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Patients with surgical wounds healing by secondary intention: A prospective, cohort study

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ABSTRACT

Background: Surgical wounds healing by secondary intention can be difficult and costly to manage and are profoundly under researched. This prospective inception, cohort study aimed to derive a better understanding of surgical wounds healing by secondary intention and to facilitate the design of future research investigating effective treatments.

Objectives: To investigate the clinical characteristics of patients with surgical wounds healing by secondary intention and the surgeries that preceded their wounds; to clearly delineate the clinical outcomes of these patients, specifically focusing on time to wound healing and its determinants; to explore the types of treatments for surgical wounds healing by secondary intention; and to assess the impact surgical wounds healing by secondary intention have on patients' quality of life.

Design: Prospective, inception cohort study.

Setting: Acute and community settings in eight sites across two large centres in the United Kingdom (Hull and Leeds, UK).

Methods: Patients with a surgical wounds healing by secondary intention (an open wound, <3 weeks' duration, resulting from surgery), were recruited and followed up for at least 12 months. Key outcome events included: time to healing; treatment type; infection; hospital re-admission and further procedures; health-related quality of life and pain.

Results: In total, 393 patients were recruited. Common co-morbidities were cardiovascular disease (38%), diabetes (26%) and peripheral vascular disease (14.5%). Baseline median SWHSI area was 6 cm^2 (range 0.01–1200). Abdominal (n = 132), foot (n = 59), leg (n = 58) and peri-anal (n = 34) wounds were common. The majority of wounds (236, 60.1%) were intentionally left open following surgery; the remainder were mostly dehisced wounds. Healing was observed in 320 (81.4%) wounds with a median time to healing of 86 days (95% CI: 75–130). Factors associated with delayed healing included wound infection at any point and baseline wound area above the median. Health-related quality of life scores were low at baseline but improved with time and healing.

Conclusions: This is the first inception cohort study in patients with surgical wounds healing by secondary intention. Patient characteristics have been clearly defined, with prolonged healing times and adverse events being common impacting on patient's health-related quality of life. Areas for, and factors crucial to the design of, future research have been identified.

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What is already known about the topic?

- Although surgical wounds healing by secondary intention are common, there is limited evidence describing the characteristics of patients or the frequency of different wound types.
- Evidence is also limited with regards the healing rates of surgical wounds healing by secondary intention and prognostic factors for healing.

What this paper adds

- The researchers have identified that surgical wounds healing by secondary intention are often planned (60.0%) and often occur following colorectal or vascular surgeries (39.7% and 20.9%).
- Time to healing of surgical wounds healing by secondary intention is often prolonged (median 86 days), and healing of foot wounds appears to be particularly problematic.
- The findings identified will help to guide the design and planning of future research studies and have highlighted areas where further investigation is warranted.

1. Introduction

Almost ten million surgical operations are performed each year within the United Kingdom (UK) National Health Service (NHS Confederation, 2016), with an estimated 313 million surgical operations being performed globally each year (Wieser et al., 2016). The majority of surgical wounds heal by primary intention following the apposition of the wound edges with clips, sutures, glue or adhesive dressings (Salcido, 2017). However a large number of surgical wounds heal by secondary intention e.g. when primary closure is not possible, or following wound dehiscence. Local audits of hospital and community UK National Health Service organisations have estimated that surgical wounds healing by secondary intention comprise approximately 28% of all prevalent surgical wounds receiving care in in-patient or community settings (Srinivasaiah et al., 2007; Vowden and Vowden, 2009).

Whilst surgical wounds healing by secondary intention are common, there are few national or international data that describe the characteristics of patients with surgical wounds healing by secondary intention or the frequency of different wound types. Furthermore little is known about the natural history or the healing rates of these wounds, and of the limited available evidence, time to healing has often been inaccurately analysed. As with wound care research more generally, there are little good epidemiological data that explore which factors are prognostic for healing. This therefore makes it almost impossible to plan new treatment trials.

Traditional management of surgical wounds healing by secondary intention involves daily or more frequent dressing changes, sometimes with packing of the wound cavity. There are different dressing options, from simple dressings such as non-adherent dressings to more modern options such as foam, hydrocolloid, alginate or negative pressure dressings. However, again there are data on which treatments are being used and how frequently. There is limited randomised controlled trial data on treatments for surgical wounds healing by secondary intention, and where these have been conducted the trials are frequently found to be underpowered and poorly designed making interpretation of the findings difficult. As a result systematic reviews exploring relative treatment effects of traditional treatments like dressings, antibiotics and antiseptics report sparse data and thus present uncertainty regarding the clinical and cost effective treatments for surgical wounds healing by secondary intention (Dumville et al., 2015; Norman et al., 2016; Vermeulen et al., 2005).

The current lack of high quality information regarding surgical wounds healing by secondary intention is a major impediment to optimising care and service delivery, communicating with patients and planning future research. There is clearly a need for broad spectrum data collection on a cohort of patients with surgical wounds healing by secondary intention.

The objectives of this prospective cohort study were:

a) To investigate the clinical characteristics of patients with surgical wounds healing by secondary intention and the surgeries that preceded their wounds
b) To clearly delineate the clinical outcomes of patients with surgical wounds healing by secondary intention, specifically focusing on time to wound healing and its determinants
c) To explore the types of treatments those with surgical wounds healing by secondary intention are receiving
d) To assess the impact surgical wounds healing by secondary intention have on patients' quality of life

2. Methods

2.1. Study design and setting

This prospective, inception, cohort study recruited consenting patients with an incident surgical wound healing by secondary intention from acute and community settings in eight sites across two large UK centres (Hull and Leeds, UK), over a nine month recruitment period. An inception cohort approach was used to enable accurate assessment of SWHSI duration, time to healing, and to provide comprehensive detail regarding treatments received over the natural history of the wound. While a prevalence cohort would have enabled increased recruitment, it would however have provided far less clarity on crucial outcomes, such as time to healing, important in this population.

Participants were followed up for a minimum of 12 months and a maximum period of 21 months. The study commenced on 18th February 2013 and completed 30th November 2014.

2.2. Participants

Patients were eligible for inclusion if they were over 18 years old and had an incident surgical wound healing by secondary intention, defined as "an acute (<3 weeks' duration), open wound resulting from surgery and requiring treatment, which was healing from the bottom up by the formation of granulation tissue". This definition included wounds left open after surgery with no primary closure planned, wounds that were originally closed but not healed and subsequently were opened or dehisced (partially or fully), and existing wounds that underwent surgical debridement e.g. foot wounds in people with diabetes. Exclusion criteria were: wounds with planned delayed primary closure or left open without planned healing (e.g. stoma, tracheotomy or gastrostomy); surgery that did not involve an incision on the skin surface (internal wounds such as tonsillectomy, dilation or curettage); surgical operations involving the eye (i.e. cataract surgery and removal of the eyeball); wounds resulting from minor dermatological or plastic surgery (e.g. removal of warts, skin tags) or diagnostic procedures (e.g. punch biopsy); recurrence of a previously healed surgical wound healing by secondary intention and patients who had been previously recruited into this study.

Health care professionals, as part of the patients clinical care team initially identified and screened potential participants for eligibility. Those meeting all of the inclusion criteria and none of

the exclusion criteria, and who provided verbal assent, were approached by a study research nurse who provided further details about the study and obtained full written informed consent from those potential participants who were willing to take part.

2.3. Assessments

2.3.1. Baseline assessment

At baseline participants' personal, clinical and surgical details were recorded using a secure on-line management database system. Clinical details included participants' height, weight and body mass index, tobacco use and co-morbidities such as diabetes or cardiovascular disease. The use of specific medication was also recorded (chemotherapy, non-steroidal anti-inflammatory, anti-coagulant/anti-platelet, corticosteroid, immunosuppressive and vasodilator medications). Surgical details included date and (sub) speciality of surgery, reason for the surgical wound healing by secondary intention, urgency and level of contamination of surgery (clean, clean-contaminated, contaminated or, dirty (Mangram et al., 1999), the name of the surgical procedure, and details of surgical implants (i.e. mesh, stent, prosthesis or other).

The study research nurses completed a prospective wound assessment which recorded the anatomical location of the surgical wound healing by secondary intention and the extent to which it penetrated and/or exposed underlying tissues (i.e. subcutaneous, muscle, tendons, bone or organs). Data was collected using a bespoke data collection tool designed for the purposes of this study. Clinical signs of infection were assessed at the wound (e.g. erythema, purulent discharge) and patient (e.g. pyrexia, tachycardia, hypotension) level in accordance with Health Protection Agency guidance on surgical site infection surveillance (Public Health England, 2013). The area of the surgical wound healing by secondary intention was determined using a wound measurement grid (Comfeel® Wound Care Grid, Coloplast Limited, Peterborough, UK). Wound treatment at baseline was also recorded. When a participant had more than one surgical wound healing by secondary intention this was noted and wound-specific study follow-up data collected on the largest wound (in terms of area) which was called the reference.

At baseline, participants' health-related quality of life were assessed using two generic preference-based, self-completion health-related quality of life instruments, the Short Form -12 v2 and the EuroQol-5D-3L. The Short Form -12 contains a subset of 12 items from the SF-36® questionnaire and assesses eight domains of health to construct physical and mental component summary measures of health (Ware et al., 1996). Physical component scores and mental component scores range from 0 (lowest level of health) to 100 (highest level of health). The Short Form -12 has been used to assess health-related quality of life in various patient populations) (Failde et al., 2010; Gandek et al., 1998; Grozdev et al., 2012; Hagell and Westergren, 2011; Konig et al., 2010; Niles et al., 2013; Pezzilli et al., 2006; Ware et al., 1996). The EuroQol-5D-3L consists of a descriptive system evaluating five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Participants report on their current health state for each dimension, selecting one of three possible levels (EuroQol Group, 2014). The EuroQol -5D-3L is a widely used tool for the assessment of health status and has been validated in many different patient groups (Hurst et al., 1997; Johnson and Pickard, 2000; Konig et al., 2002, 2010; Mahadeva et al., 2009; Oster et al., 2009; Prieto et al., 2004; Schweikert et al., 2006; van Agt et al., 1994).

Level of pain was assessed using a Brief Pain Inventory (Cleeland, 2009).The Brief Pain Inventory rates pain over a 24-h recall period, on a scale from 0 to 10, in relation to four pain severity and seven pain interference items (e.g. on what scale the pain interfered with activity, mood, sleep, etc.). Mean pain interference and pain severity scores are calculated and range between 0 and 10 with higher scores indicating more pain or interference respectively (Cleeland, 2009).

2.3.2. Outcome assessments

During follow-up, clinical and questionnaire based data were collected. A key clinical outcome of interest was wound healing, defined as complete epithelial coverage in the absence of a scab (eschar). Healing could be reported by health professionals or self-reported by participants. Where self-reporting took place, healing was verified by a health professional according to the definition. Treatments related to the surgical wound healing by secondary intention were recorded throughout follow-up, with treatment type, duration, and reason for treatment change recorded. Other important clinical events recorded during follow-up were wound infection, hospital admission, return to operating theatre and death. Study research nurses were responsible for collecting clinical data as close to real time as possible and obtained this information directly from the participants, their healthcare providers, or their medical and nursing notes. Participants also carried research booklets with data collection forms and could ask their treating healthcare professionals to complete the appropriate forms when required. Once healed, participants' were followed up for health-related quality of life and recurrence data (via monthly phone calls) only.

Health-related quality of life and pain questionnaires were collected via post with pre-paid envelopes at three monthly intervals. To limit attrition bias, non-responders were sent reminder letters after two and four weeks and a supplementary telephone call was made to those who did not respond to the second reminder, offering help in completing the questionnaires. Patients were sent an unconditional £5 with their final questionnaire in order to maximise response rates (Edwards et al., 2009).

2.4. Statistical methods

Analyses and summary statistics were produced in Stata version 13 (Stata Corporation, 2013). The analytical approach was exploratory and mainly descriptive; significance was assessed at the 5% level unless otherwise stated. Baseline data are presented using appropriate summary statistics (median, minimum and maximum for continuous variables and frequencies and percentages for categorical data). Types of treatments used over the study period and reason for changes were summarised using frequencies and percentages. The mean number of treatment changes taking into account length of follow-up is presented.

The proportion of participants whose surgical wound healing by secondary intention healed within the study follow-up period is presented both for the entire study population and stratified by pre-specified potential prognostic factors. Factors explored were age, sex, body mass index, diabetes, tobacco use, cardiovascular disease, peripheral vascular disease, wound location, contamination level of the surgery leading to the surgical wound healing by secondary intention, whether the surgery was elective or emergency, the reason for the surgical wound healing by secondary intention, wound infection, history of previous surgical wounds healing by secondary intention and baseline wound area. Chi-square and *t*-tests were used to assess differences in healing in relation to these pre-specified factors for categorical and continuous outcomes respectively. Significance was assessed at the 10% level, given the exploratory nature of these analyses. Any factors found to be associated with healing were included in a multivariate logistic regression model with healing status as the response variable, conducted on complete cases. Assessing the univariate analyses at the 10% significance level ensured variables were not

unduly excluded from this adjusted analysis for reasons such as confounding. The 10% significance level was also used to ensure that the univariate analysis allowed for a higher possibility of a chance significant finding, thus ensuring that such findings could be further explored within a multivariate analysis.

Time to healing is also presented with right censoring for participants who died, were lost to follow-up, withdrew from the study or who had not healed by the end of follow-up. An unadjusted Kaplan-Meier estimate of median time to healing is presented alongside a 95% confidence interval. Log-rank tests were used to assess differences in time to healing in relation to the pre-specified factors listed above with significance again assessed at the 10% level. Any factors found to be associated with time to healing were included in a Cox proportional hazards regression model.

Key clinical outcomes are presented in terms of proportion of participants experiencing each event.

Participant Short Form -12 physical and mental component scores were summarised at each time point and are presented for all participants and also stratified by time to healing (above/below median). Separate random intercept linear mixed models were conducted to investigate physical and mental component scores-over time; models were adjusted for the baseline values of physical and mental component scores (respectively), duration of the surgical wound healing by secondary intention, participant age, wound area and wound location. Participant EuroQol- 5D-3L utility scores (derived using the UK tariff), as well as Brief Pain Inventory severity and interference scores were summarised at each time point.

2.5. Regulatory approvals

This study was approved by the National Research Ethics Service Committee (Yorkshire and The Humber - Humber Bridge) on the 12/09/2012 (Reference number 12/YH/0350). The study was subsequently reviewed by each study sites' organisational research management and governance body and National Health Service permission was granted for each study site. This study was also included on the National Institute for Health Research Clinical Research Network Portfolio 20/12/2012 ID 13679.

3. Results

3.1. Baseline assessment

3.1.1. Participants

Between 18th February and 25th November 2013, 396 participants were recruited. Three were later excluded from the final data set since their surgical wound healing by secondary intention had been present for longer than the 3 weeks specified in the inclusion criterion at recruitment. As shown in Table 1, of the remaining 393 participants, 222 (56.5%) were men, the median age was 55 years (range 19–95) (mean 54.1 years; SD 18.2) and the median body mass index was 28.9 (range 15.4–53.0) (mean 28.9; SD 6.6). Nearly three-quarters of the cohort had no previous history of surgical wounds healing by secondary intention (n = 283/393, 72.0%). At baseline 286 (72.8%) participants had at least one co-morbidity and with two-thirds (67%) suffering multiple co-morbidities (Table 1). The most common co-morbidities at baseline were cardiovascular disease, diabetes and respiratory conditions. One hundred and twelve participants (28.5%) were current smokers. Medication use at baseline was reported in 69.2% (n = 272) of the study population. The most common medication was anti-platelets / anti-coagulants (n = 196/393, 49.9%). The number of participants taking steroids, immunosuppressants or chemotherapy was low (Table 1).

3.1.2. Wounds

The median number of surgical wounds healing by secondary intention per person was 1 (range 1–6) (mean 1.1; SD 0.5). The median area of the reference surgical wound healing by secondary intention was 6 cm^2 (range 0.01–1200) (mean 32 cm^2; SD 94.9 cm^2) (Table 2). Abdominal wounds were the most prevalent location (n = 132/393, 33.6%), with other common locations being foot (n = 59/393, 15.0%), leg (n = 58/393, 14.8%) and peri-anal area (n = 34/393, 8.7%). As detailed in Table 2, planned surgical wounds healing by secondary intention accounted for 236 (60.0%) of cases with a relatively equal split between those planned due to infection / contamination (n = 119/393, 30.3%) and those planned as the wound edges could not be approximated (n = 112/393, 28.5%). Approximately a third of surgical wounds healing by secondary intention were attributable to partial (n = 120/393, 30.5%) or full (n = 21/393, 5.3%) wound dehiscence. Only a small number (n = 16/393, 4.1%) of wounds had been surgically reopened. Antibiotics were prescribed at baseline for 182 (46.3%) participants, most commonly by the oral route (n = 126/393, 32.1%), with 155 prescriptions related to the surgical wound healing by secondary intention (Table 2). Hospital wards were the most frequent treatment site at baseline (n = 229/393, 58.3%) however 88 (22.4%) participants were being treated in their own home. The most commonly utilised dressings for surgical wounds healing by secondary intention at baseline were hydrofibre / spun hydrocolloid (n = 164/393, 41.7%), wound contact dressings (i.e. non-adherent) (n = 129/393, 32.8%) and Negative Pressure Wound Therapy (n = 114/393, 29.0%) (Table 2).

3.1.3. Surgery leading to *surgical wounds healing by secondary intention*

As shown in Table 3, colorectal (n = 156/393, 39.7%) and vascular (n = 82/393, 20.9%) were the most frequently represented surgical specialities, together accounting for almost two thirds of cases. In terms of urgency and contamination, emergency surgery (n = 236/393, 60.1%) and “dirty” (n = 247/393, 62.9%) surgery were most common (Table 3).

3.2. Follow up outcome assessment

3.2.1. Participants

Sixty six (16.8%) participants were not followed-up for the entire study duration; 31 withdrew, 29 died, and 6 were lost to follow up. Median length of follow up was 528 days (range 13–651). SWHSI infection occurred in 126 (32.1%) participants during the study period, with 79 (62.7%) cases present at baseline. Hospital re-admissions were reported for 97 (24.7%) participants, 36 (37.1%) of these were related to a surgical wound healing by secondary intention. A return to operating theatre was reported for 66 (16.8%) participants. Amputation of the limb where the reference surgical wound healing by secondary intention was located was undertaken in 13 (3.3%) participants.

3.2.2. Wound treatments

Fifty-two (13.2%) participants remained on the same type of dressing throughout the study period. Participants had a median of 0.9 changes (range 0–9) of type of dressing per month of follow up. Twelve participants had their first change of dressing type on the day of baseline data collection. Excluding these participants, the median number of days to first change of dressing type (accounting for censoring) was 13 (95% CI: 11–17 days). Common reasons for change of dressing type, which were specified on the reporting documentation, included infection (n = 174/393, 44.3%), healing (n = 169/393, 43.0%), a need for wound protection (n = 136/393, 34.6%) and exudate management (n = 115/393, 29.3%) (See Supplementary Table S1). “Other” reasons for changing the

Table 1
Patient Baseline Characteristics.

Variable	Patients (n = 393)
Age (years)	
mean (SD)	54.1 (18.2)
median (range)	55.0 (19.0–95.3)
Gender	**n (%)**
Male	222 (56.5%)
Female	171 (43.5%)
Body Mass Index	
mean (SD)	28.9 (6.6)
median (range)	28.1 (15.4–53.0)
History of Surgical Wounds Healing by Secondary Intention	**n (%)**
Yes	93 (23.7%)
No	283 (72.0%)
Don't know	17 (4.3%)
Tobacco use (%)	**n (%)**
None in last 10 years	219 (55.7%)
None current but in last 10 years	62 (15.8%)
Current (<1 pack/day) or quit in last year	84 (21.4%)
Current (>1 pack/day)	28 (7.1%)
Baseline comorbidities	Patients (n = 286)[a] n (%)
Cardiovascular disease	151 (38.4%)
Diabetes	103 (26.2%)
Airways (e.g. Asthma)	69 (17.6%)
Arthritis	65 (16.5%)
Peripheral vascular disease	57 (14.5%)
Cancer	51 (13.0%)
Orthopaedic (e.g. fractures)	27 (6.9%)
Stroke	20 (5.1%)
Auto-immune	19 (4.8%)
Neurological	11 (2.8%)
Other	31 (7.9%)
Medications Used	Patients (n = 272)[b] n (%)
Anti-coagulants/anti platelets	196 (49.9%)
Vasodilator	111 (28.2%)
Non-Steroidal Anti-Inflammatory Drugs	66 (16.8%)
Corticosteroids	11 (2.8%)
Immuno-suppressant	9 (2.3%)
Cytotoxic	5 (1.3%)

[a] N is less than total sample – 107 patients without associated comorbidity.
[b] N is less than total sample – 121 patients did not report medication use.

dressing type, which were not pre-specified, were also common (n = 251/393, 63.9%) and included allergic reactions, completion of course of antibiotics or patient preference (See Supplementary Table S1). As detailed in Supplementary Table S1, the most commonly used dressing types for surgical wounds healing by secondary intention across the whole study period were hydrofibre and basic wound contact (i.e. non-adherent) dressings, which were received at least once by 259 (65.9%) and 212 (53.9%) participants respectively. Antimicrobial dressings (those containing silver, iodine or honey) were used at some time in 148 (37.7%) participants and Negative Pressure Wound Therapy in 115 (29.3%) participants (See Supplementary Table S1).

3.2.3. Healing

Healing of the reference surgical wound healing by secondary intention occurred in 320 (81.4%) participants during study follow up (See Supplementary Table S2). Of the 73 participants who did not heal, 16 died (21.9%), one was lost to follow-up (0.3%) and three withdrew (4.1%) (See Supplementary Table S2). The median time to healing from wound start date was 86 days (95% CI: 75–130) (See Fig. 1). Recurrence of a surgical wound healing by secondary intention following healing occurred in 41 (12.9%) participants.

3.2.3.1. Patient factors and healing. In a univariate analysis, detailed in Supplementary Table S2, there was an association between healing status and diabetes ($p < 0.01$), Cardiovascular Disease ($p = 0.06$) and Peripheral Vascular Disease ($p = 0.02$). A lower proportion of SWHSI healed in participants with diabetes, cardiovascular disease, and peripheral vascular disease compared to those without. It is likely that an association exists between time to healing and gender ($p = 0.04$), diabetes ($p < 0.01$) and cardiovascular disease ($p = 0.04$). Median time to healing was longer in men than women (13 days), in diabetic compared to non-diabetic participants (61 days) and in participants with cardiovascular disease compared to those with no history of cardiovascular disease (33 days) (See Supplementary Table S2).

3.2.3.2. Surgery, wound factors and healing. In univariate analyses, there was an association between healing status and infection at any point ($p < 0.01$), baseline wound area ($p < 0.01$) and the reason for the surgical wound healing by secondary intention ($p < 0.01$)

Table 2
Wound Baseline Characteristics.

Variable	Patients (n = 393)
Number of Surgical Wounds Healing by Secondary Intention	
mean (SD)	1.1 (0.5)
median (range)	1 (1–6)
Area (cm^2)	
mean (SD)	32 (94.9)
median (range)	6 (0.01–1200)
Surgical Wound Healing by Secondary Intention Location (%)	**n (%)**
Abdomen	132 (33.6%)
Foot	59 (15.0%)
Leg	58 (14.8%)
Peri-anal	34 (8.7%)
Back	19 (4.8%)
Natal cleft	16 (4.1%)
Buttocks	16 (4.1%)
Breast	7 (1.8%)
Arm	5 (1.3%)
Perineum	5 (1.3%)
Head	3 (0.8%)
Hand	2 (0.5%)
Neck	2 (0.5%)
Missing	35 (8.9%)
Aetiology (%)	**n (%)**
Planned	236 (60.0%)
Dehisced	141 (35.9%)
Surgically re-opened	16 (4.1%)
Tissue Involvement (%)	**n (%)**
Full thickness	235 (59.8%)
Muscle, tendon or bone exposed	120 (30.5%)
Organ exposed	1 (0.3%)
Unsure	35 (8.9%)
Missing	2 (0.5%)
Infection at Baseline (%)	**n (%)**
Yes	79 (20.1%)
No	314 (79.9%)
Antibiotics Used at Baseline (%)	**n (%)**
Yes	182 (46.3%)
No	211 (53.7%)
Dressing (%)	**n (%)**
Hydro-fibre/spun hydrocolloid	164 (41.7%)
Other	129 (32.8%)
Wound contact (i.e non-adherent dressing)	114 (29.0%)
Negative Pressure Wound Therapy	89 (22.7%)
Foam	36 (9.2%)
Alginate	27 (6.9%)
Silver containing	23 (5.9%)
Iodine impregnated dressings	19 (4.8%)
Soft polymer	19 (4.8%)
Hydrocolloid	10 (2.5%)
Superabsorbent	7 (1.8%)
Cavity foam	4 (1.0%)
Hydrogel	1 (0.3%)
Silver sulfadiazine	1 (0.3%)
Treatment Environment (%)	
Hospital inpatient	229 (58.3%)
Home	88 (22.4%)
General Practitioner	55 (14.0%)
Hospital outpatient	11 (2.8%)
Other	8 (2.0%)
Missing	2 (0.5%)

(See Supplementary Table S3). A lower proportion of surgical wounds healing by secondary intention healed if there was infection at any point or if the baseline wound area was above the median. A higher proportion of surgical wounds healing by secondary intention due to partial dehiscence healed than surgical wounds healing by secondary intention due to other causes. It is likely that an association exists between time to healing and infection at any point ($p < 0.01$), wound area at baseline ($p < 0.01$), reason for the surgical wound healing by secondary intention ($p < 0.01$) and surgical contamination ($p < 0.01$) (See

Table 3
Surgery Baseline Characteristics.

Variable	Patients (n = 393)
Sub speciality (%)	**n (%)**
Colorectal	156 (39.7%)
Vascular	82 (20.9%)
Other	50 (12.7%)
Plastics	33 (8.4%)
Orthopaedic	17 (4.3%)
Obstetrics and Gynaecology	13 (3.3%)
Surgical debridement	11 (2.8%)
Upper GI	7 (1.8%)
Urology	7 (1.8%)
Cardiothoracic	7 (1.8%)
Neurosurgery	3 (0.8%)
Thoracic	3 (0.8%)
Breast	2 (0.5%)
Trauma	1 (0.3%)
Oral and maxillofacial	1 (0.3%)
Surgery Type (%)	**n (%)**
Emergency	236 (60.1%)
Elective	135 (34.4%)
Missing	22 (5.6%)
Contamination Level (%)	**n (%)**
Dirty	247 (62.9%)
Contaminated	65 (16.5%)
Clean-contaminated	51 (13.0%)
Clean	26 (6.6%)
Missing	4 (1.0%)

Supplementary Table S3). Median time to healing was longer in surgical wounds healing by secondary intention that were infected at any point than those which were not infected (52 days), and longer in surgical wounds healing by secondary intention with a baseline area above the median compared with those with a baseline area below the median (88 days). Time to healing was shortest at 54 days for planned surgical wounds healing by secondary intention due to infection and longest at 148 days for those planned due to being unable to approximate wound edges; and was shortest for clean surgery (55 days) and longest for surgery classified as contaminated (106 days) (See Supplementary Table S3).

Due to small numbers in certain categories it was not possible to formally examine the association between wound location and healing status or time to healing. For wound locations observed in more than 10 participants (abdomen, foot, leg, perianal area, back, natal cleft, buttocks) proportions healing with foot wounds were the lowest at 57.6% and highest in back wounds at 94.7% (See Supplementary Table S3). Median time to healing was shortest in perianal surgical wounds healing by secondary intention at 41 days and longest in foot wounds at 182 days (See Supplementary Table S3).

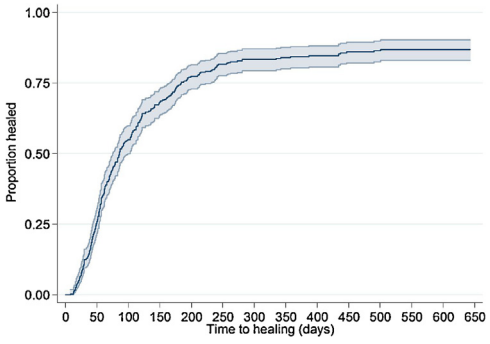

Fig. 1. Kaplan-Meier curve of time to healing in days.
*Band represents the associated 95% Confidence Interval.

3.2.3.3. Adjusted analyses. Factors associated with healing status in univariate analyses at the 10% significance level (diabetes, cardiovascular disease, peripheral vascular disease, wound infection at any point, baseline wound area and reason for the surgical wound healing by secondary intention) were included as covariates in a multivariate logistic regression model. After adjustment peripheral vascular disease ($p = 0.02$), infection at any point ($p < 0.01$), baseline wound area above the median of 6cm^2 ($p < 0.01$) and reason for the surgical wound healing by secondary intention ($p = 0.01$) (See Table 4). Odds of healing were lower for participants with peripheral vascular disease, with wound infection at any point, and with a baseline wound area above the median (See Table 4). Those with wounds planned due to infection, dehisced wounds (partially or fully) and surgically opened wounds had higher odds of healing than those with wounds planned due to inability to approximate the wound edges (See Table 4).

Factors found to be associated with time to healing (diabetes, gender, cardiovascular disease, infection at any point, baseline wound area, reason for the surgical wound healing by secondary intention and surgery contamination level) were included as covariates in a Cox proportional hazards regression model. As detailed in Table 4, after adjustment, factors persistently associated with prolonged time to healing included wound infection at any point ($p < 0.01$), baseline wound area above the median ($p < 0.01$) and high surgical contamination level ($p = 0.04$). The risk of not healing at any given time was 35% higher for surgical wounds healing by secondary intention with infection at any point compared to those without, and 64% higher for those wounds with baseline area above the median compared to those below. Risk of not being healed at any given time was also higher for surgical wounds healing by secondary intention associated with clean-contaminated, contaminated and dirty surgery compared with clean surgery (See Table 4).

3.3. Health-Related Quality of life and pain outcomes

Return rates of questionnaires reduced over time. Return rates at baseline were 392/393 (99.7%), at 3 months 275/384 (71.6%), at 6 months 234/377 (62.1%), at 9 months 228/368 (62.0%), at 12 months 195/348 (56.0%), at 15 months 154/267 (57.7%), at 18 months 81/149 (54.4%) and at 21 months 5/8 (62.5%).

3.3.1. Short form -12 results

Both median Short Form -12 physical and mental component scores improved over time and participants with shorter than median time to healing had higher (better health-related quality of life) Short Form -12 physical and mental component scores at each time point, compared to participants with a longer than median time to healing (See Supplementary Table S4).

Follow-up time point was found to be a significant predictor of physical health ($p < 0.001$), when age, duration of the surgical wound healing by secondary intention, baseline area and location, and baseline physical health score ($n = 281$), were adjusted for. Follow up time point was also found to be a significant predictor of mental health ($p = 0.03$).

Baseline physical component score, age and duration of the surgical wound healing by secondary intention duration were also found to be significant predictors ($p < 0.001$) of physical health score. Physical component score increased by 0.48 for each unit increase in baseline physical component score, decreased by −0.28 for each unit increase in age, and decreased by −0.01 for each day increase in wound duration. Baseline mental component score, age

Table 4
Multivariate analyses for predictors of healing and time to healing.

	Predictors of Healing		Time to Healing	
Covariate	Odds ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value
Diabetes present (vs not)	0.59 (0.31, 1.11)	0.10	0.81 (0.61, 1.08)	0.16
Cardiovascular disease present (vs not)	1.05 (0.56, 1.97)	0.88	1.03 (0.81, 1.22)	0.79
Peripheral vascular disease present (vs not)	0.42 (0.20, 0.88)	0.02		
Infection at any point (vs not)	0.41 (0.23, 0.74)	<0.01	0.65 (0.51, 0.84)	<0.01
Area above median (vs below)	0.40 (0.21, 0.77)	0.01	0.46 (0.36, 0.59)	<0.01
Reason for the surgical wound healing by secondary intention				
Planned due to infection	2.18 (1.06, 4.47)	0.01	1.35 (0.96, 1.89)	0.29
Planned for other reason[a]	0.28 (0.04, 1.87)		0.43 (0.10, 1.76)	
Dehisced	1.94 (0.59, 6.43)		1.16 (0.68, 1.97)	
Partially dehisced	6.36 (2.71, 14.94)		1.24 (0.89, 1.75)	
Surgically opened	1.37 (0.39, 4.76)		0.86 (0.46, 1.61)	

[a] Unable to approximate the wound edges.

and wound duration were also found to be significant predictors ($p < 0.001$) of mental health score. Mental component scores increased by 0.41 for each unit increase in baseline score, decreased by −0.09 for each unit increase in age, and decreased by −0.01 for each day increase in wound duration.

3.3.2. EuroQol-5D-3L results

The pain and discomfort dimension demonstrated the greatest change over time. At baseline 75% of participants reported some problems with pain and discomfort, which decreased to 60% at 18 months. Problems with self-care remained relatively stable, affecting 25–30% of participants at each time point (See Supplementary Fig. S1). Overall mean utility scores remained relatively consistent across the course of follow-up (See Supplementary Table S5). There was no statistically significant difference in unadjusted utility scores between participants who had healed during the study period and those who had not (See Supplementary Table S5).

3.3.3. Brief pain inventory results

The trend in Brief Pain Inventory severity and interference scores was towards an improvement over time (See Supplementary Table S6). There was no statistically significant difference in pain severity and interference between participants who had healed during the study period and those who had not (See Supplementary Table S6).

4. Discussion

This is the first inception cohort study in which researchers have reported the key clinical characteristics of a large group of patients with surgical wounds healing by secondary intention. Over a nine-month period almost 400 participants were recruited. There were slightly more men recruited than women perhaps reflecting the fact that some diseases associated with surgical wounds healing by secondary intention (e.g. Peripheral vascular disease, pilonidal sinus disease) are more common in men than in women. In the cohort population, comorbidities traditionally associated with poor wound healing (e.g. diabetes and cardiovascular disease) were also common. Participants with a surgical wound healing by secondary intention fell broadly into 3 groups; participants with abdominal wounds following colorectal surgery, those with leg/foot wounds following vascular surgery, and a mixed group. Many of these surgical procedures were performed as emergencies and were at high risk of contamination. “Planned” surgical wounds healing by secondary intention accounted for 60% of cases either due to infection/contamination or inability to approximate the wound edges

The mortality in this cohort was 7.4%. Hospital readmission (24%) and return to theatre (16.8%) were relatively common and associated significant resource implications. It is reassuring that the majority (81.4%) of wounds within this cohort healed over the follow up period, but the median time to healing was prolonged at 86 days. Healing in specific wounds (e.g. foot) appears to be particularly problematic, with only 57.6% of foot wounds healing and a median time to healing of 182 days observed for this group. Infection at any point was a relatively common occurrence experienced by 32.1% of participants, with approximately two thirds of these episodes occurring at baseline i.e. within three weeks of a surgical wound healing by secondary intention forming. Several factors with associated with a detrimental effect on healing have been identified including infection of a surgical wound healing by secondary intention at any point, wound area at baseline, high level of surgical contamination and reason for the surgical wound healing by secondary intention (e.g. inability to approximate the wound edges). Some of the variables included within the associated modelling deriving these findings may have had a non-normal distribution. We acknowledge the potential limitation arising by virtue of non-parametric testing not being completed prior to conducting this modelling work.

The investigation of the use of different treatments was also a key aim of this study. A wide range of different dressings were used and changes in dressing type were very common, for a wide variety of reasons. There was frequent use of hydrofibre dressings, basic wound contact (non-adherent) dressings, antimicrobial dressings and Negative Pressure Wound Therapy. The wide range of dressings used, and the number of treatment changes observed, likely reflects the limited randomised controlled trial data on treatments for surgical wounds healing by secondary intention, and hence the uncertainty regarding the clinical and cost effective treatments for these wounds (Dumville et al., 2015; Norman et al., 2016; Vermeulen et al., 2005). Further randomised controlled trial evidence for wound dressings is therefore required, which can subsequently inform wound management plans, including use of dressings where effectiveness in relation to wound healing has been demonstrated.

The final fundamental aim of this study was to assess the impact surgical wounds healing by secondary intention have on patients’ health-related quality of life. As observed in UK population studies, the Short Form -12 physical component scores in this cohort were consistently lower than the mental component scores and both scores decreased with age. However, the baseline Short Form -12 physical and mental component scores in this cohort were significantly inferior to UK population norms and although improved during follow up and with healing, they never approach UK normal values (Ashby et al., 2014a). Patients with

surgical wounds healing by secondary intention have health-related quality of life limitations comparable to patients with congestive cardiac failure but are significantly younger (Jenkinson and Layte, 1997).

Whilst this study aimed to recruit as many participants as possible, not all patients approached entered the study. The potential for selection bias is therefore possible, with the recruited subset differing in some systemic way to the wider population of patients with a surgical wound healing by secondary intention. The similarities between patient epidemiology, wound and surgical data in this cohort study to that in previous survey data would seem to argue against this, as the survey data did not require consent and was captured away from the bedside (Chetter et al., 2017). However the survey findings may have promoted focused recruitment into the cohort study (e.g. sub-speciality specific hospital wards), as some patient groups recognised nationally as having a high incidence of surgical wounds healing by secondary intention (e.g. post caesarean section wounds) seem underrepresented in this cohort (Mackeen et al., 2012).

The included analysis exploring the impact of factors on healing is observational thus it is difficult to draw firm conclusions. It is however proposed that the reported associations are valid, as in the development phase, existing literature and clinical expertise were drawn upon to ensure all factors with the potential to be prognostic for wound healing were captured.

The researchers have formally identified and characterised a previously poorly researched population of patients with a relatively common problem. This is a relatively young population with a condition that significantly impairs quality of life, and is associated with a potentially high resource use given the prolonged time to healing, treatments used, and incidence of re-hospitalisation / re-intervention. Wound healing is associated with significant quality of life improvement. It is therefore essential that future management is evidence based and focused on accelerating healing. Potentially modifiable patient and wound factors with prognostic implications for wound healing have been clearly identified. These are not only clinically important but may also represent future treatment targets to accelerate healing. The highly variable observed time to healing highlights the extensive chronicity of these wounds. This is important to ensure that patients and carers have realistic expectations in relation to wound healing.

This is a researchable population. Previously it has been difficult to get an overall view of this patient population, as these wounds have not been considered collectively. Excellent recruitment rates were achieved, loss to follow up was low and questionnaire completion rates were acceptable and similar to those previously reported for wound/ulcer trials (Ashby et al., 2014b).

Many factors that will help guide the design and planning of future research studies have been identified. This is crucial to ensuring robust evidence for treatment effectiveness is established, given the limited evidence for treatment effectiveness at present (Dumville et al., 2015; Norman et al., 2016; Vermeulen et al., 2005). The recruitment data and healing outcomes will inform planned duration of recruitment and follow up. Identification of surgical specialities most frequently associated with these wounds will facilitate targeted and efficient recruitment strategies, and the broad groups of patients recruited to this study have identified populations of relevance for future research. The prognostic factors for wound healing highlight potential areas for randomisation stratification in future trials.

Finally, a wide variety of dressings was used to treat these wounds and changes in dressing type were common. The use of antimicrobial dressings and Negative Pressure Wound Therapy were particularly prevalent in this cohort, despite the paucity of evidence to support their efficacy (Mangram et al., 1999; Norman et al., 2016). Further research, in the form of high quality trials, are required to investigate their effect on wound infection and healing, and so establish definitive evidence on which treatment choice can be based.

Many factors have also been identified that will be useful to those planning treatment delivery within healthcare settings. These wounds are a common occurrence, occurring from a wide range of surgical specialties and with a long healing duration. Predictors of delayed healing may therefore be useful to consider when planning treatment delivery. A wide range of treatments are available for SWHSI, however with limited effectiveness evidence, and this should be considered when identifying appropriate dressings for use in a healthcare setting.

This was a comprehensive cohort study conducted in two large UK centres. The patient, surgery, wound characteristics and outcomes were identical across the two centres and it is therefore proposed that an accurate description of this patient population has been provided. However, given the limited evidence base for different treatments used in these wounds there may be variation in management in different areas of the UK based on local guidelines and practices.

This is the first time that researchers have precisely characterised the population of patients with surgical wounds healing by secondary intention. The healing profile of these wounds, and potential prognostic factors for healing have been clearly identified. Findings have also been identified that will help guide the design and planning of future research studies and has highlighted areas where further investigation would seem essential.

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Appendix A. Supplementary data

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References

Ashby, R.L., Gabe, R., Ali, S., Adderley, U., Bland, J.M., Cullum, N.A., Dumville, J.C., Iglesias, C.P., Kang'ombe, A.R., Soares, M.O., Stubbs, N.C., Torgerson, D.J., 2014a. Clinical and cost-effectiveness of compression hosiery versus compression bandages in treatment of venous leg ulcers (Venous leg Ulcer Study IV, VenUS IV): a randomised controlled trial. Lancet 383 (9920), 871–879.

Ashby, R.L., Gabe, R., Ali, S., Saramago, P., Chuang, L.H., Adderley, U., 2014b. VenUS IV (Venous leg Ulcer Study IV) - compression hosiery compared with compression bandaging in the treatment of venous leg ulcers: a randomised controlled trial, mixed-treatment comparison and decision-analytic model, 18. National Institute for Health Research - Health Technology Assessment, pp. 1–293.

Chetter, I.C., Oswald, A., Fletcher, M., Dumville, J., Cullum, N., 2017. A survey or patients with surgical wounds healing by secondary intention: an assessment of prevalence, aetiology, duration and management. J. Tissue Viability 26, 103–107.

Cleeland, C.S., 2009. The Brief Pain Inventory User Guide. Houston, Texas, [cited 27/10/2014]. Available from: https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/symptom-research/symptom-assessment-tools.html.

Dumville, J.C., Owens, G.L., Crosbie, E.J., Peinemann, F., Liu, Z., 2015. Negative pressure wound therapy for treating surgical wounds healing by secondary intention. Cochrane Database Syst. Rev. 6, CD011278.

Edwards, P.J., Roberts, I., Clarke, M.J., Diguiseppi, C., Wentz, R., Kwan, I., et al., 2009. Methods to increase response to postal and electronic questionnaires. Cochrane Database Syst. Rev.(3) MR000008.

EuroQol Group, 2014. How to Use EQ-5D [cited 30/10/2014]. Available from:. . http://www.euroqol.org/about-eq-5d/how-to-use-eq-5d.html.

Failde, I., Medina, P., Ramirez, C., Arana, R., 2010. Construct and criterion validity of the Short Form -12 health questionnaire in patients with acute myocardial infarction and unstable angina. J. Eval. Clin. Pract. 16 (3), 569–573.

Gandek, B., Ware, J.E., Aaronson, N.K., Apolone, G., Bjorner, J.B., Brazier, J.E., et al., 1998. Cross-validation of item selection and scoring for the Short Form -12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment. J. Clin. Epidemiol. 51 (11), 1171–1178.

Grozdev, I., Kast, D., Cao, L., Carlson, D., Pujari, P., Schmotzer, B., et al., 2012. Physical and mental impact of psoriasis severity as measured by the compact Short Form-12 Health Survey (Short Form -12) quality of life tool. J. Invest. Dermatol. 132 (4), 1111–1116.

Hagell, P., Westergren, A., 2011. Measurement properties of the Short Form -12 health survey in Parkinson's disease. J. Parkinsons Dis. 1 (2), 185–196.

Hurst, N.P., Kind, P., Ruta, D., Hunter, M., Stubbings, A., 1997. Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). Br. J. Rheumatol. 36 (5), 551–559.

Jenkinson, C., Layte, R., 1997. Development and testing of the UK Short Form -12 (short form health survey). J. Health Serv. Res. Policy 2 (January (1)), 14–18.

Johnson, J.A., Pickard, A.S., 2000. Comparison of the EQ-5D and Short Form -12 health surveys in a general population survey in Alberta, Canada. Med. Care 38 (1), 115–121.

Konig, H.H., Ulshofer, A., Gregor, M., von Tirpitz, C., Reinshagen, M., Adler, G., et al., 2002. Validation of the EuroQol questionnaire in patients with inflammatory bowel disease. Eur. J. Gastroenterol. Hepatol. 14 (11), 1205–1215.

Konig, H.H., Heider, D., Lehnert, T., Riedel-Heller, S.G., Angermeyer, M.C., Matschinger, H., et al., 2010. Health status of the advanced elderly in six European countries: results from a representative survey using EQ-5D and Short Form -12. Health Qual. Life Outcomes 8, 143.

Mackeen, A.D., Berghella, V., Larsen, M.L., 2012. Techniques and materials for skin closure in caesarean section. Cochrane Database Syst. Rev. 11 doi:http://dx.doi.org/10.1002/14651858.CD003577.pub2.

Mahadeva, S., Wee, H.L., Goh, K.L., Thumboo, J., 2009. The EQ-5D (Euroqol) is a valid generic instrument for measuring quality of life in patients with dyspepsia. BMC Gastroenterol. 9, 20.

Mangram, A.J., Horan, T.C., Pearson, M.L., Silver, L.C., Jarvis, W.R., 1999. Guideline for prevention of surgical site infection. Infect. Control Hosp. Epidemiol. 20 (4), 247–264.

NHS Confederation, 2016. Key Statistics on the NHS [Internet]. [Cited 28.10.2016] Available from:. . . (Accessed 28th October 2016) http://www.nhsconfed.org/resources/key-statistics-on-the-nhs.

Niles, A.N., Sherbourne, C.D., Roy-Byrne, P.P., Stein, M.B., Sullivan, G., Bystritsky, A., et al., 2013. Anxiety treatment improves physical functioning with oblique scoring of the Short Form -12 short form health survey. Gen. Hosp. Psychiatry 35 (3), 291–296.

Norman, G., Dumville, J.C., Mohapatra, D.P., Owens, G.L., Crosbie, E.J., 2016. Antibiotics and antiseptics for surgical wounds healing by secondary intention. Cochrane Database Syst. Rev. 29 (March (3)) CD011712.

Oster, C., Willebrand, M., Dyster-Aas, J., Kildal, M., Ekselius, L., 2009. Validation of the EQ-5D questionnaire in burn injured adults. Burns 35 (5), 723–732.

Pezzilli, R., Morselli-Labate, A.M., Frulloni, L., Cavestro, G.M., Ferri, B., Comparato, G., et al., 2006. The quality of life in patients with chronic pancreatitis evaluated using the Short Form -12 questionnaire: a comparative study with the SF-36 questionnaire. Dig. Liver Dis. 38 (2), 109–115.

Prieto, L., Sacristan, J.A., Hormaechea, J.A., Casado, A., Badia, X., Gomez, J.C., 2004. Psychometric validation of a generic health-related quality of life measure (EQ-5D) in a sample of schizophrenic patients. Curr. Med. Res. Opin. 20 (6), 827–835.

Public Health England, 2013. In: England, P.H. (Ed.), Protocol for the Surveillance of Surgical Site Infection, .

Salcido, R., 2017. Healing by intention. Adv. Wound Care 30 (6), 246.

Schweikert, B., Hahmann, H., Leidl, R., 2006. Validation of the EuroQol questionnaire in cardiac rehabilitation. Heart (British Cardiac Society) 92 (1), 62–67.

Srinivasaiah, N., Dugdall, H., Barrett, S., Drew, P.J., 2007. A point prevalence survey of wounds in north-east England. J. Wound Care 16, 413–419.

STATA Corporation, 2013. Stata Statistical Software: Release 13. StataCorp LP, College Station, TX 2013.

van Agt, H.M., Essink-Bot, M.L., Krabbe, P.F., Bonsel, G.J., 1994. Test-retest reliability of health state valuations collected with the EuroQol questionnaire. Soc. Sci. Med. (1982) 39 (11), 1537–1544.

Vermeulen, H., Ubbink, D.T., Goossens, A., de Vos, R., Legemate, D.A., 2005. Systematic review of dressings and topical agents for surgical wounds healing by secondary intention. Br. J. Surg. 92, 665–672.

Vowden, K.R., Vowden, P., 2009. The prevalence, management and outcome for acute wounds identified in a wound care survey within one English health care district. J. Tissue Viability 18, 7–12.

Ware Jr., J., Kosinski, M., Keller, S.D., 1996. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med. Care 34 (3), 220–233.

Wieser, T.G., Haynes, A.B., Molina, G., Lipsitz, S.R., Esquivel, M.M., Uribe-Leitz, T., et al., 2016. Size and distribution of the global volume of surgery in 2012. Bull. World Health Organ. 94, 201–209F. doi:http://dx.doi.org/10.2471/BLT.15.159293.