of functional abnormalities of USI and DOA both before and after fistula repair referred to above, we sought to undertake a long-term follow-up in women who had undergone anatomically successful fistula repair. This was the first long-term follow-up of fistula patients, and the first use of a validated quality of life (QoL) instrument in this patient group (albeit the validation was in HIC populations with pelvic floor dysfunctions other than fistula) (Brookes *et al.*, 2004).

We chose to employ what was then known as the BFLUTS questionnaire (Jackson *et al.*, 1996) – now incorporated into the ICI modular set of questionnaires as the ICIQ - Female Lower Urinary Tract Symptoms questionnaire (ICIQ-FLUTS) (Bristol Urological Institute, 2014). It must be noted that this looks at the occurrence and impact of lower urinary symptoms and does not explore other domains of QoL. We obtained a good response rate of 89% at a median of over 4 years after treatment. In comparison, in a feasibility study to investigate the role of urodynamic investigation in women prior to surgical treatment for SUI, we obtained a 75% response rate to the ICIQ – FLUTS at 6-months follow-up (Hilton *et al.*, 2015).

We found very high rates of SUI and OAB symptoms (urgency, nocturia, and UUI) with 97% of patients reporting one or more of these symptoms. It must be noted of course that these are very common symptoms in parous women; however, the prevalence of individual symptoms was 1.5 to 2 times higher in our population of women following fistula repair than it was in the general population (Dolan and Hilton, 2010).

Despite the frequent reporting of lower urinary tract symptoms, for most (87%) these caused little or no impact of their QoL. It was also of interest to note that normal cystometry prior to fistula repair did not appear to be associated with a lower incidence of bothersome symptoms 4 years postoperatively. This might be seen to bring into question the role of bladder function testing in this patient group. That said, even where a good prognosis for fistula closure can be given, women

undergoing fistula repair should be counselled about the possibility of persisting urinary symptoms afterwards; they can however be reassured that in most cases, these will be mild, with limited impact on their QoL.

More recently other reports from LMICs including Nigeria (Umoiyoho *et al.*, 2011), Ethiopia (Donnelly *et al.*, 2015), Burkina Faso ,(Desalliers *et al.*, 2017) and Bangladesh (Imoto *et al.*, 2015), using a range of questionnaire and interview techniques, have not only shown the major adverse impact of fistula on QoL, particularly in terms of mental and social well-being, but also the beneficial effect of successful treatment. They have however also pointed out the occasional persistence of stigmatisation, physical problems, and anxiety over such issues as the sexual functioning, obstetric future and financial security.

Paper 6: Hilton P, Cromwell D. The risk of vesicovaginal and urethrovaginal fistula after hysterectomy performed in the English National Health Service – a retrospective cohort study examining patterns of care between 2000 and 2008. **BJOG** 2012; 119(12): 1447-1454.

Although there had been earlier studies of urinary tract injury at hysterectomy employing large national datasets (Harkki-Siren *et al.*, 1998; Forsgren *et al.*, 2009), this was the largest study to date, and with over 350,000 procedures over 9 years this allowed us to investigate, for the first time, the risks fistula developing after hysterectomy, both by route of operation, and by indication for the procedure.

Our '*headline rates*' of lower urinary-genital tract fistula following hysterectomy were:

- Overall, for all diagnoses and routes of hysterectomy - 1 in 788
- VH for POP - 1 in 3861
- STH for benign indications other than POP - 1 in 2279
- TAH for benign indications other than POP - 1 in 540
- TAH or RAH for cervical cancer - 1 in 102

The national cohort studies from Sweden (Forsgren *et al.*, 2009), and Finland (Harkki-Siren *et al.*, 1998), both showed lower overall rates of fistula following TAH for benign indications, of approximately 1 in 1000. The Swedish study covered the period 1973–2003 and the Finnish study 1990–95 whereas our study covered a later period (2000–08); an increasing risk over time could therefore explain these figures (*vide infra*).

The Cochrane review of approaches to hysterectomy for benign disease found no difference in the rate of fistula following abdominal, vaginal and laparoscopic routes (Nieboer *et al.*, 2009); and the VALUE study, a non-randomised cohort study of hysterectomy from the UK, found no difference in the rate of operative bladder injury between abdominal, vaginal and laparoscopic routes (McPherson *et al.*, 2004). The national cohort study from Finland on the other hand reported a higher rate of both bladder injury (relative risk 11.4) and subsequent fistula formation (relative risk 2.2) following laparoscopic procedures (Harkki-Siren *et al.*, 1998). Unfortunately, the OPCS-4 coding used in HES at the time of our study did not allow easy separation

between open and laparoscopic hysterectomies and we did not feel that much of use could be stated about the risks of fistula associated with laparoscopic hysterectomy.

As one would expect, the risks for developing postoperative fistula were highest in women undergoing hysterectomy for invasive cancer. Less intuitively, we found the risks in women undergoing surgery for benign indications to be lower in women over 50 years of age. This has not been reported previously, and indeed the study from Sweden found a higher rate of '*fistula disease*' in women over 50 years (Forsgren *et al.*, 2009). They however included both intestinal and urinary fistulas, and it is conceivable that the increase in fistulas reported in older women in these studies relates more to bowel than urinary fistulae, and to the prevalence of inflammatory bowel disease than to hysterectomy (Altman *et al.*, 2010).

Perhaps most notably, we found the risk of lower urinary genital tract fistula after hysterectomy to have increased by almost 50% between the first and last triennia of our study period (*i.e.* between 2000-2002 and 2006-2008). This trend has also been confirmed more recently in a conference abstract from the USA (Adam *et al.*, 2015). Factors that might underlie this trend are discussed after the considerations of papers 7 & 8, in Chapter 5.

Paper 7: Kiran A, Hilton P, Cromwell DA. The risk of ureteric injury associated with hysterectomy: a 10-year retrospective cohort study. **BJOG** 2016: 123(7); 1184-1191.

By using both diagnostic codes for ureteric injury, stricture, and fistula and operative codes for relevant interventions (*ICD-10 and OPCS-4 codes are included with the paper as supplementary material – see page 102*), we identified 1792 ureteric injuries arising during, or within 12 months of, 377,073 hysterectomies (0.5%). The incidence ureteric injury at hysterectomy from other large cohort studies and systematic reviews ranges between 0.2% and 30% (Harkki-Siren *et al.*, 1998; Brandes *et al.*, 2004; Likic *et al.*, 2008; Summerton *et al.*, 2012; de Ridder *et al.*, 2013). Some of these reviews have suggested that the incidence of iatrogenic ureteric injury may have diminished in the last two decades (Brandes *et al.*, 2004; Summerton *et al.*, 2012), although the evidence supporting this statement is certainly not strong. In contrast (yet in keeping with our earlier data on lower urinary tract fistulas following hysterectomy) the overall number of ureteric injuries identified in our study, and the rate of injury (for 6 of the 8 diagnoses examined) increased between the first (2001-2005) and second (2006-2010) quinquennia of this study (*see page 145: Chapter 5 for further discussion of this point in relation to papers 6, 7 & 8*).

We had not originally intended to report the risks associated with laparoscopic hysterectomies, in view of the recognised problems with their coding within OPCS, and anticipated under-reporting (National Oesophago-Gastric Cancer Audit, 2010; Hilton and Cromwell, 2012); with the encouragement of reviewers and editors however we did include these data. Women undergoing abdominal or vaginal hysterectomies had a rate of ureteric injury of 0.3%, whereas those having laparoscopic procedures had a rate of 0.6%. Whilst these figures were statistically significantly different, they are in some distinction with the figures reported from Finland in 1990s, where the rate of injury after all hysterectomies was 0.1% and that after laparoscopic procedures 1.4% (Harkki-Siren *et al.*, 1998). The earlier timeframe of this latter study may mean that it was collected at a period of less advanced laparoscopic skills generally.

The highest rate of ureteric injury was observed among women who had endometriosis, 2.2% for laparoscopic procedures and 1.0% for open procedures.

Perhaps surprisingly, the rate of ureteric injury in women undergoing surgery for malignant diagnoses was lower than for endometriosis and was also lower when undertaken by the laparoscopic (0.2%) than open routes (1.3%). This may reflect the greater level of surgical, and in particular laparoscopic, training that gynaecological oncologists currently undergo.

Paper 8: Cromwell D, Hilton P. Retrospective cohort study on patterns of care and outcomes of surgical treatment for lower urinary – genital tract fistula among English National Health Service hospitals between 2000 and 2009. **BJU Int** 2013; 111(4b): E257-E262.

Using the HES database, we demonstrated for the first time the pattern of care provided for urogenital fistula nationally within NHS hospitals in England. Specifically, we explored the fistula workload of individual NHS hospitals and consultant teams (*pseudonymised)* over a 10-year period, and by linking individual patient records longitudinally over time, were able to determine treatment outcomes - using the 'need for re-operation' as a marker for failure of the index procedure.

The difficulty of defining success in fistula treatment has been discussed earlier (*see page 12: Chapter 1 – Background literature - Outcomes of treatment for lower urinary tract fistula - Definition of cure*). Reported cure rates for surgical treatment vary with case mix, aetiology and surgical technique, in the range 45% to 100%. Whilst many series do not report outcomes at all, where they are provided, high surgical success rates are often described in case series reported from individual surgeons or hospitals. The recent Bodner-Adler *et al*., review, of VVF following benign gynaecological surgery, documented an overall success rate of 98.0% for surgical treatments (Bodner-Adler *et al.*, 2017), with 81 of the 107 included studies reporting success in 100% of cases. Despite this, only 6.4% of the 1379 included women were described as being completely symptom-free, only 55.5% completely dry, and only 30.0% reported to be healed or cured. The definition of failure used in our study – the need for a further repair operation or urinary diversion after an index repair procedure – whilst clearly not a sensitive measure of outcome, is perhaps the most specific available.

Overall, 24% of women with a diagnosis of lower urinary-genital tract fistula underwent urinary diversion; this might be seen as a particularly high rate, given that only 2.7% of women in the candidate's personal cohort underwent diversion (*see earlier comments in relation to paper* 3) (Hilton, 2012). Equally concerning, 23% of consultant teams treating fistulas undertook no repairs at all during the study period, and apparently managed all their cases by urinary diversion. Whilst it is possible that

these were all women with radiotherapy-associated fistulas, OPCS coding in HES does not include details of prior radiotherapy treatments. Even if it were possible to identify prior radiotherapy as a possible causative factor for fistula by longitudinal linkage of records, the fact that fistula may arise anything up to 50 years after radiotherapy (Hilton, 2012), would make that approach unlikely to be informative.

Even amongst those consultant teams that undertook fistula repair procedures, the workload could only be described as idiosyncratic, with 75% performing only one repair in the 10-year study period, and only 3 teams averaging more than 3 cases per year. The relationship between workload and outcome is discussed earlier (*see page 10: Chapter 1 Background literature – Patterns of care – Non-obstetric fistula in high-income countries*). We confirmed, for the first time, that such a relationship exists in fistula repair surgery, with hospitals undertaking more than 30 cases in 10 years (*i.e.* averaging more than 3 per year) having half the re-operation rate of those doing fewer procedures. Re-operation rates were up to 50%, with 10 hospitals having rates more than twice the national average (11%), and one having a rate less than half the national average. We also confirmed the finding of earlier reports (*including our submitted papers 2 & 3*) that the best prospect for success is with the primary procedure, with re-operation rates after first, second and third operations being 88%, 71% and 65% respectively, again, strengthening the arguments for centralised management of fistulas; a maximum of 3 units in England would seem to be justified (NHS England, 2013).

Chapter 5: Further commentary on emerging trends in the aetiology of urogenital fistula[3]

Recent trends in iatrogenic/surgical fistula

In papers 6 and 7 we showed the risk of lower urinary-genital tract fistulas and ureteric injury after hysterectomy to have increased by 46% and 128%, respectively, between the early and later years of our study periods. This trend has also been confirmed more recently in a conference abstract from the USA (Adam *et al.*, 2015). In paper 8, in addition to reporting on patterns of care, we also found a 68% increase in primary fistula repair procedures over a similar period.

DRIVERS FOR RECENT TRENDS SEEN IN IATROGENIC FISTULAE IN HIGH-INCOME COUNTRIES

Between 2000 and 2008, the total number of hysterectomy procedures in England fell by 12% and those for the main benign indications (excluding prolapse) fell by 27% (Hilton and Cromwell, 2012). This was mainly a result of the fall in the number of hysterectomies for menorrhagia, a trend that has been ongoing since the mid-1990s (Reid and Mukri, 2005). One explanation for the increase in risk of postoperative fistulas could therefore be an increase in the proportion of more difficult procedures among the remaining hysterectomies – the simpler operations having decreased disproportionately in number with increasing use of medical treatment for menstrual dysfunction. The fact that we did not find the rate of fistula to be significantly higher in women undergoing an TAH for fibroids or endometriosis than in those with menstrual problems, makes this explanation unlikely, however. Notwithstanding, this reduction in gynaecological surgical activity overall, the reduced length of trainees' working week, and reduced years in training, all mean that trainees, in the UK at least, obtain less surgical experience now than previously, and may therefore embark on independent practice less prepared than a decade ago.

[3] Much of the material in this chapter comes from a '*special contribution*' commissioned from the candidate by the journal editor. Hilton, P. (2016) 'Trends in the aetiology of urogenital fistula: a case of 'retrogressive evolution'?', *Int Urogynecol J*, 27(6), pp. 831-7. Although peer reviewed, it is not included amongst the submitted papers since it does not strictly contain original material.

Recent trends in of 'obstetric' fistula

There are no published longitudinal studies on trends in incidence of obstetric fistulae, although recent data suggest that there may be a reduction in new cases coming forward for treatment in Ethiopia (Wright *et al.*, 2016). There is however a growing perception that an increasing proportion of urogenital fistulae in LMICs are iatrogenic in aetiology, rather than being true 'obstetric' fistulae from ischaemic mechanisms. Although this impression relates primarily to obstetric interventions, especially caesarean section, iatrogenic fistulae are also seen increasingly following gynaecological procedures in some areas.

A study of patients managed in the 'Hamlin Fistula Ethiopia' (HFE) hospital at Barhirdar between 2004 and 2007, found 36% to be type 1 on the Goh classification (*i.e.* more than 3.5cm from the external urinary meatus) (Goh *et al.*, 2008). In a further study of fistulae managed in three other of the six HFE hospitals, Wright and colleagues found the proportion classified as being 'high' (presumed to be of iatrogenic aetiology) increased from 27% to 36% between 2011 and 2015, albeit concurrently with a significant reduction in the annual number of referrals seen (Wright *et al.*, 2016). It should be noted however that the Goh classification is more appropriate for obstetric than iatrogenic fistulae (Goh, 2004), and neither the designation as 'Goh type 1' nor 'high' can be taken as an absolute indication of aetiology, both being likely to overstate the true proportion of iatrogenic cases.

In a study of women managed in 65 facilities across 11 countries mainly in East Africa over an 18-year period, Raassen *et al.* found 13.2% of fistulas to be iatrogenic in nature (Raassen *et al.*, 2014). Waaldijk, with a personal experience of over 25,000 conservative and surgical fistula treatments in over 20,000 women treated over three decades, reported 139 of his first 1,000 cases to have had a caesarean delivery in their index pregnancy, 55 (5.5%) of which were probably iatrogenic in aetiology; this compared to 380 of his last 1,000 cases, 163 (16.3%) of which were probably iatrogenic (Waaldijk, *personal communication*). Hence, although the confirmation of the exact aetiology may not be wholly accurate, there is reasonable evidence of a 3-fold increase in the rate of iatrogenic fistulae over this period in Nigeria and Niger. Similarly, faculty surgeons from other fistula units in Nigeria (Lengmang, S. & Adeoye, S., *personal communications*), Kenya (Raassen, T. & Khisa, W., *personal*

communications), Uganda (Flynn, P., Bishop, M., Breen, M., Putman, J. & Duffy, S., *personal communications*), Ethiopia (Wright, J., & Browning, A., *personal communication*), Tanzania (Browning, A., *personal communication*), Sierra Leone (Maggi, D., *personal communication*) and Pakistan (Syed, S., *personal communication*) report an increasing number of post-caesarean section fistulae seen in recent years; although data are limited, such cases may now represent more than one third of fistulae seen in some areas.

DRIVERS FOR RECENT TRENDS SEEN IN 'OBSTETRIC' FISTULA IN LOW-INCOME COUNTRIES

Access to skilled maternity services and obstetric intervention

The significance of obstructed labour as a contributory factor to maternal and perinatal mortality and morbidity is well established; the need to relieve obstruction in order to limit these consequences, including fistula formation, is well recognised. In a recent statement, the WHO emphasised that whilst caesarean section can effectively prevent maternal and perinatal mortality and morbidity, when medically justified, there is no evidence of benefit for women or infants who do not require the procedure on medical grounds (World Health Organisation, 2015). Caesarean section is associated with risks that can extend beyond the current delivery and are greater in women with limited access to comprehensive obstetric care (World Health Organisation, 2015). The WHO statement also emphasises the imperative to provide caesarean sections to women in need, rather than striving to achieve any specific intervention rate. In many resource-poor settings, access to skilled care and crucial interventions is limited, and the rate of caesarean delivery is a marker for the availability and use of obstetric services in these situations (WHO *et al.*, 2009). In a review of trends in caesarean section rate in Asia and sub-Saharan Africa, Cavallaro *et al.* point out the association between poverty and access to healthcare; although rates up to 22% were seen (especially in wealthier urban populations), among the poorest quintile of the population, caesarean sections accounted for less than 2% of deliveries in 21/26 countries studied (Cavallaro *et al.*, 2013). Hence, limited access to obstetric intervention is likely to remain a significant contributory factor in generating fistula, particularly amongst the rural poor.

The appropriate workforce

There is a critical workforce shortage in many areas of the world, particularly in LMICs. This inevitably overstretches those staffs that are present and may contribute to patient abuse and neglect. Caesarean section is often delegated to the most junior team member, often a doctor with minimal training, supervision or mentorship. Decision-making is often poor, and hence caesarean delivery may be undertaken in inappropriate cases, with inappropriate timing, and/or using inadequate surgical techniques. Preoperative risk assessment is likely to be inadequate, with failure to recognise the increased risk of damage to the urinary tract (at caesarean section or hysterectomy) associated with a previous operative delivery (Duong and Patterson, 2014; Oliphant *et al.*, 2014). In some areas financial incentives rather than clinical priorities may dictate the choice of mode of delivery, and indeed knowledge and experience of alternative ways of delivery, especially of a dead baby, are often lacking. In the right circumstances emergency caesarean may be lifesaving, but when performed inappropriately it may increase maternal risk whilst being too late to improve perinatal outcome (Shah *et al.*, 2009).

Use of non-medically qualified clinical officers

The training of non-medically qualified clinical officers (NMQCO) has been introduced into a number of LMICs to boost the available cadre of staff able to provide emergency obstetric care. In 19 out of 47 sub-Saharan African countries, NMQCOs are authorised to provide obstetric care, and in five countries (Zaire, Burkina Faso, Malawi, Mozambique and Tanzania) are they permitted to carry out caesarean sections and other emergency obstetric surgery (Mullan and Frehywot, 2007). The use of NMQCOs in providing major obstetric surgery has been found to be cost-saving in Mozambique (Kruk *et al.*, 2007), with no significant difference in outcomes compared to medical officers in Tanzania (McCord *et al.*, 2009), and Malawi (Chilopora *et al.*, 2007). In a meta-analysis of data from 16,018 women in six non-randomised controlled cohort studies, Wilson *et al.* also reported no difference in mortalities, although they did find an increase in postoperative complications (Wilson *et al.*, 2011). None of these studies have reported comparative outcomes for more senior doctors, nor have they included data on fistulae specifically.

The appropriate working environment

Whilst taken for granted in HICs, a safe and equipped working environment is crucial to minimising risk during surgery and is often lacking in LMICs. Electricity supplies for lighting and equipment are often unreliable and running water for scrubbing and sterilisation processes may be inconsistent. Instruments are often unavailable or in need of repair, and in keeping with the workforce issue highlighted above, skilled assistance for retraction is often unavailable. Getting access to theatre may be especially problematic at night: the difficulties of finding appropriate staff and equipment are even greater; this adds to delays in preparing the theatre; in some areas patients' families may be charged with leaving the hospital to purchase drugs and materials from off-site pharmacies before an operation can begin. These are all contributors to 'Maine's third delay' (Thaddeus and Maine, 1991), and can mean that the 'decision to delivery interval' may be measured in days rather than minutes in some areas.

POST-CAESAREAN SECTION FISTULA – TRAUMATIC OR ISCHAEMIC?

Incontrovertibly, a woman neglected in obstructed labour for several days, ultimately delivering a stillborn infant vaginally, then surviving to develop a VVF, should be described as having a 'true obstetric' or ischaemic fistula. In contrast, a woman identified as being in obstructed labour who is transferred expeditiously to a healthcare facility for timely caesarean section, who is delivered of a live infant, and then goes on to develop a vesicocervical fistula, would be reasonably described as having an iatrogenic injury. But what of those women who are transferred only after considerable delay, or who undergo caesarean section for a dead baby and then develop a VVF? Or those who undergo caesarean section but then develop an urethrovaginal fistula or a mid-vaginal VVF or an ureterovaginal fistula? Should these lesions be looked on as 'obstetric', iatrogenic, or a combination?

In Tanzania it is reported that 85% of patients developing fistula now deliver in hospital, usually by caesarean section, with an increasing rate of vesicocervical and vesico-uterine (probably iatrogenic) fistulae (Browning, A. - *personal communication*). Onsrud *et al.*, also reported a higher rate of uterine or cervical involvement, with less surrounding fibrosis, and less apparent treatment delay in post-caesarean section fistulae in Democratic Republic of Congo (DRC) (Onsrud *et al.*, 2011). They considered

these to be a distinct clinical (iatrogenic) entity and highlighted the training issues discussed above. Loposso *et al.* similarly highlighted the risks of fistula in DRC despite the availability of caesarean section, but attributed this to the duration of obstructed labour prior to hospitalisation, and the delay in achieving caesarean delivery (Loposso *et al.*, 2015). The various colleagues with whom I have discussed this issue (*vide supra* - personal communications from Nigeria, Kenya, Uganda, Ethiopia, Tanzania, Sierra Leone and Pakistan), give a range of views on the point. Hence, it is likely in different circumstances fistulae following caesarean section may have varying pathophysiology, some being wholly ischaemic, some wholly traumatic, but most a combination of mechanisms.

Similar arguments may be framed around post-caesarean section ureterovaginal fistulae. Although these are commonly looked on as being exclusively iatrogenic in aetiology, operating on, or close to, the ureter within an ischaemic field defect inevitably puts it at greater risk, and means that ureterovaginal fistula developing after caesarean section for obstructed labour is also likely to be at least in part ischaemic in nature.

With the increased use of caesarean section, and consequent increase in 'repeat' procedures, the rate of placenta praevia and associated abnormal placental implantation will continue to rise (Silver *et al.*, 2006; Johnston *et al.*, 2011; Zuarez-Easton *et al.*, 2015). Given the technical difficulties of surgery in these circumstances, we might also anticipate a progressive increase in the rate of fistula following caesarean section. Although the association has been reported (Mann *et al.*, 2013), a trend is not yet evident, and in the author's own series from the UK, fistula following caesarean section or trial of attempted vaginal birth after caesarean (VBAC) have consistently represented 6%-8% of cases referred over the last three decades (Hilton, 2012).

How might one obtain further information to confirm or refute these impressions? Throughout history the establishment of causality in medicine has proved elusive (Feezer, 1921; Evans, 1978) and the confirmation of secular trends in causality presents even greater challenges. Difficult as these issues have been to establish in the context of infectious diseases (Evans, 1976), they take on a completely different magnitude with a problem as complex as obstetric fistula, given its physical, bio-

social, cultural, economic and geo-political contributors. Data collection is clearly important, but even such powerful tools as the Demographic and Health Surveys Program can provide only a small proportion of the information needed to fully investigate these issues (Johnson and Peterman, 2008; Demographic and Health Surveys, 2018). Almost all of the United Nations Millennium Development Goals potentially impact on the causation and management of fistula (United Nations General Assembly, 2000), and yet there remain substantial gaps in our achievement of these goals (United Nations, 2015). Given a worldwide fistula prevalence of up to 3,500,000(Muleta *et al.*, 2012), and incidence up to 1 in 800 births (Vangeenderhuysen *et al.*, 2001), there is clearly much to be done before we can claim to be effectively managing and preventing this condition.

Hence, it appears that with more widespread understanding of the causes of obstetric fistulae in LMICs, and increasing rates of caesarean section, there is an increase in VVF and ureterovaginal fistulae that may be at least in part iatrogenic in nature. We have also provided evidence to support the possibility of an increase in the incidence of iatrogenic (post-hysterectomy) fistulae in HICs, which coincides with a decrease in the number of hysterectomies carried out. In the first case this may reflect the amount of training, supervision and support provided to trainees; in the second it may reflect the amount of surgical experience accrued in training and workload in independent practice. In both situations it behoves governments and educational authorities to invest in training and workforce planning, and to facilitate audit and operational research, so that an appropriately trained and supervised medical workforce is maintained in the correct working environment. Alternatively, so that the right people, do the right thing, at the right time, and in the right place (NHS England, 2014a).

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Appendices

Appendix A: Group II-a publications

(***Other works put forward as evidence of the scope of the candidate's contribution to the specific field of study in which the primary submissions lie - i.e. urogenital fistula***[4])

Format	No.
Chapters and narrative reviews	21
Peer-reviewed original papers	13
Published abstracts	6
Systematic reviews	4
Letters	2
Audio-visual materials	2
Total	48

Table 6: Group II-a publications listed by format

[4] The candidate's publications are categorised as group I, IIa and IIb, as follows:

Group I - Works upon which a candidate primarily bases his claim to have satisfied the standards for the award of the degree (*see Chapter 2*);

Group II - Other works put forward as evidence of the scope of the candidate's contribution:

IIa - to the specific field of study in which the primary submissions lie - *i.e.* urogenital fistula (*Appendix A*);

IIb - to the broader field of study - *i.e.* urogynaecology (*see Appendix B*).

1. Hilton P. (1994) Sims to SMIS – an historical perspective on vesico-vaginal fistulae. In: **The Yearbook of the RCOG 1994**, pp 7-16. (*review*)
2. Hilton P. (1994) **Urethro-vaginal fistula repair** (with Martius graft). Produced by Film and Television Section, Audio-Visual Centre, Newcastle University, from a surgical workshop at the Queen Elizabeth Hospital, Gateshead, April 1994. (*live surgery video presentation*)
3. Hilton P, Ward A. Epidemiological and surgical aspects of urogenital fistulae: A review of 25 years' experience in Nigeria. **Int Urogynecol J & Pelvic Floor Dysfunct** 1995; 4: 243. (*published conference abstract*)
4. Hilton P, Ward A, Molloy M, Umana O. Peri-urethral injection with autologous fat in post fistula stress incontinence: a preliminary report. **Int Urogynecol J & Pelvic Floor Dysfunct** 1995; 4: 243. (*published conference abstract*)
5. Hilton P. Urodynamics in patients with urogenital fistula. **Int Urogynecol J & Pelvic Floor Dysfunct** 1995; 4: 243. (*published conference abstract*)
6. Hilton P. (1996) **Vesico-vaginal fistula repair**. Produced by Film and Television Section, Audio-Visual Centre, Newcastle University, from a surgical workshop at Queen Elizabeth Hospital, Gateshead, April 1996. (*live surgery video presentation*)
7. Hilton P. Debate: "Post-operative urogenital fistulae are best managed by Gynaecologists in specialist centres". **BJU Int** 1997; 80, suppl. 1: 35-42. (*review/opinion piece*)
8. Hilton P. (1997) Fistulae. In: **Gynaecology** (2nd edition) Edited by Shaw RW, Souter WP, Stanton SL, published by Churchill Livingstone, London pp 779-801. (*chapter*)
9. Hilton P. The urodynamic findings in urogenital fistula patients. **BJU Int** 1998; 81: 539-542. (*peer-reviewed paper - included in submitted work*)
10. Hilton P, Ward A, Molloy M, Umana O. Peri-urethral injection with autologous fat: a preliminary report in cases of post fistula stress incontinence. **Int Urogynecol J & Pelvic Floor Dysfunct** 1998; 9: 118-121. (*peer-reviewed paper*)

11. Hilton P, Ward A. Epidemiological and surgical aspects of urogenital fistulae: a review of 25 years' experience in south-east Nigeria. **Int Urogynecol J & Pelvic Floor Dysfunct** 1998; 9: 189-194. (*peer-reviewed paper - included in submitted work*)

12. Clement K, Hilton P. Diagnosis and management of vesico-vaginal fistulae. **The Obstetrician and Gynaecologist**. 2001; 3.4: 173-178. (*review*)

13. Hilton P. (2001) Fistula repair. In: **An Atlas of Gynaecological Oncology**. Edited by Smith RJ, del Priore G, Curtin J, Monaghan JM. Published by Martin Dunitz, London pp 187-202. (*chapter*)

14. Hilton P. (2001) Surgical fistulae. In: **Female Urology and Urogynaecology.** Edited by Cardozo LD, Staskin D. Published by Isis Medical Media, London pp 691-709. (*chapter*)

15. Hilton P. (2001) Obstetric fistulae. In: **Female Urology and Urogynaecology**. Edited by Cardozo LD, Staskin D. Published by Isis Medical Media, London pp 711-719. (*chapter*)

16. Hilton P. (2001) Vesico-vaginal fistulae – new perspectives. In: **Clinical Urogynaecology. Current Opinion in Obstetrics and Gynecology.** Edited by Stanton SL; published by Balliere-Tindall, London. 13.5: pp 513-520. (*review*)

17. Hilton P (2002) Urogenital Fistulae. In: **Incontinence in Women – proceedings of 42nd RCOG Study Group**. Maclean AB & Cardozo LD (editors). RCOG London pp 163-181. (*systematic review*)

18. Hilton P. (2002) Vesico-vaginal and urethro-vaginal fistulae. I**n: Female Pelvic Reconstructive Surgery**. Edited by Stanton SL, Zimmern P; published by Springer-Verlag, Berlin pp 273-283. (*chapter*)

19. Dolan LM, Dixon WE, Hilton P. Quality of life and urodynamic abnormality in patients following urogenital fistula repair. **Int Urogynecol J & Pelvic Floor Dysfunct**. 2003; 14, suppl. 1: S42. (*published conference abstract*)

20. Hilton P. (2003) Fistulae. In: **Gynaecology** (3rd edition) Edited by Shaw RW, Souter WP, Stanton SL, published by Elsevier Science Ltd., Edinburgh pp 835-856. (*chapter*)

21. Hilton P. Vesico-vaginal fistulas in the developing world. **Int J Gynaecol Obstet** 2003; 82.3: 285-295. (*review*)

22. Dolan LM, Easwaran SP, Hilton P. Congenital vesicovaginal fistula in association with hypoplastic kidney and uterus didelphys. **Urology** 2004; 63.1: 175i-175iii. (*peer-reviewed case report*)

23. Hilton P (2005) Maternal morbidity: vesico-vaginal fistulas in developing countries. **Textbook of Perinatal Medicine**. Edited by Kurjak A, Chervenak F, published by Parthenon, London pp 2146-2155. (*chapter*)

24. Hilton P, Dolan LM. (2005) Fistula repair. In: **An Atlas of Gynecological Oncology – investigation and surgery**. (2nd edition). Edited by Smith RJ, del Priore G, Curtin J, Monaghan JM. Published by Taylor & Francis Medical Books, London pp 253-273. (*chapter*)

25. Hilton P (2006) Urogenital fistulae - surgical. In: **Female Urology and Urogynaecology**. Edited by Cardozo LD, Staskin D. Published by Isis Medical Media, London pp 1223 – 1238. (*chapter*)

26. Dolan, L.M., Dixon, W.E. and Hilton, P. Urinary symptoms and quality of life following urogenital fistula repair: a long-term follow-up study. **BJOG** 2008; 115(12): 1570-1574. (*peer-reviewed paper - included in submitted work*)

27. Morton HC, Hilton P. Urethral injury in association with mid-urethral tape procedures used in the treatment of stress urinary incontinence. **BJOG** 2009; 116(8): 1120-1126. (*peer-reviewed paper*)

28. Hilton P, Morton HC. Urethral and bladder injuries with mid-urethral slings – do we always need to cystoscope? reply to letter from P Smith. **BJOG** 2009; 116(11); 1683-1684. (*letter*)

29. Hilton P. Urethrovaginal fistula associated with 'sterile abscess' formation following periurethral injection of dextranomer/hyaluronic acid co-polymer (Zuidex™) for the treatment of stress urinary incontinence – a case report. **BJOG** 2009; 116(11): 1527-1530. (*peer-reviewed case report*)

30. Hilton P. (2010) Fistulae. In: **Gynaecology**. (4th edition) Edited by Shaw RW, Luesley D, Monga A, published by Elsevier Science Ltd Edinburgh pp 874-895. (*chapter*)

31. Hilton P. (2011) Fistula repair. In: **An Atlas of Gynecological Oncology – investigation and surgery**. (3rd edition) Edited by Smith RJ, del Priore G, Curtin J, Monaghan JM. Published by Taylor & Francis Medical Books, London pp 236-250. (*chapter*)

32. Twemlow MRP, Narava S, Ali T, Graham JY, Hilton P. Intravesical herniation of small bowel; a very rare complication of bladder perforation. **BJUI Website** 2011; available from: http://www.bjui.org/ContentFullItem.aspx?id=764&SectionType=1&title=Intravesical-herniation-of-small-bowel:-a-very-rare-complication-of-bladder-perforation#comment. (*peer-reviewed case report*)

33. Hilton P. Urogenital fistula in the UK – a personal case series managed over 25 years. **BJU Int** 2012; 110(1): 102-110. (*peer-reviewed paper - included in submitted work*)

34. Murdoch M, Hilton P. Classical Hodgkin's lymphoma presenting as vesicovaginal fistula. **BJUI Website** 2012; available from: http://www.bjui.org/ContentFullItem.aspx?id=814&SectionType=1&title=Classical-Hodgkin's-lymphoma-presenting-as-vesicovaginal-fistula (*peer-reviewed case report*)

35. Hilton P, Cromwell D. The risk of vesicovaginal and urethrovaginal fistula after hysterectomy performed in the English National Health Service – a retrospective cohort study examining patterns of care between 2000 and 2008. **BJOG** 2012; 119(12): 1447-1454. (*peer-reviewed paper - included in submitted work*)

36. Mourad S, Haruna M, Hilton P, Saafan A, Shaker H, Vasan S. (2012) Complications of fistula surgery. In: Abrams P, editor. **ICUD-SIU – 1st International Consultation on Obstetric Fistula in the Developing World.** Societé Internationale d'Urologie, Montreal, Canada pp. 123-176. (*systematic review*)

37. De Ridder D, Hilton P, Mourad S, Pickard RS, Rovner ES (2013) Fistulae. In: **Incontinence – ICUD-EAU 5th International Consultation on Incontinence.** Abrams P, Cardozo L, Wein A (eds) Geneva. EAU publications pp. 1527-1579. (*systematic review*)

38. Cromwell D, Hilton P. Retrospective cohort study on patterns of care and outcomes of surgical treatment for lower urinary – genital tract fistula among English National Health Service hospitals between 2000 and 2009. **BJU Int** 2013; 111(4b): E257-E262. available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1464-410X.2012.11483.x/pdf (*peer-reviewed paper - included in submitted work*)

39. Kiran A, Hilton P, Cromwell DA. The risk of ureteric injury after hysterectomy performed in the English National Health Service – a retrospective cohort study examining patterns of care between 1998 and 2010. **Int Urogynecol J & Pelvic Floor Dysfunct.** 2014; 25(suppl.1): S143-S144. (*published conference abstract*)

40. Kiran A, Hilton P, Cromwell DA. The risk of ureteric injury after hysterectomy performed in the English National Health Service – a retrospective cohort study examining patterns of care between 1998 and 2010. **Female Pelvic Med & Reconst Surg**. 2014; 20(4, suppl.1): S82-S83 (*published conference abstract*)

41. Kiran A, Hilton P, Cromwell DA. The risk of ureteric injury after hysterectomy performed in the English National Health Service: a 10-year retrospective cohort study. **BJOG** 2016; 123(7); 1184-1191. (*peer-reviewed paper - included in submitted work*)

42. Hillary C, Osman N, Chapple CR, Hilton P. The aetiology, treatment and outcome of urogenital fistulae managed in well- and low-resourced countries: a systematic review. **Eur Urol** 2016; 70(3): 478-492. (*systematic review – included in submitted work*)

43. Hilton P. Trends in the aetiology of urogenital fistula: a case of 'retrogressive evolution'? **Int Urogynecol J & Pelvic Floor Dysfunct** 2016; 27.6: 831-837. Open access available from: http://rd.springer.com/article/10.1007/s00192-015-2919-y ('*special contribution*')

44. Hilton P. Author's reply to letter from Dr Ahmed Al-Badr on: Trends in the aetiology of urogenital fistula: a case of 'retrogressive evolution'? **Int Urogynecol J & Pelvic Floor Dysfunct** 2016; 27(9): 1445. Open access, available from: http://link.springer.com/article/10.1007/s00192-016-3083-8. (*letter*)

45. Hilton P, MacLaren E, Doshani, A. Urogynaecology (2017). In: **RCOG Essential Gynaecological Skills: Supporting best practice in women's health – Training & facilitators' manuals.** RCOG Global Health Unit, London pp 119-126 (Training manual) & 107-126 (Facilitators' manual). (*chapter*)

46. Hilton P. (2018) Fistula repair. In: **An Atlas of Gynecological Oncology – investigation and surgery**. (4th edition) Edited by Smith RJ, del Priore G, Coleman RL, Monaghan JM. Published by Taylor & Francis Medical Books, London. London. Pp 237-252. (*chapter*)

47. Hilton P. (2018) Operations for the repair of urinary fistulae. In: **Bonney's Gynaecological Surgery**. (12th edition) Edited by Lopes A, Spirtos N, Hilton P, & Monaghan JM. Wiley-Blackwell, London. Pp 231-265. (*chapter*)

48. Gurland B, d'Hoore A, Hilton P. (2018) Gynaecological considerations and urogenital fistulas. In: **Surgery of the Anus, Rectum and Colon.** (4th edition). Edited by Keighley MRB, Williams N. CRC Press/Taylor & Francis, London. Pp 1477-1487. (*chapter*)

Appendix B: Group II-b publications

(***Other works put forward as evidence of the scope of the candidate's contribution to the broader field of study - i.e. urogynaecology***[5])

Format	No.
Peer-reviewed original papers	93
Chapters and narrative reviews	64
Published abstracts	50
Editorial comments & letters	15
Edited books & monographs	13
Systematic reviews	13
Audio-visual materials	10
Group IIb total	248
Group I + group IIa publications	48
Other non-included publications	14
Groups I + II total	310

Table 7: Group II-b publications listed by format (above); total publications (below)

[5] Group I - Works upon which a candidate primarily bases his claim to have satisfied the standards for the award of the degree (*see Chapter 2*);

Group II - Other works put forward as evidence of the scope of the candidate's contribution:

IIa - to the specific field of study in which the primary submissions lie - *i.e.* urogenital fistula (*see Appendix A*);

IIb - to the broader field of study - *i.e.* urogynaecology (*Appendix B*).

1. Hilton P, Stanton SL. Suprapubic catheterisation. **BMJ** 1980**;** 281: 1261-1263. (*review*)
2. Hilton P, Stanton SL. Algorithmic method for assessing urinary incontinence in elderly women. **BMJ** 1980; 282: 940-942. (*peer-reviewed paper)*
3. Hilton P. (1981) Urethral pressure measurement by microtransducer: observations on methodology, the pathophysiology of genuine stress incontinence & the effects of its treatment in the female. **MD thesis**. Newcastle University – available from British Library EThOS ID: uk.bl.ethos.257745. (*thesis*)
4. Hilton P, Stanton SL. (1981) Suprapubic catheterisation. In: **Procedures in Practice.** Published by The British Medical Journal; pp 27-29. (*review*)
5. Suprapubic catheterisation. Hilton P, Stanton SL. **BMJ** (1981) **282**:479-480. (*letter)*
6. Assessing elderly incontinent patients. Hilton P, Stanton SL. **BMJ** 1981; 282:1706. (*letter)*
7. Hilton P, Stanton SL. The use of Desmopressin (DDAVP) in nocturnal urinary frequency in the female. **BJU Int** 1982; 54: 252-255. (*peer-reviewed paper)*
8. Hilton P. Urethral pressure measurement at rest: an analysis of variance. **Neurourol Urodynam** 1982; 1: 303-311. (*peer-reviewed paper; work included in MD thesis)*
9. Stanton SL, Hilton P, Norton C, Cardozo LD. Clinical and urodynamic effects of the anterior colporrhaphy and vaginal hysterectomy for prolapse with or without incontinence. **BJOG** 1982; 89: 459-463. (*peer-reviewed paper)*
10. Hilton P. Bladder function simply tested. **General Practitioner** (1982). (*review*)
11. Stanton SL, Hilton P, Hertogs K. (1982) Preliminary clinical and urodynamic results of the 'Marlex' sling procedure for stress incontinence. **BJOG** 89:775. (*published abstract)*
12. Hilton P, Stanton SL. Urethral pressure measurement by micro-transducer: the results in symptom-free women and those with genuine stress incontinence. **BJOG** 1983; 90: 919-933. (*peer-reviewed paper; work included in MD thesis)*

13. Hilton P, Stanton SL. A clinical and urodynamic evaluation of the Burch colposuspension in genuine stress incontinence. **BJOG** 1983; 90: 934-939. (*peer-reviewed paper; work included in MD thesis*)

14. Hilton P, Stanton SL. The use of intra-vaginal oestrogen cream in genuine stress incontinence. **BJOG** 1983; 90: 940-944. (*peer-reviewed paper; work included in MD thesis*)

15. Hilton P, Spathis GS, Stanton SL. Transient autonomic/sensory neuropathy in newly diagnosed insulin dependent diabetes mellitus. **BMJ** 1983; 286: 686. (*peer-reviewed paper – case report*)

16. Hilton P, Hertogs K, Stanton SL. The use of Desmopressin for nocturia in women with multiple sclerosis. **J Neurol, Neurosurg & Psych** 1983; 46: 854-855. (*peer-reviewed paper*)

17. Hilton P. Urethral pressure measurement on stress: an analysis of profiles obtained on coughing and straining. **Neurourol Urodynam** 1983; 2: 55-62. (*peer-reviewed paper; work included in MD thesis*)

18. Hilton P, Stanton SL. A clinical and urodynamic evaluation of the polypropylene (Marlex) sling for genuine stress incontinence. **Neurourol Urodynam** 1983; 2: 145-153. (*peer-reviewed paper; work included in MD thesis*)

19. Stanton SL, Ozsoy C, Hilton P. Voiding difficulties in the female: prevalence, clinical and urodynamic review. **Obstet Gynecol** 1983; 61: 144-147. (*peer-reviewed paper*)

20. Hilton P. (1984) Urethral pressure measurement. In: **Clinical Gynecologic Urology.** Edited by Stanton SL; Published by C V Mosby, St Louis pp 110-126. (*chapter*)

21. Hilton P, Varma TR. (1984) The menopause. In: **Clinical Gynecologic Urology.** Edited by Stanton SL: Published by C V Mosby, St Louis pp 343-353. (*chapter*)

22. Hilton P, Millard P. (1984) The elderly. In: **Clinical Gynecologic Urology.** Edited by Stanton SL; Published by C V Mosby, St Louis pp 354-363. (*chapter*)

23. Hilton P. A clinical and urodynamic comparison of the sub-urethral sling and Stamey endoscopic bladder neck suspension in the treatment of genuine stress incontinence. Blair-Bell Research Society, Glasgow. **BJOG** 1985; 93: 291-292. (*published abstract*)

24. Hilton P, Stanton SL (1986) **Urinary incontinence in the female: Part I – Anatomy, physiology & investigation**. Graves Medical Audio-Visual, Chelmsford, Essex. (*tape-slide presentation*)

25. Stanton SL, Hilton P (1986) **Urinary incontinence in the female: Part II - Methods of treatment.** Graves Medical Audio-Visual, Chelmsford, Essex. (*tape-slide presentation*)

26. Hilton P. Clinical algorithms: Urinary incontinence in women. **BMJ** 1987; 295: 425-432. (*peer-reviewed paper*)

27. Hilton P. (1987) The mechanism of continence. In: **Surgery for Female Urinary Incontinence**. Edited by Stanton SL, Tanagho EA; Published by Springer-Verlag, Berlin pp 1-21. (*chapter*)

28. Hilton P. (1987) Catheters and drains. In: **Principles of Gynaecological Surgery.** Edited by Stanton SL; Published by Springer-Verlag, Berlin pp 257-283. (*chapter*)

29. Hilton P. (1987) Surgery for urinary stress incontinence. In: **Operative Surgery: Gynaecology and Obstetrics**. 4th Edition, edited by Monaghan J; Published by Butterworths Scientific, London pp 105-126. (*chapter*)

30. Mayne CJ, Hilton P. A comparison of the distal urethral electrical conductance (DUEC) test with weighed pads during standardised exercise test. **Neurourol Urodynam** 1987; 6.3: 167-168. (*published abstract*)

31. Hilton P. Urinary incontinence during sexual intercourse: a common but rarely volunteered symptom. **BJOG** 1988; 95: 377-381. (*peer-reviewed paper*)

32. Hilton P. Unstable urethral pressure - towards a more relevant definition. **Neurourol Urodynam** 1988; 6: 411-418. (*peer-reviewed paper*)

33. Hilton P. Bladder drainage: a survey of practices among gynaecologists in the British Isles. **BJOG** 1988; 95: 1178-1189. (*peer-reviewed paper*)

34. Hilton P. Surgical drains: a survey of practices among gynaecologists in the British Isles. **BJOG** 1988; 95: 1063-1069. (*peer-reviewed paper)*

35. Mayne CJ, Hilton P. The distal urethral electrical conductance (DUEC) test: standardisation of method and clinical reliability. **Neurourol Urodynam** 1988; 7: 55-60. (*peer-reviewed paper)*

36. Mayne CJ, Hilton P. The short pad test: standardisation of method and a comparison with the one-hour test. **Neurourol Urodynam** 1988; 7: 443-445. (*peer-reviewed paper)*

37. Hilton P. (1988) Suprapubic catheterisation. In: **Procedures in Practice**. 2nd Edition. Published by The British Medical Journal pp 140-150. (*chapter*)

38. Hilton P, Mayne CJ. (1988) Urethral pressure variations: the correlation between pressure measurement and electrical conductance in genuine stress incontinence. **Neurourol Urodynam** 7.3: 175-176. (*published abstract)*

39. Mayne CJ, Hilton P. A comparison of urethral electrical conductance and perineometry during pelvic floor exercises for genuine stress incontinence. **Neurourol Urodynam** 1988; 7.3: 264-269. (*published abstract)*

40. Hilton P, Tweddell AL, Mayne CJ. The effect of oral and intra-vaginal oestrogens and their influence on alpha-adrenoreceptor stimulation in genuine stress incontinence. **Int Urogynecol J & Pelvic Floor Dysfunct** 1988; 1.1: 36. (*published abstract)*

41. Hilton P. A clinical and urodynamic study comparing the Stamey bladder neck suspension and sub-urethral sling procedures in the treatment of genuine stress incontinence. **BJOG** 1989; 96: 213-220. (*peer-reviewed paper)*

42. Hilton P. Sexuality and urinary incontinence. **Brit J Sex Med** 1989; 16: 230-233. (*review*)

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Appendix C: Candidate's complete cohort of patients with urogenital fistulae referred and managed in UK

i.e. updated from included paper 3, to cover the period 1985 to 2015.

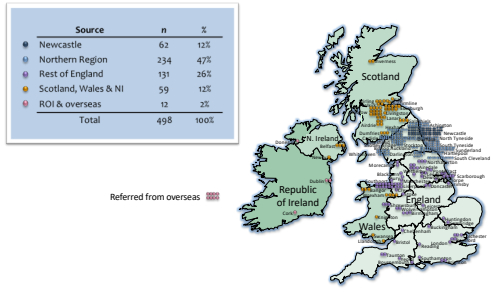
Newcastle fistula referrals 1985-2015

data updated to March 2015 from that published in 2012.†

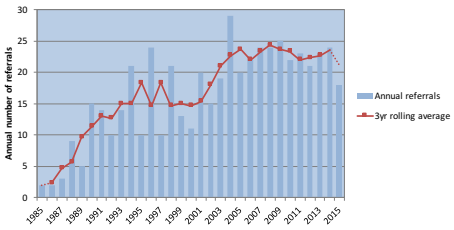
† Hilton P. Urogenital fistula in the UK - a personal case series managed over 25 years. **BJU Int.** 2012;110(1):102-110.

Newcastle fistula referrals 1985-2015

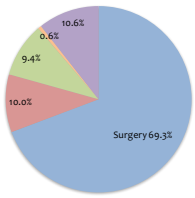
Source	n	%
Newcastle	62	12%
Northern Region	234	47%
Rest of England	131	26%
Scotland, Wales & NI	59	12%
ROI & overseas	12	2%
Total	498	100%



Newcastle fistula referrals 1985-2015

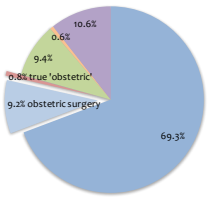


Aetiology of fistulae



	n	%
Surgery	345	69.3%
Obstetric	50	10.0%
Radiation	47	9.4%
Malignant	3	0.6%
Miscellaneous	53	10.6%
	498	100.0%

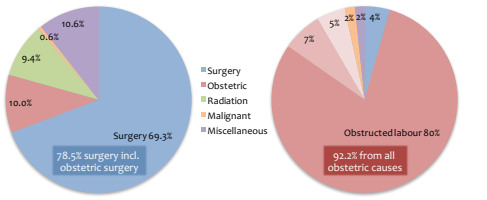
Aetiology - obstetric



Obstetric	
Caesarean section	24
Ruptured uterus	9
Forceps/ventouse	6
Caesarean hysterectomy	5
Symphysiotomy	2
Obstructed labour	2
Breech extraction	1
Placental abruption	1
subtotal	50

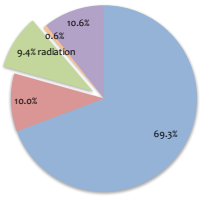
True 'obstetric' Obstetric surgery

Aetiology of fistulae



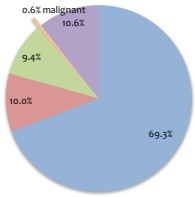
Hilton, 2018; Hilton & Ward, 1998

Aetiology - radiation



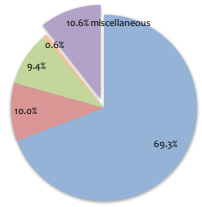
Radiation	
Ca cervix	39
Ca endometrium	7
Multifocal ca	1
subtotal	47

Aetiology – malignant



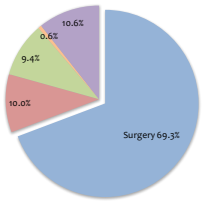
Radiation	
Ca cervix	39
Ca endometrium	7
Multifocal ca	1
subtotal	47
Malignant	3
Endometrium, ovary, rectum	

Aetiology - miscellaneous



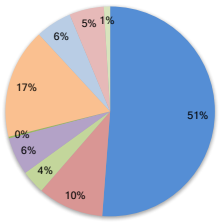
Miscellaneous	
Vaginal pessary	20
Foreign body	9
Infection	7
Congenital	6
Catheter induced	4
Trauma	3
Unexplained	3
Coital injury	1
subtotal	53

Aetiology - surgery



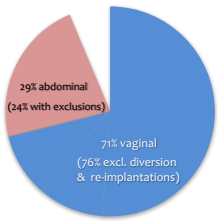
Surgical	
Abdominal hysterectomy	181
Radical hysterectomy	27
LAVH/TLH	18
Vaginal hysterectomy	9
Cervical stumpectomy	5
Subtotal hysterectomy	4
TAH and colporrhaphy	1
TAH and colposuspension	1
Colporrhaphy	19
Mid-urethral tape procedures	10
Colporrhaphy with mesh (+TVM)	4
Cystoplasty and colposuspension	3
Sling	2
Colposuspension	2
Needle suspension	2
Periurethral bulking agents	2
Sacrospinous fixation	1
Sub-trigonal phenol injection	1
Colectomy	14
LLETZ	7
Partial vaginectomy	6
Colovaginoplasty	3
Ileoanal pouch	3
Nephroureterectomy	2
Laparoscopic oophorectomy	1
Lithoclast	1
Unknown surgery in childhood	1
Urethral diverticulectomy	16
subtotal	345

Route of primary fistula surgery



- Vaginal layer dissection
- Vaginal + Martius graft
- Urethral reconstruction
- Colpocleisis
- Urethrocleisis + SPC
- Transperitoneal +/- omentum
- Transvesical
- Ureteric re-implantation/stent
- Primary urinary diversion

Route of primary fistula surgery



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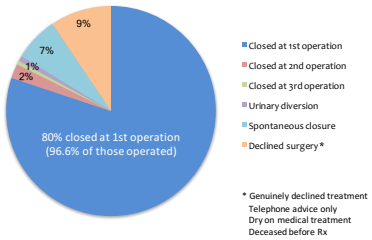
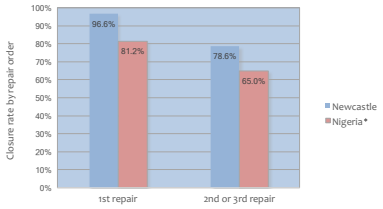
Results of surgery - overall



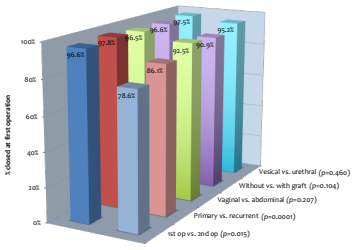
* Genuinely declined treatment
Telephone advice only
Dry on medical treatment
Deceased before Rx

Results of surgery - by procedure

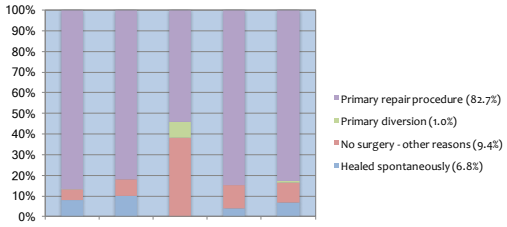


Hilton & Ward, 1998

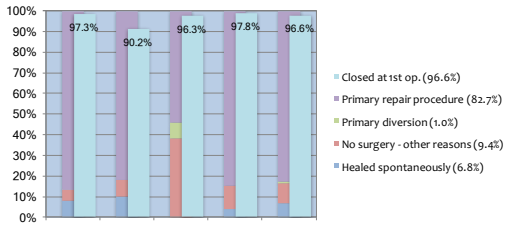
Results of surgery – other variables



Results of surgery – by aetiology



Results of surgery – by aetiology



Results of surgery – by aetiology