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ORIGINAL RESEARCH

IMPACT OF COVID-19 ON VENOUS LEG ULCER MANAGEMENT AND ASSOCIATED CLINICAL OUTCOMES IN CLINICAL PRACTICE IN THE UK

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Running title: Impact of Covid-19 on VLU management and outcomes in clinical practice in the UK.

ABSTRACT

Objective: To assess the impact of the Covid-19 pandemic on venous leg ulcer (VLU) management by the UK's health services and associated outcomes.

Design: Retrospective cohort analysis of the electronic records of patients from the THIN database.

Setting: Primary and secondary care sectors.

Participants: A cohort of 1,946 patients of whom 1,263, 1,153 and 733 had a VLU in 2019, 2020 and 2021, respectively.

Primary and secondary outcome measures: Clinical outcomes and wound-related healthcare resource use.

Results: VLU healing rate in 2020 and 2021 decreased by 16% and 42%, respectively, compared with 2019 and time to heal increased by >85%. An estimated 3% of patients in 2020 and 2021 had a covid-19 infection. Also, 1% of patients in both years had sepsis, 0.1-0.2% developed gangrene and 0.3% and 0.6% underwent an amputation on part of the foot or lower limb in 2020 and 2021, respectively. The number of face-to-face clinician visits in the community decreased by >55% in both years and >35% fewer patients were referred to a hospital specialist. In 2020 and 2021, up to 20% of patients were prescribed dressings without compression compared to 5% in 2019. Furthermore, the total number of wound care products prescribed in 2020 and 2021 was >50% less than that prescribed in 2019, possibly as a consequence of the increased frequency of dressing change from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021.

Conclusions: There was a significant trend toward decreasing care during 2020 and 2021 which was outside the boundaries considered to be good care. This led to poorer outcomes including lower VLU healing rates and increased risk of sepsis, gangrene and amputation. Hence, the Covid-19 pandemic appears to have had a deleterious impact on the health of patients with a VLU.

Keywords: Covid-19, venous leg ulcer, wound management.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study to estimate how the Covid-19 pandemic affected the management of venous leg ulcers and patients' outcomes.
- This study was undertaken using real-world evidence derived from the anonymised records of a sample of 1,946 patients in The Health Improvement Network database (a nationally representative database of clinical practice among >11 million patients registered with general practitioners in the UK).
- The estimates were derived following a systematic analysis of patients' characteristics, clinical outcomes, and community-based and secondary care resource use pertaining to wound care contained in the patients' electronic records.
- The analysis was based on clinicians' entries into their patients' records and inevitably subject to a certain amount of imprecision and lack of detail.
- The analysis excluded the potential impact of managing patients with a VLU being cared for in residential and nursing homes.

INTRODUCTION

The Covid-19 pandemic in the UK was part of the worldwide pandemic of coronavirus disease 2019 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus started to circulate in the UK by the end of January 2020 [1-4]. The UK government and each of the three devolved governments (in Scotland, Wales and Northern Ireland) introduced public health and economic measures, including new laws, to mitigate the impact of the pandemic [2, 4, 5]. A national lockdown was introduced on 23 March 2020 [4, 5]. By mid-April it was reported that restrictions had "flattened the curve" of the epidemic and the daily number of new cases had passed its peak after 26,000 deaths [1, 6-9]. The national lockdown was lifted in May and replaced with specific regional restrictions which were gradually eased in late spring and early summer of that year [4, 5].

A second wave with a new variant began circulating in the autumn of 2020 [1, 3]. This led to the introduction of tiered restrictions in both England and Scotland in October 2020, and in England this was followed by a month-long lockdown during November followed by new tiered restrictions in December [2, 4, 5]. Multi-week 'circuit-breaker' lockdowns were imposed in Wales and Northern Ireland [2, 4, 5].

A third wave, principally due to the Delta variant, began in July 2021, although most restrictions were lifted during this third wave. In early December 2021, a fourth wave began, fuelled by the Omicron variant, resulting in the reintroduction of some social restrictions. During February 2022, all remaining legally enforced restrictions were ended in England and Northern Ireland [2, 4, 5]. All restrictions were ended in Wales and Scotland by the end of March and April 2022, respectively [2, 4, 5]. The number of cases rose following the relaxation of restrictions, but began to decline shortly after [1].

In the UK, the pandemic has resulted in over 23 million confirmed cases and over >187,000 deaths within 28 days of a positive Covid-19 test [6-10]. In December 2020, the first Covid-19 vaccine was approved and began being deployed across the UK with a staggered rollout prioritising the most vulnerable and then moving to progressively younger age groups [11]. By August 2021, more than 75% of adults in the UK had been fully vaccinated against Covid-19 [3, 11].

Before the pandemic, around 85% of the burden of disease in the UK was due to long-term conditions rather than infectious diseases [12]. Although the Government put measures in place to protect and support vulnerable people, there were, and are, increasing concerns about the impact of the pandemic on the health care needs of those with longer-term health conditions [13, 14]. The UK's health services were reprioritised to manage the increased demand from Covid-19-related illness and to allow for new social distancing restrictions, resulting in fewer patients being treated [14, 15]. Consequently, the treatment of existing conditions was reduced leading to a backlog of unmet care need [14, 15].

Despite the restrictions, in April 2020, 98% of people with a long-term condition who needed prescription medications were still able to obtain them. Moreover, 73% of those who needed treatment via a GP were able to access primary care, often through telemedicine and e-consults and 65% were able to see a pharmacist [14]. An unintended consequence of the use of digital technology is that people who did not have access to such technology or are reliant on face-to-face services found accessing health care challenging [14]. The greatest reduction in primary care consultations was among patients without a pre-existing condition [14], suggesting that a large number of people with undiagnosed conditions will come into contact with the health system at a more advanced stage of their condition [14]. Furthermore, in 2020, an estimated 6 million patients did not seek treatment in England, implying that many people could be living with poor health [14].

The surge in Covid-19-related care was also accompanied by a reduction in demand and supply of care for other illness within the hospital environment [13, 14, 16]. Many elective admissions were postponed to maintain capacity for Covid-19 patients [16]. Between March and December 2020 in England, there were 2.9 million (34.4%) fewer elective in-patient admissions, 1.2 million (21.4%) fewer non-Covid-19 emergency in-patient admissions and 17.1 million (21.8%) fewer out-patient appointments compared with the same period in 2019 [16]. There were also fewer accident and emergency visits [16]. The pressure has continued with only 73% of people attending accident and emergency departments in February 2022 seen within 4 hours, compared to a target of 95% [15]. By June 2022, the waiting list for routine hospital care in England had reached 6.7 million, with 355,000 patients waiting over a year [17].

Long Covid is limiting people's ability to return to activities of daily living. By early January 2022, an estimated 1.3 million people self-reported being affected by long Covid in the UK [18]. The social restrictions during the pandemic have also affected people's mental health through reduced social interaction, changing work conditions and loss of work and income [14, 15]. Access to social care services also declined during the pandemic despite an increasing need [14, 15].

Venous leg ulcers (VLUs) are a major cause of morbidity and decreased health-related quality of life [19]. In 2017/2018, the annual prevalence of VLUs in adults over 18 years of age in the UK was estimated at 1 per 100 individuals, equivalent to 560,000 patients with a leg ulcer in that period [20]. Compression bandages are the mainstay of treatment for VLUs. Up to 49% of newly-presenting VLUs can be induced to heal by applying adequate levels of sustained, graduated compression [21]. Once healed, some VLUs recur and patients can experience a repeated cycle of ulceration, healing and recurrence. Some VLUs fail to heal in a timely manner and they then become hard-to-heal [22].

During the pandemic many tissue viability services reported they were operating at reduced capacity, with a few trusts struggling to provide even basic wound care [23]. There was also a change or temporary reduction of many community-based services that would have been providing wound care [24, 25]. Against this background, this study aimed to assess the impact of the Covid-19 pandemic on the management of patients with a VLU in clinical practice in the UK and associated clinical outcomes, within the context of the health services.

METHODS

Study Design

This study was a retrospective cohort analysis of an anonymised sample of records of patients with a VLU obtained from the THIN database. The perspective of the analysis was the UK's health services.

The THIN Database

The THIN database contains electronic records on >11 million anonymised patients entered by general practitioners (GPs) from >560 practices across the UK. The patient composition within the THIN database has been shown to be representative of the UK population in terms of demographics and disease distribution [26] and the database theoretically contains patients' entire medical history.

In particular, the database collects data on the dates that patients registered or left their practice as well as demographic data, such as date of birth and gender. All medical conditions and symptoms recorded electronically during a patient's consultation in the general practice are recorded in the THIN database, thereby building up long computerised medical histories using Read Codes [27]. General practice prescribing is computerised and entered directly into the database. Prescriptions not issued electronically (e.g. during home visits) are also entered, however there is a possibility of under-recording of such items. Information is also recorded on referrals to secondary care, including the specialty. Secondary care information and other medically-related information received by the practice are entered into the database. This includes details on hospital admissions, discharge medication, diagnosis, outpatient consultations, investigations and treatment outcomes. Details on a range of variables such as height, weight, body mass index, blood pressure, smoking are also recorded. Hence, the information contained in the THIN database reflects actual clinical practice.

(THIN is a registered trademark of Cegedim SA in the UK and other countries. IQVIA Medical Research Data (IMRD) incorporates data from THIN, A Cegedim Database. Reference made to THIN is intended to be descriptive of the data asset licensed by IQVIA.)

Study Population

The study population comprised the anonymised case records of a cohort of patients from the THIN database (provided to the authors by IQVIA) who had a VLU in 2019 and/or 2020 and/or 2021. Patients were included in the data set if they:

- Were ≥18 years of age.
- Had a Read code for a VLU in 2019 and/or 2020 and/or 2021.
- Had continuous medical history in their case record from the first mention of a VLU up to the time the data were extracted from the database, unless they died, in order to exclude patients who had moved or changed their general practice

Patients were excluded from the data set if they:

- Were <18 years of age.
- Did not have continuous medical history in their case record from the first mention of a VLU.
- Had a dermatological tumour.

The records of 2,000 patients were reviewed, of which 54 records were excluded from the analysis because they had >5% missing data. The records of the remaining 1,946 patients fulfilled the study's inclusion and exclusion criteria and were included in the data set. Patients' complete electronic records were supplied to the authors, which enabled analysis of data both within and outside of the study period.

Patient and Public Involvement

Patients and members of the public were not directly involved in this study. The study population was limited to the anonymised records of patients in the THIN database.

Study Variables and Statistical Analyses

The following information was systematically extracted from the patients' electronic records

from the time a patient entered the data set (i.e. from the start of 2019 or the start time of their wound if it occurred later) up to the time their wound healed or the end of the study period (i.e. the end of 2021), whichever came first.

- Patients' characteristics.
- Patients' comorbidities (defined as a non-acute condition that patients were suffering from in the year before the start of their wound and not necessarily the year before the start of the study period).
- Wound-related healthcare resource use (which included dressings, bandages, district nurse visits (who provide care within a patient's home), practice nurse visits (who provide care within the general practice), GP visits, hospital outpatient visits, prescribed medication (i.e. analgesics, and antibiotics).
- Clinical outcomes (i.e. healing, infections, sepsis, gangrene and amputation).

If a patient received a dressing or bandage on a specific date, but a clinician visit was not documented in their record, it was assumed the patient had been seen outside of the general practice by a district nurse. No other assumptions were made regarding missing data and there were no other interpolations.

The use of individual healthcare resources was quantified for all the patients, individually. These quantities were then used to estimate the mean utilisation of each healthcare resource attributable to VLU management in each year and were compared with our published estimate of resource use in 2017/2018 [20].

Differences between 2019, 2020 and 2021 were tested for statistical significance using a Kruskal-Wallis test or Chi-Square test. Logistic regression was used to investigate relationships between baseline variables and clinical outcomes and linear regression was used to assess the impact of the pandemic years on healthcare resource use. The p values <0.05 were considered statistically significant and have been reported. All p values ≥ 0.05 were not considered to be statistically significant and these numerical values have not been reported.

All statistical analyses were performed using IBM SPSS Statistics (IBM UK, Portsmouth, Hampshire, UK).

Cost of Patient Management

The health service cost of VLU management for each patient was estimated by assigning unit costs at 2020/2021 prices [28-30] to the quantity of healthcare resources used by individual patients. The total cost of utilisation of each healthcare resource for the sample of patients was then combined in order to estimate the mean total health service cost of VLU management in each year. These costs were compared with our published estimated costs of VLU management in 2017/2018 [2], which were uprated to 2020/21 prices. Accordingly, the study only considers the cost of patient management attributable to VLUs in primary and secondary care settings, and does not estimate patients' overall healthcare costs.

Sensitivity Analysis

Deterministic sensitivity analyses were undertaken to examine the effect of independently varying the values of individual parameters. The parameter estimates were individually varied over plausible ranges by altering them to ±20% around the base case value. However, the percentages were bounded by 0% and 100%.

RESULTS

Patients' Characteristics

The study population comprised 1,946 patients with a VLU. Of these:

- 1,263 patients had a VLU in 2019.
- 1,153 patients had a VLU in 2020.
- 733 patients had a VLU in 2021.

The number of new and existing VLUs in each year is summarised in Figure 1.

There were no differences in patients' baseline characteristics between each year. However, the percentage of patients with a new VLU was less in 2021 than in 2020 and 2019 (Table 1). A total of 44% and 48% of patients presented with a new wound in 2019 and 2020. However, in 2021, only 17% of patients in the cohort presented with a new VLU, probably indicative of patients with a new ulcer not seeking or obtaining health care.

Clinical Outcomes

The THIN database does not define wound healing. Wound healing was a clinical observation documented in the patient's record by their managing clinician, but not necessarily confirmed by a specialist, and it is unknown if the clinicians who managed these patients used any consistent definition. Furthermore, if a wound was not recorded as being healed it was considered to be unhealed. This assumption was supported by continued clinician visits for wound care and the continued prescribing of wound care products. On this basis the VLU healing rate in 2020 and 2021 decreased by 16% and 42%, respectively, compared with 2019 (Table 2). Additionally, the time to heal increased by >85% (Table 2).

An estimated 3% of patients in both 2020 and 2021 were recorded as having a Covid-19 infection. Furthermore, 1% of patients in both years had sepsis, 0.1-0.2% developed gangrene and 0.3% and 0.6% underwent an amputation on part of the foot or lower limb in 2020 and 2021, respectively (Table 2). Of the patients who underwent an amputation, 50% had diabetes.

Binary logistic regression suggested that smoking (OR 0.72 (95% CI 0.60 to 0.88); p<0.001), years of the pandemic (OR 0.77 (95% CI 0.64 to 0.93); p=0.007) and wound duration (OR 0.98 (95% CI 0.97 to 0.99); p<0.001) were independent risk factors for VLUs not healing.

Healthcare Resource Use Associated with Patient Management

Table 3 summarises the percentage of patients who utilised different resources in each year and the mean amount of resource that was used. Patients were predominantly managed in the community by practice nurses and district/community nurses (Table 3). In 2019, an average patient with a VLU had a mean of 50 face-to-face visits with a clinician in the community. In 2020 and 2021, an average patient had a mean of 21-23 such visits each year (>50% reduction). Moreover, the distribution of visits between the different types of clinician increased towards practice nurses over the three consecutive years (Figure 2). Additionally, 38% and 48% fewer patients were referred to a specialist in a hospital outpatient clinic in 2020 and 2021, respectively.

There were no differences in the percentage of patients being admitted into hospital or attending an accident and emergency department between the three years. Linear regression indicated that sepsis, amputation, covid-19 infection and wound infection all increased the risk of hospital admission (Table 4).

Patients' treatment varied over the three years with 80% of patients having been prescribed a combination of dressings and compression in 2019, decreasing to 74% of patients in 2021 (a decrease of 8%). In 2020 and 2021, 19-20% of patients were prescribed dressings without any compression compared to 5% in 2019 (Figure 4). Overall, the total number of wound care products prescribed in 2020 and 2021 was >50% less than that prescribed in 2019. This may be a consequence of the frequency of dressing change having increased from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021. In 2017/2018 the frequency of dressing change was once every 3.5 days [20].

The total number of prescriptions for analgesics and antibiotics prescribed in 2020 and 2021 was >40% less and >30% less, respectively, than that prescribed in 2019.

There was no difference in resource use between managing a new onset VLU and an existing ulcer in 2019. However, in 2020 and 2021 an average patient with a new onset VLU had a mean of 17 face-to-face visits with a community-based clinician each year. In contrast, the patients with an existing VLU had 13 such visits each year (a 24% reduction). There were no differences in the number of prescribed wound care products between patients with a new onset or existing VLU. Neither were there any differences in referrals to hospital-based clinicians or hospital admissions.

Assessment of peripheral perfusion is a recognised requirement for leg ulcer management. However, only 16%, 11% and 15% of patients in 2019, 2020 and 2021, respectively, had a Doppler ankle brachial pressure index (ABPI) recorded in their records. Of these patients, 100%, 92% and 88% in 2019, 2020 and 2021, respectively, were prescribed some form of compression. Of the patients who did not have their ABPI recorded, 86%, 71% and 67% were prescribed compression bandages/hosiery in 2019, 2020 and 221, respectively.

Health Service Cost of Patient Management

The total annual health service cost of VLU management was estimated to be a mean of £3,920 per VLU in 2019, decreasing to £2,470 in 2020 and £3,355 in 2021 (Table 5). In 2019, 32% of the cost was attributable to district nurse visits and 39% due to hospital admissions. In 2020 and 2021, 65-68% of the cost was attributable to hospital admissions and 9% was due to district nurse visits (Table 5).

In 2019, 58% of the total cost of VLU management was incurred in the community and the remaining 42% in secondary care. In 2020 and 2021, 70% and 73%, respectively, of the total cost of VLU management was incurred in secondary care and the remainder in the community. In 2017/2018, 15% of the total cost of VLU management was incurred in secondary care and 85% in the community [20].

Sensitivity Analysis

Deterministic sensitivity analyses (Table 6) showed that by individually varying the parameter estimates, the total cost of VLU management was affected to a greater extent by changing the number of hospital admissions. The costs were affected to a lesser extent by changing the number of district nurse visits and the VLU healing rate. Varying other parameters appeared to have a minimal impact on the total cost of VLU management.

Impact of the Covid-19 Pandemic

Linear regression estimated the change in healthcare resource utilisation between the pandemic (2020 and 2021) and pre-pandemic (2019) periods. This showed there was a significant reduction in prescriptions for compression, district nurse visits, prescriptions for dressings, GP visits, prescriptions for analgesics, prescriptions for antibiotics and hospital outpatient visits during the pandemic period compared with the pre-pandemic period. Conversely, the number of tele consults with practice nurses and GPs both significantly increased during the pandemic years (Table 7).

DISCUSSION

This study aimed to assess the impact of the Covid-19 pandemic [1-4] together with the associated lockdowns and social restrictions [2, 4, 5] on the management of VLUs and the consequential outcomes. The study was based on a retrospective analysis of patients' records in the THIN database. Inevitably there were some limitations, since the analysis was based on clinicians' entries into their patients' records and unavoidably subject to a certain amount of imprecision and lack of detail. One such limitation is that some patients in our data set may have had multiple wounds, but this was not specifically listed within the database and was not transparent in the patients' records. Furthermore, it would be very difficult to retrospectively extricate resource use for different wounds from the records of a patient with multiple wounds of the same aetiology. Notwithstanding this, it would be unusual for an individual to have two wounds of different aetiologies at the same time. Consequently, some patients may have had a second ulcer on their lower limb. The implication of this would be negligible since resource use and corresponding costs as presented would remain unchanged because all the resources and wound care products used in managing each patient were documented in their record (despite the lack of granularity surrounding the number of VLUs they may have had).

There were no significant differences in baseline characteristics of the patients in the different study years, which were comparable to those with a VLU in our 2017/2018 burden of wounds data set [20]. Nevertheless, the possibility that undetected differences existed between the cohorts in the different study years cannot be excluded. The smaller percentage of patients with a new VLU in 2021 is likely to be a reflection of patients with a new-onset wound self-managing and not accessing primary care. This is consistent with the aforementioned report that the greatest reduction in primary care consultations during the pandemic was among patients without a pre-existing condition [14]. Consequently, a large number of people with undiagnosed VLUs will probably come into contact with the health system once their wound has deteriorated, contributing to the backlog of unmet care need.

Notwithstanding, the data indicated that the percentage of healed VLUs increased from 37% in 2017/2018 [20] to 55% in 2019, possibly reflecting better management as a result of various programmes including the National Wound Care Strategy Programme [31] and campaigns, such as Legs Matter [32]. However, the impact of the pandemic [1-4] together with the

associated lockdowns and social restrictions [2, 3, 5] led to the VLU healing rate being reduced to 46% and 32% in 2020 and 2021, respectively and a simultaneous increase in the time to healing from a mean of 3 months in 2019 to >5 months in 2020 and 2021. These poorer outcomes may be a consequence of the reduction in face-to-face visits and associated hands-on management by clinicians. An average patient with a VLU had a >50% reduction in the number of face-to-face visits with a clinician in the community during 2020 and 2021 compared with the pre-pandemic period (from a mean of 50 to a mean of 21-23 visits). Additionally, 38% and 48% fewer patients were referred for specialist involvement in 2020 and 2021, respectively. This inevitably led to a reduction in the frequency of dressing change from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021 and a >50% reduction in the number of wound care products that were prescribed. This 'perfect storm' would not only have contributed to the poorer healing rates in 2020 and 2021, but also to a small percentage of patients having developed sepsis, or gangrene or undergone an amputation on part of the foot or lower limb in 2020 and 2021. In all our previous studies on the management of VLUs in clinical practice, we never encountered a single patient who had sepsis or gangrene or underwent an amputation on part of the foot or lower limb [20, 22, 33-38]. This analysis indicated a significant trend towards decreasing standards of care during 2020 and 2021 which was outside the boundaries of what is considered to be 'good care', leading to these poorer outcomes.

It is noteworthy that between March and December 2020 compared with the same period in 2019 there were 17.1 million fewer hospital outpatient appointments, 2.9 million fewer elective hospital admissions, 1.2 million fewer non-Covid-19 emergency hospital admissions in England [16]. There was also 7.6 million fewer accident and emergency attendances in 2020/21 than in 2019/20 [39]. In this study's cohort of patients with a VLU, there were fewer hospital outpatient appointments in 2020 and 2021 compared with 2019, but there were no significant differences in hospital admissions and accident and emergency attendances across the three years.

It was not possible to determine which professional groups were the decision makers in relation to VLU management as this information was not specifically recorded in the patients' records. However, <20% of patients in any year had a vascular assessment with a Doppler ABPI recorded in their records, contrary to national guidance [40, 41]. It remains unclear and

disappointing to find that records still lacked documentation of this essential investigation, particularly in 2019.

The reduced levels of healthcare resource use in 2020 and 2021 inevitably resulted in a smaller cost of VLU management when compared to 2019. While the levels of resource use in the community decreased during the years of the pandemic, hospital admissions and accident and emergency attendances remained relatively static. Sensitivity analysis showed that the total cost of VLU management was affected to a greater extent by changing the number of hospital admissions rather than by changing any other parameter. Moreover, the risk of hospital admission was increased among those either with sepsis or covid-19 infection or wound infection or having to undergo an amputation. The shift towards less utilisation of community-based resources is reflected in the distribution of the cost of leg ulcer care between the community and secondary care. In 2019, 42% of the total cost of VLU management was incurred in secondary care. In 2020 and 2021, this increased to 70% and 73%, respectively, with the remainder being incurred in the community. In 2017/2018, 15% of the total cost of VLU management was incurred in secondary care and 85% in the community [20].

Whilst there was a reprioritisation of health care services to manage Covid-19-related demand [14, 15], it seems unclear how the health services can best manage its backlog of unmet care need [14]. While e-consults and telemedicine consultations with GPs and practice nurses are planned to increase [42], this analysis has indicated the consequences of patients with VLUs not having an adequate number of face-to-face visits with clinicians. The massive reduction in healthcare resource utilisation in managing patients with a VLU makes a compelling case for prioritising efforts that address the unmet needs of these patients. Health services for leg ulcer care needs to be restored and a plan needs to be implemented for managing those wounds that have not had the attention from clinicians that they would normally receive, in order to facilitate healing and prevent any further exacerbation of outcomes. As we have previously suggested [20], the authors are advocating the establishment of dedicated tissue viability clinics in the community across the country, at which patients receive consistent and integrated care from clinicians with qualified experience in wound care. These clinics could provide both direct wound care and holistic assessments of patients allowing coordinated management of any comorbidities which may impact on wound healing.

The advantages and disadvantages of using the THIN database for this study have been previously discussed [33]. In summary, the advantage of using the THIN database is that the patient pathways and associated resource use were based on real-world evidence derived from clinical practice. However, the possibility of resource use associated with managing a comorbidity being conflated with that of wound management cannot be excluded. Prescriptions issued by GPs and practice nurses were recorded in the database, but it did not specify whether the prescriptions were dispensed or detail patient compliance with the product. Despite these limitations, it is the authors' opinion that the THIN database affords one of the best sources of real-world evidence for clinical practice in the UK. Furthermore, a review of Medline in August 2022 identified 1,938 articles in peer-reviewed journals in which the THIN database had been used as the source of real world evidence to characterise clinical practice in a wide range of therapeutic areas [27].

The analysis did not consider the potential impact of those wounds that remained unhealed beyond the study period. The THIN database may have under-recorded the use of some healthcare resources, particularly outside the GP's surgery if not documented in the GP records. In particular, not all community records may have been linked to the GP records. The impact of this was addressed in sensitivity analyses. Also excluded is the potential impact of managing patients with wounds being cared for in residential and nursing homes. The analysis only considered resource use for the 'average adult patient', and did not stratify resource use according to gender, comorbidities, wound size and severity of underlying venous disease.

The analysis was unable to consider the level of a clinician's skills in managing VLUs. It was also unable to discern the challenges clinicians may have had in VLU management during the pandemic. The possibility that the analysis may not have identified all the confounding variables that could have influenced the impact of the pandemic cannot be excluded, in particular the impact of long Covid.

Notwithstanding the study's limitations, real-world evidence highlighted a significant trend toward decreasing care for VLUs during 2020 and 2021 which was outside the boundaries considered to be good care. This led to poorer outcomes including an increased risk of amputation. Hence, the Covid-19 pandemic appears to have had a deleterious impact on the health of patients with a VLU.

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CONTRIBUTORS

JFG designed the study, obtained the THIN data set, managed the analyses, performed some analyses, checked all the other analyses, and wrote the manuscript. GWF conducted much of the analyses. Both the authors were involved in revising the manuscript and gave final approval. JFG is the guarantor of this work and, as such, 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.

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This study was commissioned by 3M Healthcare, Loughborough, UK.

COMPETING INTERESTS

None declared.

PATIENT CONSENT FOR PUBLICATION

Not required.

ETHICS APPROVAL

Ethics approval to use patients' records from the THIN database for this study was obtained from the Research Ethics Committee that appraises studies using the THIN database (Reference number 22SRC014).

DATA AVAILABILITY STATEMENT

All data relevant to the study are included in the article. The THIN data set cannot be shared as this restriction was a condition of the ethics approval obtained from the Research Ethics Committee (Reference number 22SRC014). Questions concerning the data underlying the results can be sent to the corresponding author.

Table 1: Patients' characteristics.

	2017/2018 [20]	2019	2020	2021
Percentage new ulcers	59%	44%	48%	17%
Mean age per patient (years)	70.9±14.0	72.6±13.5	72.7±14.1	72.2±14.4
Percentage >=65 years of age	74%	75%	75%	74%
Percentage male	48%	48%	49%	48%
Percentage smokers	7%	22%	23%	24%
Percentage non-smokers	92%	67%	67%	64%
Percentage with unknown smoking status	1%	11%	10%	12%
Mean body mass index per patient (kg/m^2)	31.5±6.8	27.7±9.4	29.1±10.6	29.0±10.6
Percentage with cardiovascular disease	72%	59%	56%	59%
Percentage with respiratory disorders	33%	44%	43%	42%
Percentage with musculoskeletal disorders	59%	37%	38%	40%
Percentage with endocrinological disorders	52%	41%	39%	38%
Percentage with dermatological disorders	41%	38%	38%	36%
Percentage with gastrointestinal disorders	19%	37%	34%	36%
Percentage with genito-urinary disorders	19%	21%	20%	22%
Percentage with ophthalmological disorders	4%	25%	23%	21%
Percentage with psychiatric illness	15%	19%	19%	20%
Percentage with cancer	7%	26%	22%	20%
Percentage with neurological disorders	33%	18%	16%	15%
Percentage with renal disease	30%	14%	14%	13%
Percentage with haematological disease	3%	13%	11%	11%
Percentage with cerebrovascular disease	3%	10%	10%	9%
Mean number of comorbidities per patient	4.0±2.0	4.6±2.4	4.7±3.0	4.5±3.0

Table 2: Clinical outcomes.

	2017/2018 [20]	2019	2020	2021	p value
Percentage who developed an infected wound during the year	41%	47%	49%	47%	ns
Percentage who had a covid-19 infection	0%	0%	3%	3%	ns
Percentage who had sepsis	0%	0%	1%	1%	ns
Percentage who had gangrene	0%	0%	0.2%	0.1%	ns
Percentage who had amputation	0%	0%	0.3%	0.6%	ns
Percentage of all VLUs that healed	37%	55%	46%	32%	< 0.001*
Percentage of new VLUs that healed	56%	60%	50%	53%	0.001**
Mean time of a VLU to heal (months)	4.5±4.0	2.8±3.9	5.6±4.4	5.3±4.5	< 0.001**

* Differences between the 3 years

** Difference between 2019 and 2020/2021:

Table 3: Healthcare resource use associated with VLU management.

	2017/2018 [20]		2019		2020		2021		
	%	N	%	N	%	N	%	N	p value
GP surgery visits	100%	17.6	82%	7.1±6.0	73%	3.1±2.0	89%	3.9±2.8	< 0.001*
GP tele consults	<1%	1.0	11%	1.4±0.4	37%	1.8±0.9	36%	2.4±1.4	< 0.001**
Practice nurse visits	96%	25.8	80%	10.4±9.4	95%	8.2±7.0	92%	9.1±8.0	< 0.001**
Practice nurse tele consults	<1%	1.0	5%	1.5±0.4	25%	1.7±0.6	24%	1.6±0.5	< 0.001**
District nurse visits	85%	62.6	78%	29.2±26.4	67%	6.4±5.3	74%	7.3±6.1	< 0.001*
Practice nurse and district nurse combined	100%	88.4	96%	39.6±35.5	97%	14.6±12.1	94%	16.4±14.3	< 0.001**
Tissue viability nurse visits	1%	1.0	2%	2.0±0.4	4%	1.6±0.4	4%	1.4±0.3	ns
Podiatry visits	1%	1.0	2%	1.3±0.3	7%	1.8±0.6	6%	1.5±0.4	ns
Hospital outpatient visits	41%	6.6	21%	1.8±0.8	13%	1.5±0.4	11%	1.7±0.6	< 0.001**
Hospital admissions	7%	1.5	21%	1.6±0.4	22%	1.5±0.5	22%	2.1±1.0	ns
Accident and emergency attendances	30%	1.5	31%	1.3±0.3	32%	1.4±0.3	29%	2.0±0.9	ns
Compression systems	74%	49.9	88%	26.6±24.4	70%	5.8±4.7	56%	8.1±7.0	< 0.001*
Compression hosiery	70%	12.5	29%	2.1±1.0	31%	2.3±1.2	32%	2.6±1.5	ns
All compression	93%	62.4	89%	28.7±26.3	78%	8.1±6.1	74%	10.7±8.3	ns
Dressings	98%	142.6	85%	25.5±24.2	97%	10.8±9.5	94%	14.2±12.9	0.01*
Prescribed analgesics	81%	8.9	65%	12.3±11.1	47%	7.6±5.0	50%	8.6±6.4	0.01*
Prescribed antibiotics	81%	3.1	71%	5.2±4.3	56%	4.5±3.1	56%	4.6±3.6	0.01*

% = percentage of patients who utilised a resource in the study year; N = Annual amount of resource use per patient who used the resource in the study year * Differences between the 3 years; ** Difference between 2019 and 2020/2021

Table 4: Linear regression assessing the impact of clinical outcomes on hospital admission.

	Unstandardised B coefficient (95% confidence intervals)	p value
Sepsis	1.511 (1.128, 1.893)	0.001
Amputation	0.780 (0.198, 1.362)	0.009
Covid infection	0.416 (0.232, 0.601)	0.001
Years of the pandemic	0.215 (0.144, 0.285)	0.001
Wound infection	0.214 (0.152, 0.275)	0.001

Table 5: Cost of healthcare resource use associated with VLU management per patient.

	2017/2018 [20]		2019		2020		2021	
District nurse/healthcare assistant visits	£1,338.30	(30%)	£1,260.34	(32%)	£234.00	(9%)	£309.00	(9%)
Hospital admissions	£217.27	(5%)	£1,520.53	(39%)	£1,614.01	(65%)	£2,286.44	(68%)
GP visits and tele consults	£792.84	(18%)	£446.85	(11%)	£188.00	(8%)	£236.00	(7%)
Compression	£623.78	(14%)	£204.30	(5%)	£46.00	(2%)	£62.00	(2%)
Practice nurse visits and tele consults	£326.76	(7%)	£193.78	(5%)	£174.00	(7%)	£197.00	(6%)
Dressings	£643.49	(14%)	£76.81	(2%)	£37.00	(1%)	£49.00	(1%)
Prescribed drugs	£90.77	(2%)	£61.71	(2%)	£33.00	(1%)	£34.00	(1%)
Hospital outpatient visits	£389.75	(9%)	£87.41	(2%)	£43.00	(2%)	£47.87	(1%)
Accident & emergency attendances	£42.92	(1%)	£53.71	(1%)	£83.46	(3%)	£117.01	(3%)
Podiatrist visits	£0.00	(0%)	£9.96	(<1%)	£10.01	(<1%)	£10.18	(<1%)
Tissue viability nurse visits	£0.00	(0%)	£6.02	(<1%)	£6.52	(<1%)	£4.26	(<1%)
TOTAL	£4,465.88	(100%)	£3,921.42	(100%)	£2,469.00	(100%)	£3,352.76	(100%)

Table 6. Deterministic sensitivity analyses showing the range in the cost of VLU management when individual variables were changed by ±20%, but bounded by 0% and 100%. Values in parentheses indicate percentage change from the base case value.

Scenario	2019	2020	2021
Base case value	£3,921	£2,470	£3,353
Number of hospital admissions changed by ±20% of the estimated value	£3,617-£4,226 (8%)	£2,148-£2,793 (13%)	£2897-£3,812 (14%)
Number of district nurse visits changed by ±20% of the estimated value	£3,669-£4,173 (6%)	£2,424-£2,517 (2%)	£3,293-£3,417 (2%)
Percentage of VLUs healed changed by ±20% of the estimated value	£3,775-£4,069 (4%)	£2,371-£2,571 (4%)	£3,267-£3,438 (3%)
Number of GP visits changed by ±20% of the estimated value	£3,832-£4,010 (2%)	£2,435-£2,506 (1%)	£3,310-£3,399 (1%)
Number of accident and emergency attendances visits changed by ±20% of the estimated value	£3,911-£3,932 (<1%)	£2,454-£,2487 (1%)	£3,331-£3,378 (1%)
Number of prescribed compression bandages changed by ±20% of the estimated value	£3,881-£3,962 (1%)	£2,461-£2,480 (<1%)	£3,342-£3,367 (<1%)
Number of prescribed dressings changed by ±20% of the estimated value	£3,906-£3,937 (<1%)	£2,463-£2,478 (<1%)	£3,345-£3,365 (<1%)
Number of hospital outpatient visits changed by ±20% of the estimated value	£3,904-£3,939 (<1%)	£2,462-£2,479 (<1%)	£3,345-£3,364 (<1%)
Percentage of patients who underwent an amputation changed by ±20% of the estimated value	£3,921-£3,921 (0%)	£2,461-£2,480 (<1%)	£3,347-£3,363 (<1%)
Percentage of patients with sepsis or gangrene changed by ±20% of the estimated value	£3,921-£3,921 (0%)	£2,465-£2,476 (<1%)	£3,350-£3,359 (<1%)
Number of GP and practice nurse tele consults changed by ±20% of the estimated value	£3,921-£3,922 (<1%)	£2,468-£2,473 (<1%)	£3,351-£3,358 (<1%)
Number of practice nurse visits changed by ±20% of the estimated value	£3,921-£3,922 (<1%)	£2,470-£2,471 (<1%)	£3,354-£3,355 (<1%)

Table 7. Linear regression assessing the impact of the pandemic on key variables.

	Unstandardised B coefficient (95% confidence intervals)	p value
Compression	-18.83 (-20.39, -17.27)	0.001
District nurse visits	-18.31 (-19.81, -16.81)	0.001
Dressings	-10.36 (-12.01, -8.72)	0.001
GP visits	-3.38 (-3.79, -2.98)	0.001
Prescriptions for analgesics	-2.32 (-3.13, -1.51)	0.001
Prescriptions for antibiotics	-1.19 (-1.52, -0.89)	0.001
Hospital outpatient visits	-0.2 (-0.26, -0.14)	0.001
Practice nurse tele consults	0.33 (0.27, 0.38)	0.001
GP tele consults	0.58 (0.50, 0.66)	0.001

Figure 1. Flow diagram showing the number of patients in each period.

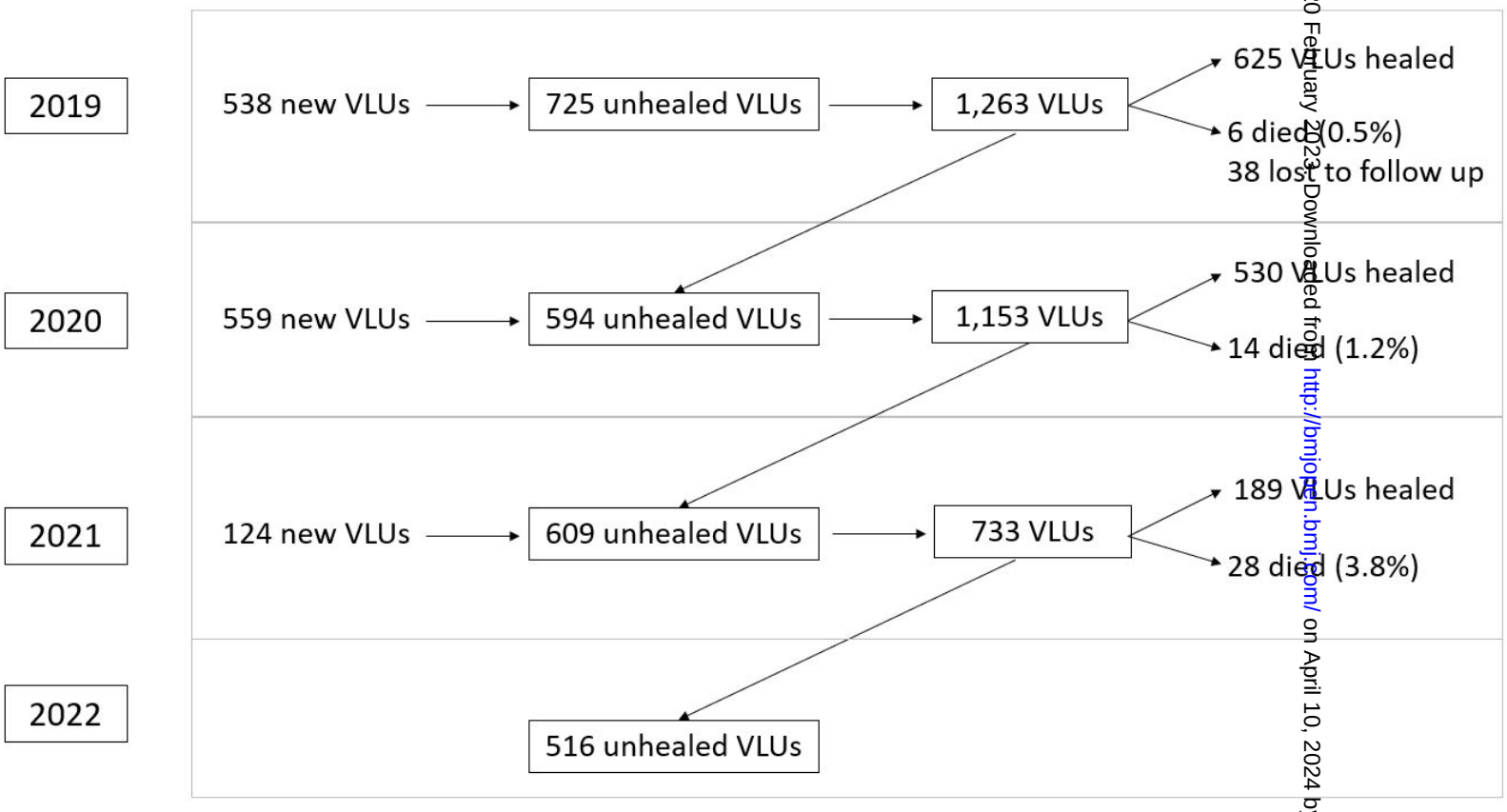


Figure 2: Distribution of face-to-face visits.

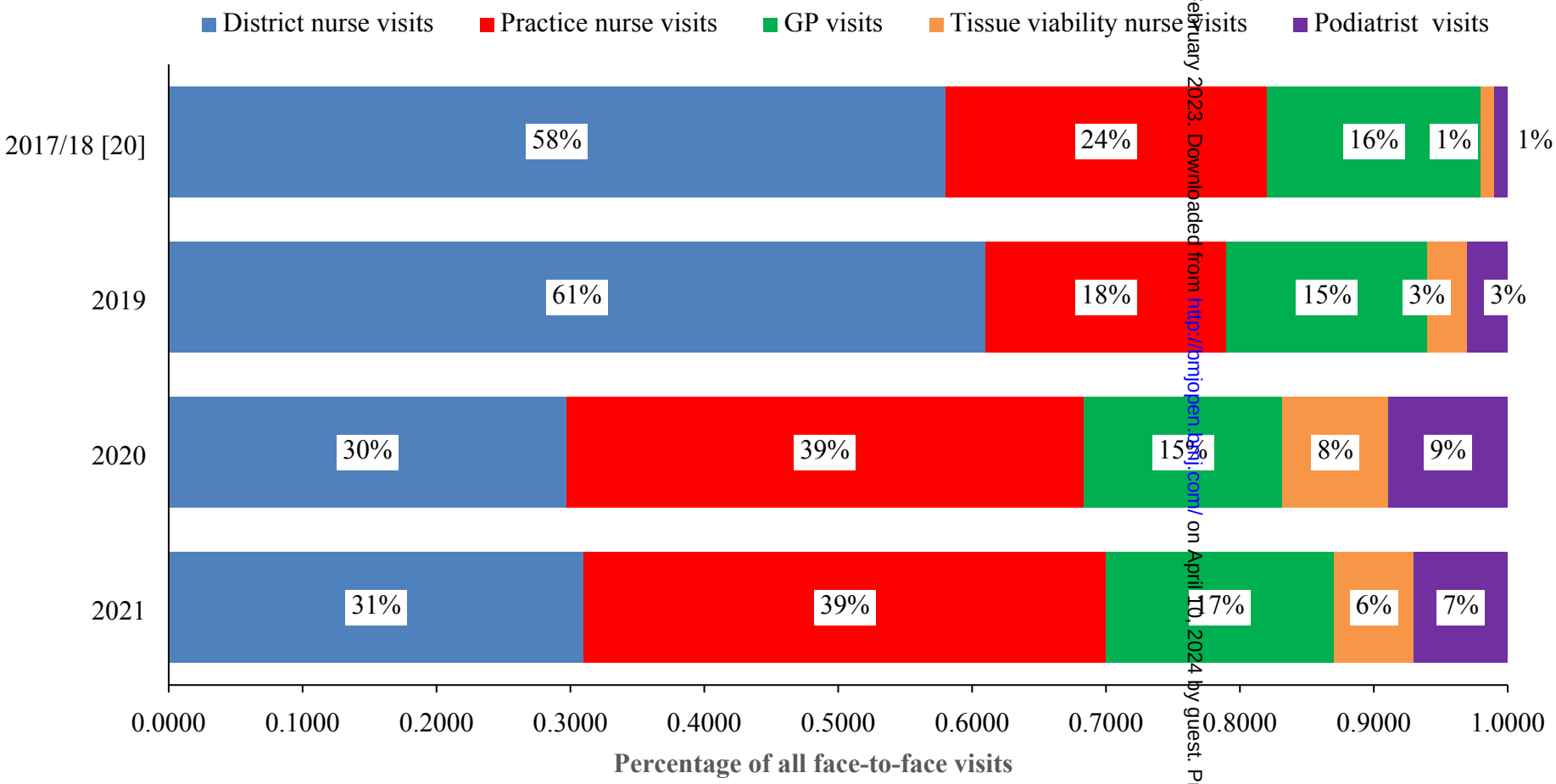
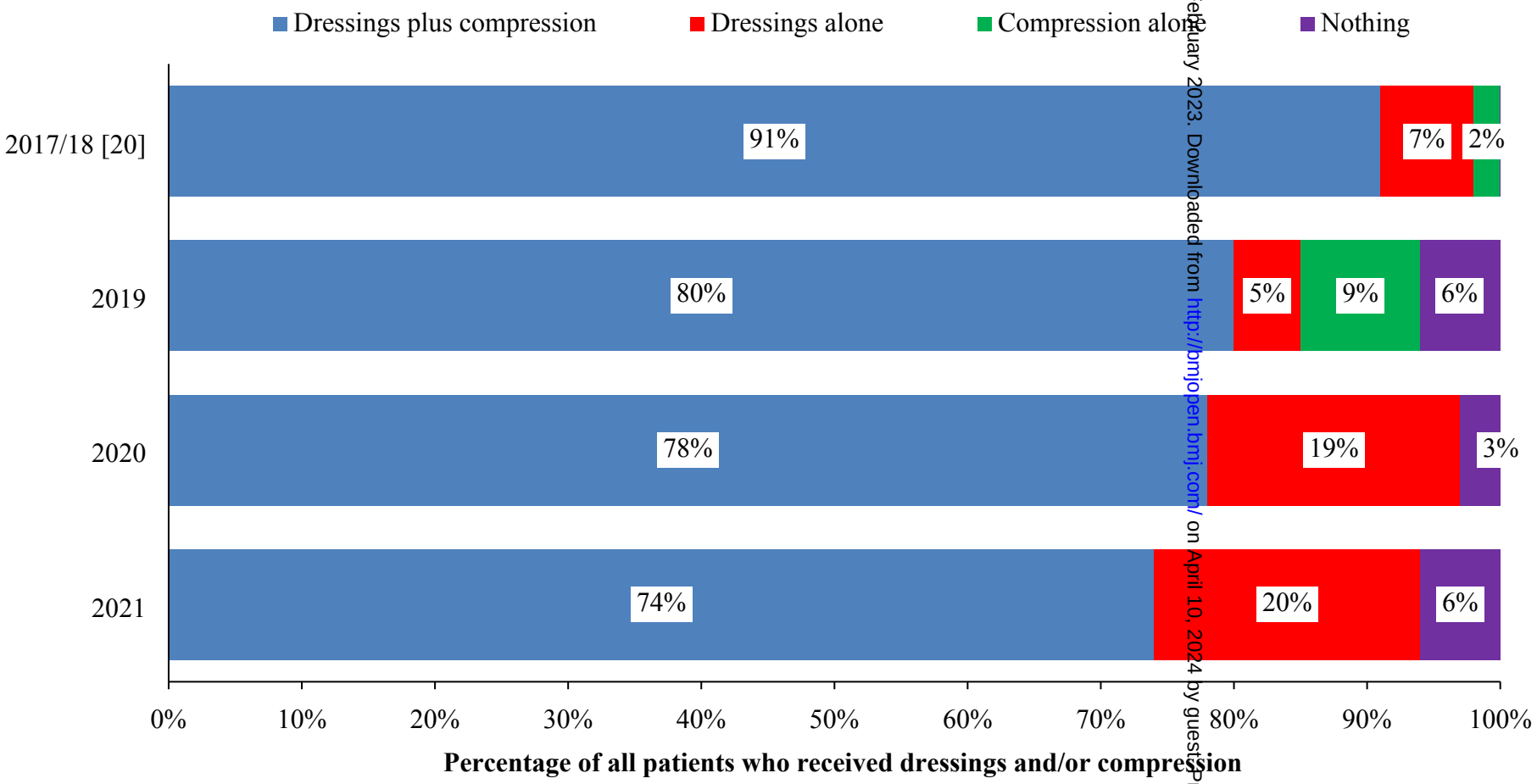


Figure 3. Distribution of prescribed dressings and compression.



STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3,4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8,9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	31
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	24
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	26

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	26
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	27,29,30
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

IMPACT OF COVID-19 ON VENOUS LEG ULCER MANAGEMENT AND ASSOCIATED CLINICAL OUTCOMES IN CLINICAL PRACTICE IN THE UK

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ORIGINAL RESEARCH

IMPACT OF COVID-19 ON VENOUS LEG ULCER MANAGEMENT AND ASSOCIATED CLINICAL OUTCOMES IN CLINICAL PRACTICE IN THE UK

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Running title: Impact of Covid-19 on VLU management and outcomes in clinical practice in the UK.

ABSTRACT

Objective: To assess the impact of the Covid-19 pandemic on venous leg ulcer (VLU) management by the UK's health services and associated outcomes.

Design: Retrospective cohort analysis of the electronic records of patients from the THIN database.

Setting: Primary and secondary care sectors.

Participants: A cohort of 1,946 patients of whom 1,263, 1,153 and 733 had a VLU in 2019, 2020 and 2021, respectively.

Primary and secondary outcome measures: Clinical outcomes and wound-related healthcare resource use.

Results: VLU healing rate in 2020 and 2021 decreased by 16% and 42%, respectively, compared with 2019 and time to heal increased by >85%. An estimated 3% of patients in 2020 and 2021 had a covid-19 infection. Also, 1% of patients in both years had VLU-related sepsis, 0.1-0.2% developed gangrene and 0.3% and 0.6% underwent an amputation on part of the foot or lower limb in 2020 and 2021 (of whom 57% had diabetes), respectively. The number of community-based face-to-face clinician visits decreased by >55% in both years and >35% fewer patients were referred to a hospital specialist. In 2020 and 2021, up to 20% of patients were prescribed dressings without compression compared to 5% in 2019. Furthermore, the total number of wound care products prescribed in 2020 and 2021 was >50% less than that prescribed in 2019, possibly due to the increased frequency of dressing change from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021.

Conclusions: There was a significant trend toward decreasing care during 2020 and 2021 which was outside the boundaries considered to be good care. This led to poorer outcomes including lower VLU healing rates and increased risk of amputation. Hence, the Covid-19 pandemic appears to have had a deleterious impact on the health of patients with a VLU.

Keywords: Covid-19, venous leg ulcer, wound management.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study to estimate how the Covid-19 pandemic affected the management of venous leg ulcers and patients' outcomes.
- This study was undertaken using real-world evidence derived from the anonymised records of a sample of 1,946 patients in The Health Improvement Network database (a nationally representative database of clinical practice among >11 million patients registered with general practitioners in the UK).
- The data set was analysed retrospectively, and no other data sources are available to check or verify the completeness and accuracy of the data.
- The analysis was based on clinicians' entries into their patients' records and inevitably subject to a certain amount of imprecision and lack of detail.
- The analysis excluded the potential impact of managing patients with a VLU being cared for in residential and nursing homes.

INTRODUCTION

The Covid-19 pandemic in the UK was part of the worldwide pandemic of coronavirus disease 2019 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus started to circulate in the UK by the end of January 2020 [1-4]. The UK government and each of the three devolved governments (in Scotland, Wales and Northern Ireland) introduced public health and economic measures, including new laws, to mitigate the impact of the pandemic [2, 4, 5]. A national lockdown was introduced on 23 March 2020 [4, 5]. By mid-April it was reported that restrictions had "flattened the curve" of the epidemic and the daily number of new cases had passed its peak after 26,000 deaths [1, 6-9]. The national lockdown was lifted in May and replaced with specific regional restrictions which were gradually eased in late spring and early summer of that year [4, 5].

A second wave with a new variant began circulating in the autumn of 2020 [1, 3]. This led to the introduction of tiered restrictions in both England and Scotland in October 2020, and in England this was followed by a month-long lockdown during November followed by new tiered restrictions in December [2, 4, 5]. Multi-week 'circuit-breaker' lockdowns were imposed in Wales and Northern Ireland [2, 4, 5].

A third wave, principally due to the Delta variant, began in July 2021, although most restrictions were lifted during this third wave. In early December 2021, a fourth wave began, fuelled by the Omicron variant, resulting in the reintroduction of some social restrictions. During February 2022, all remaining legally enforced restrictions were ended in England and Northern Ireland [2, 4, 5]. All restrictions were ended in Wales and Scotland by the end of March and April 2022, respectively [2, 4, 5]. The number of cases rose following the relaxation of restrictions, but began to decline shortly after [1].

In the UK, the pandemic has resulted in over 23 million confirmed cases and over >187,000 deaths within 28 days of a positive Covid-19 test [6-10]. In December 2020, the first Covid-19 vaccine was approved and began being deployed across the UK with a staggered rollout prioritising the most vulnerable and then moving to progressively younger age groups [11]. By August 2021, more than 75% of adults in the UK had been fully vaccinated against Covid-19 [3, 11].

Before the pandemic, around 85% of the burden of disease in the UK was due to long-term conditions rather than infectious diseases [12]. Although the Government put measures in place to protect and support vulnerable people, there were, and are, increasing concerns about the impact of the pandemic on the health care needs of those with longer-term health conditions [13, 14]. The UK's health services were reprioritised to manage the increased demand from Covid-19-related illness and to allow for new social distancing restrictions, resulting in fewer patients being treated [14, 15]. Consequently, the treatment of existing conditions was reduced leading to a backlog of unmet care need [14, 15].

Despite the restrictions, in April 2020, 98% of people with a long-term condition who needed prescription medications were still able to obtain them. Moreover, 73% of those who needed treatment via a GP were able to access primary care, often through telemedicine and e-consults and 65% were able to see a pharmacist [14]. An unintended consequence of the use of digital technology is that people who did not have access to such technology or were reliant on face-to-face services found accessing health care challenging [14]. The greatest reduction in primary care consultations was among patients without a pre-existing condition [14], suggesting that a large number of people with undiagnosed conditions will come into contact with the health system at a more advanced stage of their condition [14]. Furthermore, in 2020, an estimated 6 million patients did not seek treatment in England, implying that many people could be living with poor health [14].

The surge in Covid-19-related care was also accompanied by a reduction in demand and supply of care for other illness within the hospital environment [13, 14, 16]. Many elective admissions were postponed to maintain capacity for Covid-19 patients [16]. Between March and December 2020 in England, there were 2.9 million (34.4%) fewer elective in-patient admissions, 1.2 million (21.4%) fewer non-Covid-19 emergency in-patient admissions and 17.1 million (21.8%) fewer out-patient appointments compared with the same period in 2019 [16]. There were also fewer accident and emergency visits [16]. The pressure has continued with only 73% of people attending accident and emergency departments in February 2022 seen within 4 hours, compared to a target of 95% [15]. By June 2022, the waiting list for routine hospital care in England had reached 6.7 million, with 355,000 patients waiting over a year [17].

Long Covid is limiting people's ability to return to activities of daily living. By early January 2022, an estimated 1.3 million people self-reported being affected by long Covid in the UK [18]. The social restrictions during the pandemic have also affected people's mental health through reduced social interaction, changing work conditions and loss of work and income [14, 15]. Access to social care services also declined during the pandemic despite an increasing need [14, 15].

Venous leg ulcers (VLUs) are a major cause of morbidity and decreased health-related quality of life [19]. In 2017/2018, the annual prevalence of VLUs in adults over 18 years of age in the UK was estimated at 1 per 100 individuals, equivalent to 560,000 patients with a leg ulcer in that period [20]. Compression bandages are the mainstay of treatment for VLUs. Up to 49% of newly-presenting VLUs can be induced to heal by applying adequate levels of sustained, graduated compression [21]. Once healed, some VLUs recur and patients can experience a repeated cycle of ulceration, healing and recurrence. Some VLUs fail to heal in a timely manner and they then become hard-to-heal [22].

During the pandemic many tissue viability services reported they were operating at reduced capacity, with a few trusts struggling to provide even basic wound care [23]. There was also a change or temporary reduction of many community-based services that would have been providing wound care [24, 25]. Against this background, this study aimed to assess the impact of the Covid-19 pandemic on the management of patients with a VLU in clinical practice in the UK and associated clinical outcomes, within the context of the health services.

METHODS

Study Design

This study was a retrospective cohort analysis of an anonymised sample of records of patients with a VLU obtained from the Health Improvement Network (THIN) database. The perspective of the analysis was the UK's health services.

The Health Improvement Network (THIN) Database

The THIN database contains electronic records on >11 million anonymised patients entered by general practitioners (GPs) from >560 practices across the UK. The patient composition within the THIN database has been shown to be representative of the UK population in terms of demographics and disease distribution [26] and the database theoretically contains patients' entire medical history.

In particular, the database collects data on the dates that patients registered or left their practice as well as demographic data, such as date of birth and gender. All medical conditions and symptoms recorded electronically during a patient's consultation in the general practice are recorded in the THIN database, thereby building up long computerised medical histories using Read Codes [27]. General practice prescribing is computerised and entered directly into the database. Prescriptions not issued electronically (e.g. during home visits) are also entered, however there is a possibility of under-recording of such items. Information is also recorded on referrals to secondary care, including the specialty. Secondary care information and other medically-related information received by the practice are entered into the database. This includes details on hospital admissions, discharge medication, diagnosis, outpatient consultations, investigations and treatment outcomes. Details on a range of variables such as height, weight, body mass index, blood pressure, smoking are also recorded. Hence, the information contained in the THIN database reflects actual clinical practice.

(THIN is a registered trademark of Cegedim SA in the UK and other countries. IQVIA Medical Research Data (IMRD) incorporates data from THIN, A Cegedim Database. Reference made to THIN is intended to be descriptive of the data asset licensed by IQVIA.)

Study Population

The study population comprised the anonymised case records of a cohort of patients from the THIN database (provided to the Authors by IQVIA) who had a VLU in 2019 and/or 2020 and/or 2021. Patients were included in the data set if they:

- Were ≥18 years of age.
- Had a Read code for a VLU in 2019 and/or 2020 and/or 2021.
- Had continuous medical history in their case record from the first mention of a VLU up to the time the data were extracted from the database, unless they died, in order to exclude patients who had moved or changed their general practice

Patients were excluded from the data set if they:

- Were <18 years of age.
- Did not have continuous medical history in their case record from the first mention of a VLU.
- Had a dermatological tumour.

The records of 2,000 patients were reviewed, of which 54 records were excluded from the analysis because they had >5% missing data. The records of the remaining 1,946 patients fulfilled the study's inclusion and exclusion criteria and were included in the data set. Patients' complete electronic records were supplied to the Authors, which enabled analysis of data both within and outside of the study period.

Patient and Public Involvement

Patients and members of the public were not directly involved in this study. The study population was limited to the anonymised records of patients in the THIN database.

Study Variables and Statistical Analyses

The following information was systematically extracted from the patients' electronic records

from the time a patient entered the data set (i.e. from the start of 2019 or the start time of their wound if it occurred later) up to the time their wound healed or the end of the study period (i.e. the end of 2021), whichever came first.

- Patients' characteristics.
- Patients' comorbidities (defined as a non-acute condition that patients were suffering from in the year before the start of their wound and not necessarily the year before the start of the study period).
- Wound-related healthcare resource use (which included dressings, bandages, district nurse visits (who provide care within a patient's home), practice nurse visits (who provide care within the general practice), GP visits, hospital outpatient visits, prescribed medication (i.e. analgesics, and antibiotics).
- Clinical outcomes (i.e. healing, infections, sepsis, gangrene and amputation).

If a patient received a dressing or bandage on a specific date, but a clinician visit was not documented in their record, it was assumed the patient had been seen outside of the general practice by a district nurse. No other assumptions were made regarding missing data and there were no other interpolations.

The use of individual healthcare resources was quantified for all the patients, individually. These quantities were then used to estimate the mean utilisation of each healthcare resource attributable to VLU management in each year and were compared with our published estimate of resource use in 2017/2018 [20].

Differences between 2019, 2020 and 2021 were tested for statistical significance using a Kruskal-Wallis test or Chi-Square test. Logistic regression was used to investigate relationships between baseline variables and clinical outcomes and linear regression was used to assess the impact of the pandemic years on healthcare resource use. The p values <0.05 were considered statistically significant and have been reported. All p values ≥ 0.05 were not considered to be statistically significant and these numerical values have not been reported.

All statistical analyses were performed using IBM SPSS Statistics (IBM UK, Portsmouth, Hampshire, UK).

Cost of Patient Management

The health service cost of VLU management for each patient was estimated by assigning unit costs at 2020/2021 prices [28-30] to the quantity of healthcare resources used by individual patients. The total cost of utilisation of each healthcare resource for the sample of patients was then combined in order to estimate the mean total health service cost of VLU management in each year. These costs were compared with our published estimated costs of VLU management in 2017/2018 [2], which were uprated to 2020/21 prices. Accordingly, the study only considers the cost of patient management attributable to VLUs in primary and secondary care settings, and does not estimate patients' overall healthcare costs.

Sensitivity Analysis

Deterministic sensitivity analyses were undertaken to examine the effect of independently varying the values of individual parameters. The parameter estimates were individually varied over plausible ranges by altering them to ±20% around the base case value. However, the percentages were bounded by 0% and 100%.

RESULTS

Patients' Characteristics

The study population comprised 1,946 patients with a VLU. Of these:

- 1,263 patients had a VLU in 2019.
- 1,153 patients had a VLU in 2020.
- 733 patients had a VLU in 2021.

The number of new and existing VLUs in each year is summarised in Figure 1.

There were no differences in patients' baseline characteristics between each year. However, the percentage of patients with a new VLU was less in 2021 than in 2020 and 2019 (Table 1). A total of 44% and 48% of patients presented with a new wound in 2019 and 2020. However, in 2021, only 17% of patients in the cohort presented with a new VLU, probably indicative of patients with a new ulcer not seeking or obtaining health care.

Clinical Outcomes

The THIN database does not define wound healing. Wound healing was a clinical observation documented in the patient's record by their managing clinician, but not necessarily confirmed by a specialist, and it is unknown if the clinicians who managed these patients used any consistent definition. Furthermore, if a wound was not recorded as being healed it was considered to be unhealed. This assumption was supported by continued clinician visits for wound care and the continued prescribing of wound care products. On this basis the VLU healing rate in 2020 and 2021 decreased by 16% and 42%, respectively, compared with 2019 (Table 2). Additionally, the time to heal increased by >85% (Table 2).

An estimated 3% of patients in both 2020 and 2021 were recorded as having a Covid-19 infection. Furthermore, 1% of patients in both years had VLU-related sepsis, 0.1-0.2% developed gangrene and 0.3% and 0.6% underwent an amputation on part of the foot or lower limb in 2020 and 2021, respectively (Table 2). None of the patients who developed gangrene had diabetes or underwent an amputation. Also, 57% of those who underwent an amputation did have diabetes, indicating some arterial involvement in these patients.

Binary logistic regression suggested that smoking (OR 0.72 (95% CI 0.60 to 0.88); p<0.001), years of the pandemic (OR 0.77 (95% CI 0.64 to 0.93); p=0.007) and wound duration (OR 0.98 (95% CI 0.97 to 0.99); p<0.001) were independent risk factors for VLUs not healing.

Healthcare Resource Use Associated with Patient Management

Table 3 summarises the percentage of patients who utilised different resources in each year and the mean amount of resource that was used. Patients were predominantly managed in the community by practice nurses and district/community nurses (Table 3). In 2019, an average patient with a VLU had a mean of 50 face-to-face visits with a clinician in the community. In 2020 and 2021, an average patient had a mean of 21-23 such visits each year (>50% reduction). Moreover, the distribution of visits between the different types of clinician increased towards practice nurses over the three consecutive years (Figure 2). Additionally, 38% and 48% fewer patients were referred to a specialist in a hospital outpatient clinic in 2020 and 2021, respectively.

There were no differences in the percentage of patients being admitted into hospital or attending an accident and emergency department between the three years. Linear regression indicated that sepsis, amputation, covid-19 infection and wound infection all increased the risk of hospital admission (Table 4).

Patients' treatment varied over the three years with 80% of patients having been prescribed a combination of dressings and compression in 2019, decreasing to 74% of patients in 2021 (a decrease of 8%). In 2020 and 2021, 19-20% of patients were prescribed dressings without any compression compared to 5% in 2019 (Figure 3). Overall, the total number of wound care products prescribed in 2020 and 2021 was >50% less than that prescribed in 2019. This may be a consequence of the frequency of dressing change having increased from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021. In 2017/2018 the frequency of dressing change was once every 3.5 days [20].

The total number of prescriptions for analgesics and antibiotics prescribed in 2020 and 2021 was >40% less and >30% less, respectively, than that prescribed in 2019. This reduction in

prescribing may be due to clinicians' reluctance to prescribe without seeing a patient in person, rather than a reduction in the frequency of pain or infection.

There was no difference in resource use between managing a new onset VLU and an existing ulcer in 2019. However, in 2020 and 2021 an average patient with a new onset VLU had a mean of 17 face-to-face visits with a community-based clinician each year. In contrast, the patients with an existing VLU had 13 such visits each year (a 24% reduction). There were no differences in the number of prescribed wound care products between patients with a new onset or existing VLU. Neither were there any differences in referrals to hospital-based clinicians or hospital admissions.

Assessment of peripheral perfusion is a recognised requirement for leg ulcer management. However, only 16%, 11% and 15% of patients in 2019, 2020 and 2021, respectively, had a Doppler ankle brachial pressure index (ABPI) recorded in their records. Of these patients, 100%, 92% and 88% in 2019, 2020 and 2021, respectively, were prescribed some form of compression. Of the patients who did not have their ABPI recorded, 86%, 71% and 67% were prescribed compression bandages/hosiery in 2019, 2020 and 221, respectively.

Health Service Cost of Patient Management

The total annual health service cost of VLU management was estimated to be a mean of £3,920 per VLU in 2019, decreasing to £2,470 in 2020 and £3,355 in 2021 (Table 5). In 2019, 32% of the cost was attributable to district nurse visits and 39% due to hospital admissions. In 2020 and 2021, 65-68% of the cost was attributable to hospital admissions and 9% was due to district nurse visits (Table 5).

In 2019, 58% of the total cost of VLU management was incurred in the community and the remaining 42% in secondary care. In 2020 and 2021, 70% and 73%, respectively, of the total cost of VLU management was incurred in secondary care and the remainder in the community. In 2017/2018, 15% of the total cost of VLU management was incurred in secondary care and 85% in the community [20].

Sensitivity Analysis

Deterministic sensitivity analyses (Table 6) showed that by individually varying the parameter estimates, the total cost of VLU management was affected to a greater extent by changing the number of hospital admissions. The costs were affected to a lesser extent by changing the number of district nurse visits and the VLU healing rate. Varying other parameters appeared to have a minimal impact on the total cost of VLU management.

Impact of the Covid-19 Pandemic

Linear regression estimated the change in healthcare resource utilisation between the pandemic (2020 and 2021) and pre-pandemic (2019) periods. This showed there was a significant reduction in prescriptions for compression, district nurse visits, prescriptions for dressings, GP visits, prescriptions for analgesics, prescriptions for antibiotics and hospital outpatient visits during the pandemic period compared with the pre-pandemic period. Conversely, the number of tele consults with practice nurses and GPs both significantly increased during the pandemic years (Table 7).

DISCUSSION

This study aimed to assess the impact of the Covid-19 pandemic [1-4] together with the associated lockdowns and social restrictions [2, 4, 5] on the management of VLUs and the consequential outcomes. The study was based on a retrospective analysis of patients' records in the THIN database. Inevitably there were some limitations, since the analysis was based on clinicians' entries into their patients' records and unavoidably subject to a certain amount of imprecision and lack of detail. One such limitation is that some patients in our data set may have had multiple wounds, but this was not specifically listed within the database and was not transparent in the patients' records. Furthermore, it would be very difficult to retrospectively extricate resource use for different wounds from the records of a patient with multiple wounds of the same aetiology. Notwithstanding this, it would be unusual for an individual to have two wounds of different aetiologies at the same time. Consequently, some patients may have had a second ulcer on their lower limb. The implication of this would be negligible since resource use and corresponding costs as presented would remain unchanged because all the resources and wound care products used in managing each patient were documented in their record (despite the lack of granularity surrounding the number of VLUs they may have had).

There were no significant differences in baseline characteristics of the patients in the different study years, which were comparable to those with a VLU in our 2017/2018 burden of wounds data set [20]. Nevertheless, the possibility that undetected differences existed between the cohorts in the different study years cannot be excluded. The smaller percentage of patients with a new VLU in 2021 is likely to be a reflection of patients with a new-onset wound self-managing and not accessing primary care. This is consistent with the aforementioned report that the greatest reduction in primary care consultations during the pandemic was among patients without a pre-existing condition [14]. Consequently, a large number of people with undiagnosed VLUs will probably come into contact with the health system once their wound has deteriorated, contributing to the backlog of unmet care need.

Notwithstanding, the data indicated that the percentage of healed VLUs increased from 37% in 2017/2018 [20] to 55% in 2019, possibly reflecting better management as a result of various programmes including the National Wound Care Strategy Programme [31] and campaigns, such as Legs Matter [32]. However, the impact of the pandemic [1-4] together with the

associated lockdowns and social restrictions [2, 3, 5] led to the VLU healing rate being reduced to 46% and 32% in 2020 and 2021, respectively and a simultaneous increase in the time to healing from a mean of 3 months in 2019 to >5 months in 2020 and 2021. These poorer outcomes may be a consequence of the reduction in face-to-face visits and associated hands-on management by clinicians. An average patient with a VLU had a >50% reduction in the number of face-to-face visits with a clinician in the community during 2020 and 2021 compared with the pre-pandemic period (from a mean of 50 to a mean of 21-23 visits). Additionally, 38% and 48% fewer patients were referred for specialist involvement in 2020 and 2021, respectively. This inevitably led to a reduction in the frequency of dressing change from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021 and a >50% reduction in the number of wound care products that were prescribed. This 'perfect storm' would not only have contributed to the poorer healing rates in 2020 and 2021, but also to a small percentage of patients having developed sepsis, or gangrene or undergone an amputation on part of the foot or lower limb in 2020 and 2021. In all our previous studies on the management of VLUs in clinical practice, we never encountered a single patient who had sepsis or gangrene or underwent an amputation on part of the foot or lower limb [20, 22, 33-38]. This analysis indicated a significant trend towards decreasing standards of care during 2020 and 2021 which was outside the boundaries of what is considered to be 'good care', leading to these poorer outcomes. Notwithstanding, anecdotally clinicians informed the Authors that they are not aware of any compression regime that is able to maintain adequate compression pressure for 11 or more days, indicating that even pre-pandemic, the frequency of face-to-face clinician visits was not optimal.

It is noteworthy that between March and December 2020 compared with the same period in 2019 there were 17.1 million fewer hospital outpatient appointments, 2.9 million fewer elective hospital admissions, 1.2 million fewer non-Covid-19 emergency hospital admissions in England [16]. There was also 7.6 million fewer accident and emergency attendances in 2020/21 than in 2019/20 [39]. In this study's cohort of patients with a VLU, there were fewer hospital outpatient appointments in 2020 and 2021 compared with 2019, but there were no significant differences in hospital admissions and accident and emergency attendances across the three years.

It was not possible to determine which professional groups were the decision makers in relation to VLU management as this information was not specifically recorded in the patients' records. However, <20% of patients in any year had a vascular assessment with a Doppler ABPI recorded in their records, contrary to national guidance [40, 41]. This was not a pandemic-related observation since successive studies have reported that compression is routinely applied to the leg without assessment of arterial status in the limb in the majority of patients in clinical practice [20, 22, 33, 34]. It remains unclear and disappointing to find that records still lacked documentation of this essential investigation, particularly in 2019.

The reduced levels of healthcare resource use in 2020 and 2021 inevitably resulted in a smaller cost of VLU management when compared to 2019. While the levels of resource use in the community decreased during the years of the pandemic, hospital admissions and accident and emergency attendances remained relatively static. Sensitivity analysis showed that the total cost of VLU management was affected to a greater extent by changing the number of hospital admissions rather than by changing any other parameter. Moreover, the risk of hospital admission was increased among those either with sepsis or covid-19 infection or wound infection or having to undergo an amputation. The shift towards less utilisation of community-based resources during the pandemic is reflected in the distribution of the cost of leg ulcer care between the community and secondary care. In 2019, 42% of the total cost of VLU management was incurred in secondary care. In 2020 and 2021, this increased to 70% and 73%, respectively, with the remainder being incurred in the community. In 2017/2018, 15% of the total cost of VLU management was incurred in secondary care and 85% in the community [20].

Whilst there was a reprioritisation of health care services to manage Covid-19-related demand [14, 15], it seems unclear how the health services can best manage its backlog of unmet care need [14]. While e-consults and telemedicine consultations with GPs and practice nurses are planned to increase [42], this analysis has indicated the consequences of patients with VLUs not having an adequate number of face-to-face visits with clinicians. The massive reduction in healthcare resource utilisation in managing patients with a VLU makes a compelling case for prioritising efforts that address the unmet needs of these patients. An assessment of the impact of the pandemic on other wound types was beyond the remit of the current study, but it may be comparable to that observed for VLUs. Notwithstanding, health services for wound care need to be restored and a plan needs to be implemented for managing those wounds that have not

had the attention from clinicians that they would normally receive, in order to facilitate healing and prevent any further exacerbation of outcomes. There have been many calls for monitoring the long-term impact of missed care and public campaigns have urged people to seek medical care when they need it [43]. As previously suggested [20], the Authors advocate the establishment of dedicated tissue viability clinics in the community across the country, at which patients receive consistent and integrated care from clinicians with qualified experience in wound care. These clinics could provide both direct wound care and holistic assessments of patients allowing coordinated management of any comorbidities which may impact on wound healing.

Due to the retrospective nature of the analysis, it was not possible to validate the study's findings with other sources at the current time. Nevertheless, the detrimental impact of the pandemic is not limited to wounds. A systematic review of the impact of the Covid-19 pandemic on utilisation of healthcare services across 20 countries found a median 37% reduction in healthcare service provision between pre-pandemic and pandemic periods [43]. This included a median 42% reduction in clinician visits and a median 28% reduction in hospital admissions [43]. Furthermore, the pandemic's disruption to healthcare globally, became a serious threat to patients who were incapable of managing their condition without caregiver support [44]. Moreover, there was in increase in bed shortages during the pandemic due to hospitalisation of Covid-19-infected patients. This made it increasingly difficult for hospitals to address the needs of non-Covid patients with serious conditions, such as those with cancer [45]. The pandemic has had a detrimental affect on cancer services leading to delays in diagnosis and management, resulting in an increase in mortality rate for many cancer types [46, 47].

Future research should assess the impact of ongoing changes in healthcare utilisation on population health, costs and equity. There is a need to fully understand how the pandemic differentially impacted on different patient groups and a need to prioritise ongoing healthcare provision accordingly. For example, what were patients' experiences of avoiding or missing care and what were the clinicians' responses to changes in process and practice? Did some patients who didn't receive the requisite care not incur any poorer outcomes or even improve? Have the changes that occurred during the pandemic subsequently been maintained or optimised? The extent and effects of replacing face-to-face care with telemedicine or self-care

also require investigation. Clearly, the establishment of a national wound registry would help to answer many of these questions.

The advantages and disadvantages of using the THIN database for this study have been previously discussed [33]. In summary, the advantage of using the THIN database is that the patient pathways and associated resource use were based on real-world evidence derived from clinical practice. However, the possibility of resource use associated with managing a comorbidity being conflated with that of wound management cannot be excluded. Prescriptions issued by GPs and practice nurses were recorded in the database, but it did not specify whether the prescriptions were dispensed or detail patient compliance with the product.

The analysis did not consider the potential impact of those wounds that remained unhealed beyond the study period. The THIN database may have under-recorded the use of some healthcare resources, particularly outside the GP's surgery if not documented in the GP records. In particular, not all community records may have been linked to the GP records. The impact of this was addressed in sensitivity analyses. Also excluded is the potential impact of managing patients with wounds being cared for in residential and nursing homes. The analysis only considered resource use for the 'average adult patient', and did not stratify resource use according to gender, comorbidities, wound size and severity of underlying venous disease. Despite these limitations, it is the Authors' opinion that the THIN database affords one of the best sources of real-world evidence for clinical practice in the UK. Furthermore, a review of Medline in August 2022 identified 1,938 articles in peer-reviewed journals in which the THIN database had been used as the source of real world evidence to characterise clinical practice in a wide range of therapeutic areas [27].

The analysis was unable to consider the level of a clinician's skills in managing VLUs. It was also unable to discern the challenges clinicians may have had in VLU management during the pandemic. The possibility that the analysis may not have identified all the confounding variables that could have influenced the impact of the pandemic cannot be excluded, in particular the impact of long Covid.

Notwithstanding the study's limitations, real-world evidence highlighted a significant trend toward decreasing care for VLUs during 2020 and 2021 which was outside the boundaries

considered to be good care. This led to poorer outcomes including an increased risk of amputation. Hence, the Covid-19 pandemic appears to have had a deleterious impact on the health of patients with a VLU.

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CONTRIBUTORS

JFG designed the study, obtained the THIN data set, managed the analyses, performed some analyses, checked all the other analyses, and wrote the manuscript. GWF conducted much of the analyses. Both the Authors were involved in revising the manuscript and gave final approval. JFG is the guarantor of this work and, as such, 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.

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This study was commissioned by 3M Healthcare, Loughborough, UK.

COMPETING INTERESTS

None declared.

PATIENT CONSENT FOR PUBLICATION

Not required.

ETHICS APPROVAL

Ethics approval to use patients' records from the THIN database for this study was obtained from the Research Ethics Committee that appraises studies using the THIN database (Reference number 22SRC014).

DATA AVAILABILITY STATEMENT

All data relevant to the study are included in the article. The THIN data set cannot be shared as this restriction was a condition of the ethics approval obtained from the Research Ethics Committee (Reference number 22SRC014). Questions concerning the data underlying the results can be sent to the corresponding author.

Table 1: Patients' characteristics.

	2017/2018 [20]	2019	2020	2021
Percentage new ulcers	59%	44%	48%	17%
Mean (± standard deviation) age per patient (years)	70.9±14.0	72.6±13.5	72.7±14.1	72.2±14.4
Percentage >=65 years of age	74%	75%	75%	74%
Percentage male	48%	48%	49%	48%
Percentage smokers	7%	22%	23%	24%
Percentage non-smokers	92%	67%	67%	64%
Percentage with unknown smoking status	1%	11%	10%	12%
Mean (± standard deviation) body mass index per patient (kg/m^2)	31.5±6.8	27.7±9.4	29.1±10.6	29.0±10.6
Percentage with cardiovascular disease	72%	59%	56%	59%
Percentage with respiratory disorders	33%	44%	43%	42%
Percentage with musculoskeletal disorders	59%	37%	38%	40%
Percentage with endocrinological disorders	52%	41%	39%	38%
Percentage with dermatological disorders	41%	38%	38%	36%
Percentage with gastrointestinal disorders	19%	37%	34%	36%
Percentage with genito-urinary disorders	19%	21%	20%	22%
Percentage with ophthalmological disorders	4%	25%	23%	21%
Percentage with psychiatric illness	15%	19%	19%	20%
Percentage with cancer	7%	26%	22%	20%
Percentage with neurological disorders	33%	18%	16%	15%
Percentage with renal disease	30%	14%	14%	13%
Percentage with haematological disease	3%	13%	11%	11%
Percentage with cerebrovascular disease	3%	10%	10%	9%
Mean (± standard deviation) number of comorbidities per patient	4.0±2.0	4.6±2.4	4.7±3.0	4.5±3.0

Table 2: Clinical outcomes.

	2017/2018 [20]	2019	2020	2021	p value
Percentage who developed an infected wound during the year	41%	47%	49%	47%	ns
Percentage who had a covid-19 infection	0%	0%	3%	3%	ns
Percentage who had sepsis	0%	0%	1%	1%	ns
Percentage who had gangrene	0%	0%	0.2%	0.1%	ns
Percentage who had amputation	0%	0%	0.3%	0.6%	ns
Percentage of all VLUs that healed	37%	55%	46%	32%	< 0.001*
Percentage of new VLUs that healed	56%	60%	50%	53%	0.001**
Mean (± standard deviation) time of a VLU to heal (months)	4.5±4.0	2.8±3.9	5.6±4.4	6.3±4.5	< 0.001**

* Differences between the 3 years

** Difference between 2019 and 2020/2021:

Table 3: Healthcare resource use associated with VLU management.

	2017/2018 [20]		2019		2020		2021		
	%	N	%	N	%	N	%	N	p value
GP surgery visits	100%	17.6	82%	7.1±6.0	73%	3.1±2.0	89%	3.9±2.8	< 0.001*
GP tele consults	<1%	1.0	11%	1.4±0.4	37%	1.8±0.9	36%	2.4±1.4	< 0.001**
Practice nurse visits	96%	25.8	80%	10.4±9.4	95%	8.2±7.0	92%	9.1±8.0	< 0.001**
Practice nurse tele consults	<1%	1.0	5%	1.5±0.4	25%	1.7±0.6	24%	1.6±0.5	< 0.001**
District nurse visits	85%	62.6	78%	29.2±26.4	67%	6.4±5.3	74%	7.3±6.1	< 0.001*
Practice nurse and district nurse combined	100%	88.4	96%	39.6±35.5	97%	14.6±12.1	94%	16.4±14.3	< 0.001**
Tissue viability nurse visits	1%	1.0	2%	2.0±0.4	4%	1.6±0.4	4%	1.4±0.3	ns
Podiatry visits	1%	1.0	2%	1.3±0.3	7%	1.8±0.6	6%	1.5±0.4	ns
Hospital outpatient visits	41%	6.6	21%	1.8±0.8	13%	1.5±0.4	11%	1.7±0.6	< 0.001**
Hospital admissions	7%	1.5	21%	1.6±0.4	22%	1.5±0.5	22%	2.1±1.0	ns
Accident and emergency attendances	30%	1.5	31%	1.3±0.3	32%	1.4±0.3	29%	2.0±0.9	ns
Compression systems	74%	49.9	88%	26.6±24.4	70%	5.8±4.7	56%	8.1±7.0	< 0.001*
Compression hosiery	70%	12.5	29%	2.1±1.0	31%	2.3±1.2	32%	2.6±1.5	ns
All compression	93%	62.4	89%	28.7±26.3	78%	8.1±6.1	74%	10.7±8.3	ns
Dressings	98%	142.6	85%	25.5±24.2	97%	10.8±9.5	94%	14.2±12.9	0.01*
Prescribed analgesics	81%	8.9	65%	12.3±11.1	47%	7.6±5.0	50%	8.6±6.4	0.01*
Prescribed antibiotics	81%	3.1	71%	5.2±4.3	56%	4.5±3.1	56%	4.6±3.6	0.01*

% = percentage of patients who utilised a resource in the study year; N = Annual amount (± standard deviation) of resource use per patient who used the resource in the study year * Differences between the 3 years; ** Difference between 2019 and 2020/2021

Table 4: Linear regression assessing the impact of clinical outcomes on hospital admission.

	Unstandardised B coefficient (95% confidence intervals)	p value
Sepsis	1.51 (1.13, 1.89)	0.001
Amputation	0.78 (0.20, 1.36)	0.009
Covid infection	0.42 (0.23, 0.60)	0.001
Years of the pandemic	0.22 (0.14, 0.29)	0.001
Wound infection	0.21 (0.15, 0.28)	0.001

Table 5: Mean cost of healthcare resource use associated with VLU management per patient.

	2017/2018 [20]		2019		2020		2021	
District nurse/healthcare assistant visits	£1,338.30	(30%)	£1,260.34	(32%)	£234.00	(9%)	£309.00	(9%)
Hospital admissions	£217.27	(5%)	£1,520.53	(39%)	£1,614.01	(65%)	£2,286.44	(68%)
GP visits and tele consults	£792.84	(18%)	£446.85	(11%)	£188.00	(8%)	£236.00	(7%)
Compression	£623.78	(14%)	£204.30	(5%)	£46.00	(2%)	£62.00	(2%)
Practice nurse visits and tele consults	£326.76	(7%)	£193.78	(5%)	£174.00	(7%)	£197.00	(6%)
Dressings	£643.49	(14%)	£76.81	(2%)	£37.00	(1%)	£49.00	(1%)
Prescribed drugs	£90.77	(2%)	£61.71	(2%)	£33.00	(1%)	£34.00	(1%)
Hospital outpatient visits	£389.75	(9%)	£87.41	(2%)	£43.00	(2%)	£47.87	(1%)
Accident & emergency attendances	£42.92	(1%)	£53.71	(1%)	£83.46	(3%)	£117.01	(3%)
Podiatrist visits	£0.00	(0%)	£9.96	(<1%)	£10.91	(<1%)	£10.18	(<1%)
Tissue viability nurse visits	£0.00	(0%)	£6.02	(<1%)	£6.52	(<1%)	£4.26	(<1%)
TOTAL	£4,465.88	(100%)	£3,921.42	(100%)	£2,469.90	(100%)	£3,352.76	(100%)

Table 6. Deterministic sensitivity analyses showing the range in the cost of VLU management when individual variables were changed by ±20%, but bounded by 0% and 100%. Values in parentheses indicate percentage change from the base case value.

Scenario	2019	2020	2021
Base case value	£3,921	£2,470	£3,353
Number of hospital admissions changed by ±20% of the estimated value	£3,617-£4,226 (8%)	£2,148-£2,793 (13%)	£2897-£3,812 (14%)
Number of district nurse visits changed by ±20% of the estimated value	£3,669-£4,173 (6%)	£2,424-£2,517 (2%)	£3,293-£3,417 (2%)
Percentage of VLUs healed changed by ±20% of the estimated value	£3,775-£4,069 (4%)	£2,371-£2,571 (4%)	£3,267-£3,438 (3%)
Number of GP visits changed by ±20% of the estimated value	£3,832-£4,010 (2%)	£2,435-£2,506 (1%)	£3,310-£3,399 (1%)
Number of accident and emergency attendances visits changed by ±20% of the estimated value	£3,911-£3,932 (<1%)	£2,454-£,2487 (1%)	£3,331-£3,378 (1%)
Number of prescribed compression bandages changed by ±20% of the estimated value	£3,881-£3,962 (1%)	£2,461-£2,480 (<1%)	£3,342-£3,367 (<1%)
Number of prescribed dressings changed by ±20% of the estimated value	£3,906-£3,937 (<1%)	£2,463-£2,478 (<1%)	£3,345-£3,365 (<1%)
Number of hospital outpatient visits changed by ±20% of the estimated value	£3,904-£3,939 (<1%)	£2,462-£2,479 (<1%)	£3,345-£3,364 (<1%)
Percentage of patients who underwent an amputation changed by ±20% of the estimated value	£3,921-£3,921 (0%)	£2,461-£2,480 (<1%)	£3,347-£3,363 (<1%)
Percentage of patients with sepsis or gangrene changed by ±20% of the estimated value	£3,921-£3,921 (0%)	£2,465-£2,476 (<1%)	£3,350-£3,359 (<1%)
Number of GP and practice nurse tele consults changed by ±20% of the estimated value	£3,921-£3,922 (<1%)	£2,468-£2,473 (<1%)	£3,351-£3,358 (<1%)
Number of practice nurse visits changed by ±20% of the estimated value	£3,921-£3,922 (<1%)	£2,470-£2,471 (<1%)	£3,354-£3,355 (<1%)

Table 7. Linear regression assessing the impact of the pandemic on key variables.

	Unstandardised B coefficient (95% confidence intervals)	p value
Compression	-18.83 (-20.39, -17.27)	0.001
District nurse visits	-18.31 (-19.81, -16.81)	0.001
Dressings	-10.36 (-12.01, -8.72)	0.001
GP visits	-3.38 (-3.79, -2.98)	0.001
Prescriptions for analgesics	-2.32 (-3.13, -1.51)	0.001
Prescriptions for antibiotics	-1.19 (-1.52, -0.89)	0.001
Hospital outpatient visits	-0.2 (-0.26, -0.14)	0.001
Practice nurse tele consults	0.33 (0.27, 0.38)	0.001
GP tele consults	0.58 (0.50, 0.66)	0.001

Figure 1. Flow diagram showing the number of patients in each period.

Figure 2: Distribution of face-to-face visits.

Figure 3. Distribution of prescribed dressings and compression.

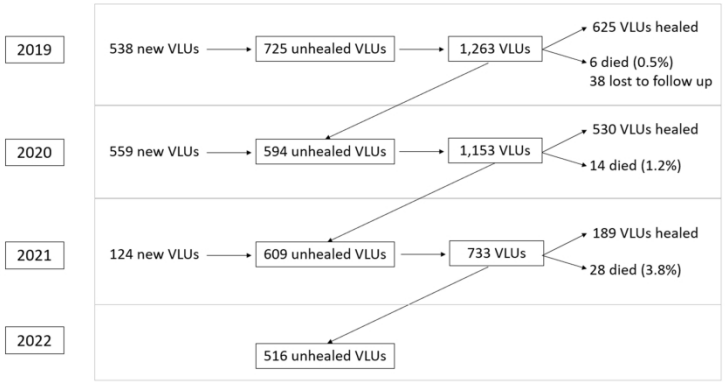

Figure 1

338x190mm (300 x 300 DPI)

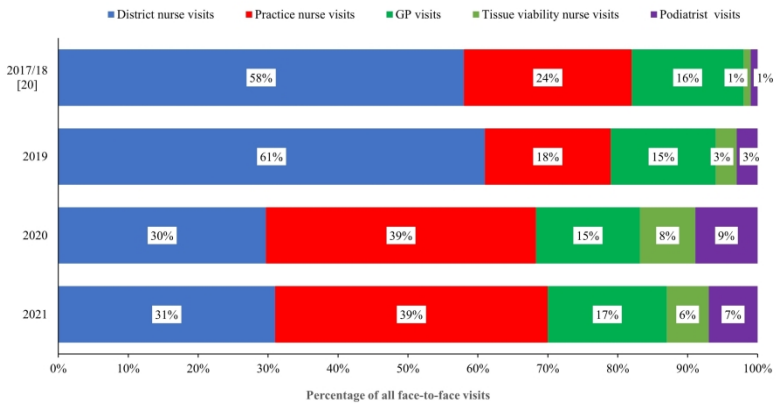

Figure 2

338x190mm (300 x 300 DPI)

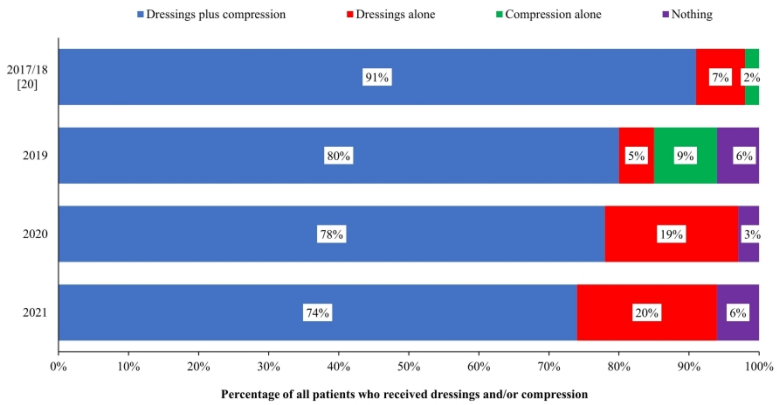

Figure 3

338x190mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3,4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8,9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	33
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	26
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	28

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	28 N/A N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	29,31,32
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

COHORT STUDY ASSESSING THE IMPACT OF COVID-19 ON VENOUS LEG ULCER MANAGEMENT AND ASSOCIATED CLINICAL OUTCOMES IN CLINICAL PRACTICE IN THE UK

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ORIGINAL RESEARCH

COHORT STUDY ASSESSING THE IMPACT OF COVID-19 ON VENOUS LEG ULCER MANAGEMENT AND ASSOCIATED CLINICAL OUTCOMES IN CLINICAL PRACTICE IN THE UK

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Running title: Impact of Covid-19 on VLU management and outcomes in clinical practice in the UK.

ABSTRACT

Objective: To assess the impact of the Covid-19 pandemic on venous leg ulcer (VLU) management by the UK's health services and associated outcomes.

Design: Retrospective cohort analysis of the electronic records of patients from the THIN database.

Setting: Clinical practice in primary and secondary care.

Participants: A cohort of 1,946 patients of whom 1,263, 1,153 and 733 had a VLU in 2019, 2020 and 2021, respectively.

Primary and secondary outcome measures: Clinical outcomes and wound-related healthcare resource use.

Results: VLU healing rate in 2020 and 2021 decreased by 16% and 42%, respectively, compared with 2019 and time to heal increased by >85%. An estimated 3% of patients in 2020 and 2021 had a covid-19 infection. Also, 1% of patients in both years had VLU-related sepsis, 0.1-0.2% developed gangrene and 0.3% and 0.6% underwent an amputation on part of the foot or lower limb in 2020 and 2021 (of whom 57% had diabetes), respectively. The number of community-based face-to-face clinician visits decreased by >55% in both years and >35% fewer patients were referred to a hospital specialist. In 2020 and 2021, up to 20% of patients were prescribed dressings without compression compared to 5% in 2019. The total number of wound care products prescribed in 2020 and 2021 was >50% less than that prescribed in 2019, possibly due to the increased frequency of dressing change from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021.

Conclusions: There was a significant trend toward decreasing care during 2020 and 2021 which was outside the boundaries considered to be good care. This led to poorer outcomes including lower VLU healing rates and increased risk of amputation. Hence, the Covid-19 pandemic appears to have had a deleterious impact on the health of patients with a VLU.

Keywords: Covid-19, venous leg ulcer, wound management.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study to estimate how the Covid-19 pandemic affected the management of venous leg ulcers and patients' outcomes.
- This study was undertaken using real-world evidence derived from the anonymised records of a sample of 1,946 patients in The Health Improvement Network database (a nationally representative database of clinical practice among >11 million patients registered with general practitioners in the UK).
- The data set was analysed retrospectively, and no other data sources are available to check or verify the completeness and accuracy of the data.
- The analysis was based on clinicians' entries into their patients' records and inevitably subject to a certain amount of imprecision and lack of detail.
- The analysis excluded the potential impact of managing patients with a VLU being cared for in residential and nursing homes.

INTRODUCTION

The Covid-19 pandemic in the UK was part of the worldwide pandemic of coronavirus disease 2019 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus started to circulate in the UK by the end of January 2020 [1-4]. The UK government and each of the three devolved governments (in Scotland, Wales and Northern Ireland) introduced public health and economic measures, including new laws, to mitigate the impact of the pandemic [2, 4, 5]. A national lockdown was introduced on 23 March 2020 [4, 5]. By mid-April it was reported that restrictions had "flattened the curve" of the epidemic and the daily number of new cases had passed its peak after 26,000 deaths [1, 6-9]. The national lockdown was lifted in May and replaced with specific regional restrictions which were gradually eased in late spring and early summer of that year [4, 5].

A second wave with a new variant began circulating in the autumn of 2020 [1, 3]. This led to the introduction of tiered restrictions in both England and Scotland in October 2020, and in England this was followed by a month-long lockdown during November followed by new tiered restrictions in December [2, 4, 5]. Multi-week 'circuit-breaker' lockdowns were imposed in Wales and Northern Ireland [2, 4, 5].

A third wave, principally due to the Delta variant, began in July 2021, although most restrictions were lifted during this third wave. In early December 2021, a fourth wave began, fuelled by the Omicron variant, resulting in the reintroduction of some social restrictions. During February 2022, all remaining legally enforced restrictions were ended in England and Northern Ireland [2, 4, 5]. All restrictions were ended in Wales and Scotland by the end of March and April 2022, respectively [2, 4, 5]. The number of cases rose following the relaxation of restrictions, but began to decline shortly after [1].

In the UK, the pandemic has resulted in over 23 million confirmed cases and over >187,000 deaths within 28 days of a positive Covid-19 test [6-10]. In December 2020, the first Covid-19 vaccine was approved and began being deployed across the UK with a staggered rollout prioritising the most vulnerable and then moving to progressively younger age groups [11]. By August 2021, more than 75% of adults in the UK had been fully vaccinated against Covid-19 [3, 11].

Before the pandemic, around 85% of the burden of disease in the UK was due to long-term conditions rather than infectious diseases [12]. Although the Government put measures in place to protect and support vulnerable people, there were, and are, increasing concerns about the impact of the pandemic on the health care needs of those with longer-term health conditions [13, 14]. The UK's health services were reprioritised to manage the increased demand from Covid-19-related illness and to allow for new social distancing restrictions, resulting in fewer patients being treated [14, 15]. Consequently, the treatment of existing conditions was reduced leading to a backlog of unmet care need [14, 15].

Despite the restrictions, in April 2020, 98% of people with a long-term condition who needed prescription medications were still able to obtain them. Moreover, 73% of those who needed treatment via a GP were able to access primary care, often through telemedicine and e-consults and 65% were able to see a pharmacist [14]. An unintended consequence of the use of digital technology is that people who did not have access to such technology or were reliant on face-to-face services found accessing health care challenging [14]. The greatest reduction in primary care consultations was among patients without a pre-existing condition [14], suggesting that a large number of people with undiagnosed conditions will come into contact with the health system at a more advanced stage of their condition [14]. Furthermore, in 2020, an estimated 6 million patients did not seek treatment in England, implying that many people could be living with poor health [14].

The surge in Covid-19-related care was also accompanied by a reduction in demand and supply of care for other illness within the hospital environment [13, 14, 16]. Many elective admissions were postponed to maintain capacity for Covid-19 patients [16]. Between March and December 2020 in England, there were 2.9 million (34.4%) fewer elective in-patient admissions, 1.2 million (21.4%) fewer non-Covid-19 emergency in-patient admissions and 17.1 million (21.8%) fewer out-patient appointments compared with the same period in 2019 [16]. There were also fewer accident and emergency visits [16]. The pressure has continued with only 73% of people attending accident and emergency departments in February 2022 seen within 4 hours, compared to a target of 95% [15]. By June 2022, the waiting list for routine hospital care in England had reached 6.7 million, with 355,000 patients waiting over a year [17].

Long Covid is limiting people's ability to return to activities of daily living. By early January 2022, an estimated 1.3 million people self-reported being affected by long Covid in the UK [18]. The social restrictions during the pandemic have also affected people's mental health through reduced social interaction, changing work conditions and loss of work and income [14, 15]. Access to social care services also declined during the pandemic despite an increasing need [14, 15].

Venous leg ulcers (VLUs) are a major cause of morbidity and decreased health-related quality of life [19]. In 2017/2018, the annual prevalence of VLUs in adults over 18 years of age in the UK was estimated at 1 per 100 individuals, equivalent to 560,000 patients with a leg ulcer in that period [20]. Compression bandages are the mainstay of treatment for VLUs. Up to 49% of newly-presenting VLUs can be induced to heal by applying adequate levels of sustained, graduated compression [21]. Once healed, some VLUs recur and patients can experience a repeated cycle of ulceration, healing and recurrence. Some VLUs fail to heal in a timely manner and they then become hard-to-heal [22].

During the pandemic many tissue viability services reported they were operating at reduced capacity, with a few trusts struggling to provide even basic wound care [23]. There was also a change or temporary reduction of many community-based services that would have been providing wound care [24, 25]. Against this background, this study aimed to assess the impact of the Covid-19 pandemic on the management of patients with a VLU in clinical practice in the UK and associated clinical outcomes, within the context of the health services.

METHODS

Study Design

This study was a retrospective cohort analysis of an anonymised sample of records of patients with a VLU obtained from the Health Improvement Network (THIN) database. The perspective of the analysis was the UK's health services.

The Health Improvement Network (THIN) Database

The THIN database contains electronic records on >11 million anonymised patients entered by general practitioners (GPs) from >560 practices across the UK. The patient composition within the THIN database has been shown to be representative of the UK population in terms of demographics and disease distribution [26] and the database theoretically contains patients' entire medical history.

In particular, the database collects data on the dates that patients registered or left their practice as well as demographic data, such as date of birth and gender. All medical conditions and symptoms recorded electronically during a patient's consultation in the general practice are recorded in the THIN database, thereby building up long computerised medical histories using Read Codes [27]. General practice prescribing is computerised and entered directly into the database. Prescriptions not issued electronically (e.g. during home visits) are also entered, however there is a possibility of under-recording of such items. Information is also recorded on referrals to secondary care, including the specialty. Secondary care information and other medically-related information received by the practice are entered into the database. This includes details on hospital admissions, discharge medication, diagnosis, outpatient consultations, investigations and treatment outcomes. Details on a range of variables such as height, weight, body mass index, blood pressure, smoking are also recorded. Hence, the information contained in the THIN database reflects actual clinical practice.

(THIN is a registered trademark of Cegedim SA in the UK and other countries. IQVIA Medical Research Data (IMRD) incorporates data from THIN, A Cegedim Database. Reference made to THIN is intended to be descriptive of the data asset licensed by IQVIA.)

Study Population

The study population comprised the anonymised case records of a cohort of patients from the THIN database (provided to the Authors by IQVIA) who had a VLU in 2019 and/or 2020 and/or 2021. Patients were included in the data set if they:

- Were ≥18 years of age.
- Had a Read code for a VLU in 2019 and/or 2020 and/or 2021.
- Had continuous medical history in their case record from the first mention of a VLU up to the time the data were extracted from the database, unless they died, in order to exclude patients who had moved or changed their general practice

Patients were excluded from the data set if they:

- Were <18 years of age.
- Did not have continuous medical history in their case record from the first mention of a VLU.
- Had a dermatological tumour.

The records of 2,000 patients were reviewed, of which 54 records were excluded from the analysis because they had >5% missing data. The records of the remaining 1,946 patients fulfilled the study's inclusion and exclusion criteria and were included in the data set. Patients' complete electronic records were supplied to the Authors, which enabled analysis of data both within and outside of the study period.

Patient and Public Involvement

Patients and members of the public were not directly involved in this study. The study population was limited to the anonymised records of patients in the THIN database.

Study Variables and Statistical Analyses

The following information was systematically extracted from the patients' electronic records

from the time a patient entered the data set (i.e. from the start of 2019 or the start time of their wound if it occurred later) up to the time their wound healed or the end of the study period (i.e. the end of 2021), whichever came first.

- Patients' characteristics.
- Patients' comorbidities (defined as a non-acute condition that patients were suffering from in the year before the start of their wound and not necessarily the year before the start of the study period).
- Wound-related healthcare resource use (which included dressings, bandages, district nurse visits (who provide care within a patient's home), practice nurse visits (who provide care within the general practice), GP visits, hospital outpatient visits, prescribed medication (i.e. analgesics, and antibiotics).
- Clinical outcomes (i.e. healing, infections, sepsis, gangrene and amputation).

If a patient received a dressing or bandage on a specific date, but a clinician visit was not documented in their record, it was assumed the patient had been seen outside of the general practice by a district nurse. No other assumptions were made regarding missing data and there were no other interpolations.

The use of individual healthcare resources was quantified for all the patients, individually. These quantities were then used to estimate the mean utilisation of each healthcare resource attributable to VLU management in each year and were compared with our published estimate of resource use in 2017/2018 [20].

Differences between 2019, 2020 and 2021 were tested for statistical significance using a Kruskal-Wallis test or Chi-Square test. Logistic regression was used to investigate relationships between baseline variables and clinical outcomes and linear regression was used to assess the impact of the pandemic years on healthcare resource use. The p values <0.05 were considered statistically significant and have been reported. All p values ≥ 0.05 were not considered to be statistically significant and these numerical values have not been reported.

All statistical analyses were performed using IBM SPSS Statistics (IBM UK, Portsmouth, Hampshire, UK).

Cost of Patient Management

The health service cost of VLU management for each patient was estimated by assigning unit costs at 2020/2021 prices [28-30] to the quantity of healthcare resources used by individual patients. The total cost of utilisation of each healthcare resource for the sample of patients was then combined in order to estimate the mean total health service cost of VLU management in each year. These costs were compared with our published estimated costs of VLU management in 2017/2018 [2], which were uprated to 2020/21 prices. Accordingly, the study only considers the cost of patient management attributable to VLUs in primary and secondary care settings, and does not estimate patients' overall healthcare costs.

Sensitivity Analysis

Deterministic sensitivity analyses were undertaken to examine the effect of independently varying the values of individual parameters. The parameter estimates were individually varied over plausible ranges by altering them to ±20% around the base case value. However, the percentages were bounded by 0% and 100%.

RESULTS

Patients' Characteristics

The study population comprised 1,946 patients with a VLU. Of these:

- 1,263 patients had a VLU in 2019.
- 1,153 patients had a VLU in 2020.
- 733 patients had a VLU in 2021.

The number of new and existing VLUs in each year is summarised in Figure 1.

There were no differences in patients' baseline characteristics between each year. However, the percentage of patients with a new VLU was less in 2021 than in 2020 and 2019 (Table 1). A total of 44% and 48% of patients presented with a new wound in 2019 and 2020. However, in 2021, only 17% of patients in the cohort presented with a new VLU, probably indicative of patients with a new ulcer not seeking or obtaining health care.

Clinical Outcomes

The THIN database does not define wound healing. Wound healing was a clinical observation documented in the patient's record by their managing clinician, but not necessarily confirmed by a specialist, and it is unknown if the clinicians who managed these patients used any consistent definition. Furthermore, if a wound was not recorded as being healed it was considered to be unhealed. This assumption was supported by continued clinician visits for wound care and the continued prescribing of wound care products. On this basis the VLU healing rate in 2020 and 2021 decreased by 16% and 42%, respectively, compared with 2019 (Table 2). Additionally, the time to heal increased by >85% (Table 2).

An estimated 3% of patients in both 2020 and 2021 were recorded as having a Covid-19 infection. Furthermore, 1% of patients in both years had VLU-related sepsis, 0.1-0.2% developed gangrene and 0.3% and 0.6% underwent an amputation on part of the foot or lower limb in 2020 and 2021, respectively (Table 2). None of the patients who developed gangrene had diabetes or underwent an amputation. Also, 57% of those who underwent an amputation did have diabetes, indicating some arterial involvement in these patients.

Binary logistic regression suggested that smoking (OR 0.72 (95% CI 0.60 to 0.88); p<0.001), years of the pandemic (OR 0.77 (95% CI 0.64 to 0.93); p=0.007) and wound duration (OR 0.98 (95% CI 0.97 to 0.99); p<0.001) were independent risk factors for VLUs not healing.

Healthcare Resource Use Associated with Patient Management

Table 3 summarises the percentage of patients who utilised different resources in each year and the mean amount of resource that was used. Patients were predominantly managed in the community by practice nurses and district/community nurses (Table 3). In 2019, an average patient with a VLU had a mean of 50 face-to-face visits with a clinician in the community. In 2020 and 2021, an average patient had a mean of 21-23 such visits each year (>50% reduction). Moreover, the distribution of visits between the different types of clinician increased towards practice nurses over the three consecutive years (Figure 2). Additionally, 38% and 48% fewer patients were referred to a specialist in a hospital outpatient clinic in 2020 and 2021, respectively.

There were no differences in the percentage of patients being admitted into hospital or attending an accident and emergency department between the three years. Linear regression indicated that sepsis, amputation, covid-19 infection and wound infection all increased the risk of hospital admission (Table 4).

Patients' treatment varied over the three years with 80% of patients having been prescribed a combination of dressings and compression in 2019, decreasing to 74% of patients in 2021 (a decrease of 8%). In 2020 and 2021, 19-20% of patients were prescribed dressings without any compression compared to 5% in 2019 (Figure 3). Overall, the total number of wound care products prescribed in 2020 and 2021 was >50% less than that prescribed in 2019. This may be a consequence of the frequency of dressing change having increased from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021. In 2017/2018 the frequency of dressing change was once every 3.5 days [20].

The total number of prescriptions for analgesics and antibiotics prescribed in 2020 and 2021 was >40% less and >30% less, respectively, than that prescribed in 2019. This reduction in

prescribing may be due to clinicians' reluctance to prescribe without seeing a patient in person, rather than a reduction in the frequency of pain or infection.

There was no difference in resource use between managing a new onset VLU and an existing ulcer in 2019. However, in 2020 and 2021 an average patient with a new onset VLU had a mean of 17 face-to-face visits with a community-based clinician each year. In contrast, the patients with an existing VLU had 13 such visits each year (a 24% reduction). There were no differences in the number of prescribed wound care products between patients with a new onset or existing VLU. Neither were there any differences in referrals to hospital-based clinicians or hospital admissions.

Assessment of peripheral perfusion is a recognised requirement for leg ulcer management. However, only 16%, 11% and 15% of patients in 2019, 2020 and 2021, respectively, had a Doppler ankle brachial pressure index (ABPI) recorded in their records. Of these patients, 100%, 92% and 88% in 2019, 2020 and 2021, respectively, were prescribed some form of compression. Of the patients who did not have their ABPI recorded, 86%, 71% and 67% were prescribed compression bandages/hosiery in 2019, 2020 and 221, respectively.

Health Service Cost of Patient Management

The total annual health service cost of VLU management was estimated to be a mean of £3,920 per VLU in 2019, decreasing to £2,470 in 2020 and £3,355 in 2021 (Table 5). In 2019, 32% of the cost was attributable to district nurse visits and 39% due to hospital admissions. In 2020 and 2021, 65-68% of the cost was attributable to hospital admissions and 9% was due to district nurse visits (Table 5).

In 2019, 58% of the total cost of VLU management was incurred in the community and the remaining 42% in secondary care. In 2020 and 2021, 70% and 73%, respectively, of the total cost of VLU management was incurred in secondary care and the remainder in the community. In 2017/2018, 15% of the total cost of VLU management was incurred in secondary care and 85% in the community [20].

Sensitivity Analysis

Deterministic sensitivity analyses (Table 6) showed that by individually varying the parameter estimates, the total cost of VLU management was affected to a greater extent by changing the number of hospital admissions. The costs were affected to a lesser extent by changing the number of district nurse visits and the VLU healing rate. Varying other parameters appeared to have a minimal impact on the total cost of VLU management.

Impact of the Covid-19 Pandemic

Linear regression estimated the change in healthcare resource utilisation between the pandemic (2020 and 2021) and pre-pandemic (2019) periods. This showed there was a significant reduction in prescriptions for compression, district nurse visits, prescriptions for dressings, GP visits, prescriptions for analgesics, prescriptions for antibiotics and hospital outpatient visits during the pandemic period compared with the pre-pandemic period. Conversely, the number of tele consults with practice nurses and GPs both significantly increased during the pandemic years (Table 7).

DISCUSSION

This study aimed to assess the impact of the Covid-19 pandemic [1-4] together with the associated lockdowns and social restrictions [2, 4, 5] on the management of VLUs and the consequential outcomes. The study was based on a retrospective analysis of patients' records in the THIN database. Inevitably there were some limitations, since the analysis was based on clinicians' entries into their patients' records and unavoidably subject to a certain amount of imprecision and lack of detail. One such limitation is that some patients in our data set may have had multiple wounds, but this was not specifically listed within the database and was not transparent in the patients' records. Furthermore, it would be very difficult to retrospectively extricate resource use for different wounds from the records of a patient with multiple wounds of the same aetiology. Notwithstanding this, it would be unusual for an individual to have two wounds of different aetiologies at the same time. Consequently, some patients may have had a second ulcer on their lower limb. The implication of this would be negligible since resource use and corresponding costs as presented would remain unchanged because all the resources and wound care products used in managing each patient were documented in their record (despite the lack of granularity surrounding the number of VLUs they may have had).

There were no significant differences in baseline characteristics of the patients in the different study years, which were comparable to those with a VLU in our 2017/2018 burden of wounds data set [20]. Nevertheless, the possibility that undetected differences existed between the cohorts in the different study years cannot be excluded. The smaller percentage of patients with a new VLU in 2021 is likely to be a reflection of patients with a new-onset wound self-managing and not accessing primary care. This is consistent with the aforementioned report that the greatest reduction in primary care consultations during the pandemic was among patients without a pre-existing condition [14]. Consequently, a large number of people with undiagnosed VLUs will probably come into contact with the health system once their wound has deteriorated, contributing to the backlog of unmet care need.

Notwithstanding, the data indicated that the percentage of healed VLUs increased from 37% in 2017/2018 [20] to 55% in 2019, possibly reflecting better management as a result of various programmes including the National Wound Care Strategy Programme [31] and campaigns, such as Legs Matter [32]. However, the impact of the pandemic [1-4] together with the

associated lockdowns and social restrictions [2, 3, 5] led to the VLU healing rate being reduced to 46% and 32% in 2020 and 2021, respectively and a simultaneous increase in the time to healing from a mean of 3 months in 2019 to >5 months in 2020 and 2021. These poorer outcomes may be a consequence of the reduction in face-to-face visits and associated hands-on management by clinicians. An average patient with a VLU had a >50% reduction in the number of face-to-face visits with a clinician in the community during 2020 and 2021 compared with the pre-pandemic period (from a mean of 50 to a mean of 21-23 visits). Additionally, 38% and 48% fewer patients were referred for specialist involvement in 2020 and 2021, respectively. This inevitably led to a reduction in the frequency of dressing change from a mean of once every 11 days in 2019 to once every 21 days in 2020 and 2021 and a >50% reduction in the number of wound care products that were prescribed. This 'perfect storm' would not only have contributed to the poorer healing rates in 2020 and 2021, but also to a small percentage of patients having developed sepsis, or gangrene or undergone an amputation on part of the foot or lower limb in 2020 and 2021. In all our previous studies on the management of VLUs in clinical practice, we never encountered a single patient who had sepsis or gangrene or underwent an amputation on part of the foot or lower limb [20, 22, 33-38]. This analysis indicated a significant trend towards decreasing standards of care during 2020 and 2021 which was outside the boundaries of what is considered to be 'good care', leading to these poorer outcomes. Notwithstanding, anecdotally clinicians informed the Authors that they are not aware of any compression regime that is able to maintain adequate compression pressure for 11 or more days, indicating that even pre-pandemic, the frequency of face-to-face clinician visits was not optimal.

It is noteworthy that between March and December 2020 compared with the same period in 2019 there were 17.1 million fewer hospital outpatient appointments, 2.9 million fewer elective hospital admissions, 1.2 million fewer non-Covid-19 emergency hospital admissions in England [16]. There was also 7.6 million fewer accident and emergency attendances in 2020/21 than in 2019/20 [39]. In this study's cohort of patients with a VLU, there were fewer hospital outpatient appointments in 2020 and 2021 compared with 2019, but there were no significant differences in hospital admissions and accident and emergency attendances across the three years.

It was not possible to determine which professional groups were the decision makers in relation to VLU management as this information was not specifically recorded in the patients' records. However, <20% of patients in any year had a vascular assessment with a Doppler ABPI recorded in their records, contrary to national guidance [40, 41]. This was not a pandemic-related observation since successive studies have reported that compression is routinely applied to the leg without assessment of arterial status in the limb in the majority of patients in clinical practice [20, 22, 33, 34]. It remains unclear and disappointing to find that records still lacked documentation of this essential investigation, particularly in 2019.

The reduced levels of healthcare resource use in 2020 and 2021 inevitably resulted in a smaller cost of VLU management when compared to 2019. While the levels of resource use in the community decreased during the years of the pandemic, hospital admissions and accident and emergency attendances remained relatively static. Sensitivity analysis showed that the total cost of VLU management was affected to a greater extent by changing the number of hospital admissions rather than by changing any other parameter. Moreover, the risk of hospital admission was increased among those either with sepsis or covid-19 infection or wound infection or having to undergo an amputation. The shift towards less utilisation of community-based resources during the pandemic is reflected in the distribution of the cost of leg ulcer care between the community and secondary care. In 2019, 42% of the total cost of VLU management was incurred in secondary care. In 2020 and 2021, this increased to 70% and 73%, respectively, with the remainder being incurred in the community. In 2017/2018, 15% of the total cost of VLU management was incurred in secondary care and 85% in the community [20].

Whilst there was a reprioritisation of health care services to manage Covid-19-related demand [14, 15], it seems unclear how the health services can best manage its backlog of unmet care need [14]. While e-consults and telemedicine consultations with GPs and practice nurses are planned to increase [42], this analysis has indicated the consequences of patients with VLUs not having an adequate number of face-to-face visits with clinicians. The massive reduction in healthcare resource utilisation in managing patients with a VLU makes a compelling case for prioritising efforts that address the unmet needs of these patients. An assessment of the impact of the pandemic on other wound types was beyond the remit of the current study, but it may be comparable to that observed for VLUs. Notwithstanding, health services for wound care need to be restored and a plan needs to be implemented for managing those wounds that have not

had the attention from clinicians that they would normally receive, in order to facilitate healing and prevent any further exacerbation of outcomes. There have been many calls for monitoring the long-term impact of missed care and public campaigns have urged people to seek medical care when they need it [43]. As previously suggested [20], the Authors advocate the establishment of dedicated tissue viability clinics in the community across the country, at which patients receive consistent and integrated care from clinicians with qualified experience in wound care. These clinics could provide both direct wound care and holistic assessments of patients allowing coordinated management of any comorbidities which may impact on wound healing.

Due to the retrospective nature of the analysis, it was not possible to validate the study's findings with other sources at the current time. Nevertheless, the detrimental impact of the pandemic is not limited to wounds. A systematic review of the impact of the Covid-19 pandemic on utilisation of healthcare services across 20 countries found a median 37% reduction in healthcare service provision between pre-pandemic and pandemic periods [43]. This included a median 42% reduction in clinician visits and a median 28% reduction in hospital admissions [43]. Furthermore, the pandemic's disruption to healthcare globally, became a serious threat to patients who were incapable of managing their condition without caregiver support [44]. Moreover, there was in increase in bed shortages during the pandemic due to hospitalisation of Covid-19-infected patients. This made it increasingly difficult for hospitals to address the needs of non-Covid patients with serious conditions, such as those with cancer [45]. The pandemic has had a detrimental affect on cancer services leading to delays in diagnosis and management, resulting in an increase in mortality rate for many cancer types [46, 47].

Future research should assess the impact of ongoing changes in healthcare utilisation on population health, costs and equity. There is a need to fully understand how the pandemic differentially impacted on different patient groups and a need to prioritise ongoing healthcare provision accordingly. For example, what were patients' experiences of avoiding or missing care and what were the clinicians' responses to changes in process and practice? Did some patients who didn't receive the requisite care not incur any poorer outcomes or even improve? Have the changes that occurred during the pandemic subsequently been maintained or optimised? The extent and effects of replacing face-to-face care with telemedicine or self-care

also require investigation. Clearly, the establishment of a national wound registry would help to answer many of these questions.

The advantages and disadvantages of using the THIN database for this study have been previously discussed [33]. In summary, the advantage of using the THIN database is that the patient pathways and associated resource use were based on real-world evidence derived from clinical practice. However, the possibility of resource use associated with managing a comorbidity being conflated with that of wound management cannot be excluded. Prescriptions issued by GPs and practice nurses were recorded in the database, but it did not specify whether the prescriptions were dispensed or detail patient compliance with the product.

The analysis did not consider the potential impact of those wounds that remained unhealed beyond the study period. The THIN database may have under-recorded the use of some healthcare resources, particularly outside the GP's surgery if not documented in the GP records. In particular, not all community records may have been linked to the GP records. The impact of this was addressed in sensitivity analyses. Also excluded is the potential impact of managing patients with wounds being cared for in residential and nursing homes. The analysis only considered resource use for the 'average adult patient', and did not stratify resource use according to gender, comorbidities, wound size and severity of underlying venous disease. Despite these limitations, it is the Authors' opinion that the THIN database affords one of the best sources of real-world evidence for clinical practice in the UK. Furthermore, a review of Medline in August 2022 identified 1,938 articles in peer-reviewed journals in which the THIN database had been used as the source of real world evidence to characterise clinical practice in a wide range of therapeutic areas [27].

The analysis was unable to consider the level of a clinician's skills in managing VLUs. It was also unable to discern the challenges clinicians may have had in VLU management during the pandemic. The possibility that the analysis may not have identified all the confounding variables that could have influenced the impact of the pandemic cannot be excluded, in particular the impact of long Covid.

Notwithstanding the study's limitations, real-world evidence highlighted a significant trend toward decreasing care for VLUs during 2020 and 2021 which was outside the boundaries

considered to be good care. This led to poorer outcomes including an increased risk of amputation. Hence, the Covid-19 pandemic appears to have had a deleterious impact on the health of patients with a VLU.

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CONTRIBUTORS

JFG designed the study, obtained the THIN data set, managed the analyses, performed some analyses, checked all the other analyses, and wrote the manuscript. GWF conducted much of the analyses. Both the Authors were involved in revising the manuscript and gave final approval. JFG is the guarantor of this work and, as such, 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.

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COMPETING INTERESTS

None declared.

PATIENT CONSENT FOR PUBLICATION

Not required.

ETHICS APPROVAL

Use of IQVIA Medical Research Data (IMRD-THIN) is approved by the UK Research Ethics Committee (reference number: 18/LO/0441). In accordance with this approval, this study's protocol was reviewed and approved by an independent Scientific Review Committee (Reference number 22SRC014).

DATA AVAILABILITY STATEMENT

All data relevant to the study are included in the article. The THIN data set cannot be shared as this restriction was a condition of the ethics approval obtained from the Scientific Review Committee (Reference number 22SRC014). Questions concerning the data underlying the results can be sent to the corresponding author.

Table 1: Patients' characteristics.

	2017/2018 [20]	2019	2020	2021
Percentage new ulcers	59%	44%	48%	17%
Mean (± standard deviation) age per patient (years)	70.9±14.0	72.6±13.5	72.7±14.1	72.2±14.4
Percentage >=65 years of age	74%	75%	75%	74%
Percentage male	48%	48%	49%	48%
Percentage smokers	7%	22%	23%	24%
Percentage non-smokers	92%	67%	67%	64%
Percentage with unknown smoking status	1%	11%	10%	12%
Mean (± standard deviation) body mass index per patient (kg/m^2)	31.5±6.8	27.7±9.4	29.1±10.6	29.0±10.6
Percentage with cardiovascular disease	72%	59%	56%	59%
Percentage with respiratory disorders	33%	44%	43%	42%
Percentage with musculoskeletal disorders	59%	37%	38%	40%
Percentage with endocrinological disorders	52%	41%	39%	38%
Percentage with dermatological disorders	41%	38%	38%	36%
Percentage with gastrointestinal disorders	19%	37%	34%	36%
Percentage with genito-urinary disorders	19%	21%	20%	22%
Percentage with ophthalmological disorders	4%	25%	23%	21%
Percentage with psychiatric illness	15%	19%	19%	20%
Percentage with cancer	7%	26%	22%	20%
Percentage with neurological disorders	33%	18%	16%	15%
Percentage with renal disease	30%	14%	14%	13%
Percentage with haematological disease	3%	13%	11%	11%
Percentage with cerebrovascular disease	3%	10%	10%	9%
Mean (± standard deviation) number of comorbidities per patient	4.0±2.0	4.6±2.4	4.7±3.0	4.5±3.0

Table 2: Clinical outcomes.

	2017/2018 [20]	2019	2020	2021	p value
Percentage who developed an infected wound during the year	41%	47%	49%	47%	ns
Percentage who had a covid-19 infection	0%	0%	3%	3%	ns
Percentage who had sepsis	0%	0%	1%	1%	ns
Percentage who had gangrene	0%	0%	0.2%	0.1%	ns
Percentage who had amputation	0%	0%	0.3%	0.6%	ns
Percentage of all VLUs that healed	37%	55%	46%	32%	< 0.001*
Percentage of new VLUs that healed	56%	60%	50%	53%	0.001**
Mean (± standard deviation) time of a VLU to heal (months)	4.5±4.0	2.8±3.9	5.6±4.4	6.3±4.5	< 0.001**

* Differences between the 3 years

** Difference between 2019 and 2020/2021:

Table 3: Healthcare resource use associated with VLU management.

	2017/2018 [20]		2019		2020		2021		
	%	N	%	N	%	N	%	N	p value
GP surgery visits	100%	17.6	82%	7.1±6.0	73%	3.1±2.0	89%	3.9±2.8	< 0.001*
GP tele consults	<1%	1.0	11%	1.4±0.4	37%	1.8±0.9	36%	2.4±1.4	< 0.001**
Practice nurse visits	96%	25.8	80%	10.4±9.4	95%	8.2±7.0	92%	9.1±8.0	< 0.001**
Practice nurse tele consults	<1%	1.0	5%	1.5±0.4	25%	1.7±0.6	24%	1.6±0.5	< 0.001**
District nurse visits	85%	62.6	78%	29.2±26.4	67%	6.4±5.3	74%	7.3±6.1	< 0.001*
Practice nurse and district nurse combined	100%	88.4	96%	39.6±35.5	97%	14.6±12.1	94%	16.4±14.3	< 0.001**
Tissue viability nurse visits	1%	1.0	2%	2.0±0.4	4%	1.6±0.4	4%	1.4±0.3	ns
Podiatry visits	1%	1.0	2%	1.3±0.3	7%	1.8±0.6	6%	1.5±0.4	ns
Hospital outpatient visits	41%	6.6	21%	1.8±0.8	13%	1.5±0.4	11%	1.7±0.6	< 0.001**
Hospital admissions	7%	1.5	21%	1.6±0.4	22%	1.5±0.5	22%	2.1±1.0	ns
Accident and emergency attendances	30%	1.5	31%	1.3±0.3	32%	1.4±0.3	29%	2.0±0.9	ns
Compression systems	74%	49.9	88%	26.6±24.4	70%	5.8±4.7	56%	8.1±7.0	< 0.001*
Compression hosiery	70%	12.5	29%	2.1±1.0	31%	2.3±1.2	32%	2.6±1.5	ns
All compression	93%	62.4	89%	28.7±26.3	78%	8.1±6.1	74%	10.7±8.3	ns
Dressings	98%	142.6	85%	25.5±24.2	97%	10.8±9.5	94%	14.2±12.9	0.01*
Prescribed analgesics	81%	8.9	65%	12.3±11.1	47%	7.6±5.0	50%	8.6±6.4	0.01*
Prescribed antibiotics	81%	3.1	71%	5.2±4.3	56%	4.5±3.1	56%	4.6±3.6	0.01*

% = percentage of patients who utilised a resource in the study year; N = Annual amount (± standard deviation) of resource use per patient who used the resource in the study year * Differences between the 3 years; ** Difference between 2019 and 2020/2021

Table 4: Linear regression assessing the impact of clinical outcomes on hospital admission.

	Unstandardised B coefficient (95% confidence intervals)	p value
Sepsis	1.51 (1.13, 1.89)	0.001
Amputation	0.78 (0.20, 1.36)	0.009
Covid infection	0.42 (0.23, 0.60)	0.001
Years of the pandemic	0.22 (0.14, 0.29)	0.001
Wound infection	0.21 (0.15, 0.28)	0.001

Table 5: Mean cost of healthcare resource use associated with VLU management per patient.

	2017/2018 [20]		2019		2020		2021	
District nurse/healthcare assistant visits	£1,338.30	(30%)	£1,260.34	(32%)	£234.00	(9%)	£309.00	(9%)
Hospital admissions	£217.27	(5%)	£1,520.53	(39%)	£1,614.01	(65%)	£2,286.44	(68%)
GP visits and tele consults	£792.84	(18%)	£446.85	(11%)	£188.00	(8%)	£236.00	(7%)
Compression	£623.78	(14%)	£204.30	(5%)	£46.00	(2%)	£62.00	(2%)
Practice nurse visits and tele consults	£326.76	(7%)	£193.78	(5%)	£174.00	(7%)	£197.00	(6%)
Dressings	£643.49	(14%)	£76.81	(2%)	£37.00	(1%)	£49.00	(1%)
Prescribed drugs	£90.77	(2%)	£61.71	(2%)	£33.00	(1%)	£34.00	(1%)
Hospital outpatient visits	£389.75	(9%)	£87.41	(2%)	£43.00	(2%)	£47.87	(1%)
Accident & emergency attendances	£42.92	(1%)	£53.71	(1%)	£83.46	(3%)	£117.01	(3%)
Podiatrist visits	£0.00	(0%)	£9.96	(<1%)	£10.91	(<1%)	£10.18	(<1%)
Tissue viability nurse visits	£0.00	(0%)	£6.02	(<1%)	£6.52	(<1%)	£4.26	(<1%)
TOTAL	£4,465.88	(100%)	£3,921.42	(100%)	£2,469.90	(100%)	£3,352.76	(100%)

Table 6. Deterministic sensitivity analyses showing the range in the cost of VLU management when individual variables were changed by ±20%, but bounded by 0% and 100%. Values in parentheses indicate percentage change from the base case value.

Scenario	2019	2020	2021
Base case value	£3,921	£2,470	£3,353
Number of hospital admissions changed by ±20% of the estimated value	£3,617-£4,226 (8%)	£2,148-£2,793 (13%)	£2897-£3,812 (14%)
Number of district nurse visits changed by ±20% of the estimated value	£3,669-£4,173 (6%)	£2,424-£2,517 (2%)	£3,293-£3,417 (2%)
Percentage of VLUs healed changed by ±20% of the estimated value	£3,775-£4,069 (4%)	£2,371-£2,571 (4%)	£3,267-£3,438 (3%)
Number of GP visits changed by ±20% of the estimated value	£3,832-£4,010 (2%)	£2,435-£2,506 (1%)	£3,310-£3,399 (1%)
Number of accident and emergency attendances visits changed by ±20% of the estimated value	£3,911-£3,932 (<1%)	£2,454-£,2487 (1%)	£3,331-£3,378 (1%)
Number of prescribed compression bandages changed by ±20% of the estimated value	£3,881-£3,962 (1%)	£2,461-£2,480 (<1%)	£3,342-£3,367 (<1%)
Number of prescribed dressings changed by ±20% of the estimated value	£3,906-£3,937 (<1%)	£2,463-£2,478 (<1%)	£3,345-£3,365 (<1%)
Number of hospital outpatient visits changed by ±20% of the estimated value	£3,904-£3,939 (<1%)	£2,462-£2,479 (<1%)	£3,345-£3,364 (<1%)
Percentage of patients who underwent an amputation changed by ±20% of the estimated value	£3,921-£3,921 (0%)	£2,461-£2,480 (<1%)	£3,347-£3,363 (<1%)
Percentage of patients with sepsis or gangrene changed by ±20% of the estimated value	£3,921-£3,921 (0%)	£2,465-£2,476 (<1%)	£3,350-£3,359 (<1%)
Number of GP and practice nurse tele consults changed by ±20% of the estimated value	£3,921-£3,922 (<1%)	£2,468-£2,473 (<1%)	£3,351-£3,358 (<1%)
Number of practice nurse visits changed by ±20% of the estimated value	£3,921-£3,922 (<1%)	£2,470-£2,471 (<1%)	£3,354-£3,355 (<1%)

Table 7. Linear regression assessing the impact of the pandemic on key variables.

	Unstandardised B coefficient (95% confidence intervals)	p value
Compression	-18.83 (-20.39, -17.27)	0.001
District nurse visits	-18.31 (-19.81, -16.81)	0.001
Dressings	-10.36 (-12.01, -8.72)	0.001
GP visits	-3.38 (-3.79, -2.98)	0.001
Prescriptions for analgesics	-2.32 (-3.13, -1.51)	0.001
Prescriptions for antibiotics	-1.19 (-1.52, -0.89)	0.001
Hospital outpatient visits	-0.2 (-0.26, -0.14)	0.001
Practice nurse tele consults	0.33 (0.27, 0.38)	0.001
GP tele consults	0.58 (0.50, 0.66)	0.001

Figure 1. Flow diagram showing the number of patients in each period.

Figure 2: Distribution of face-to-face visits.

Figure 3. Distribution of prescribed dressings and compression.

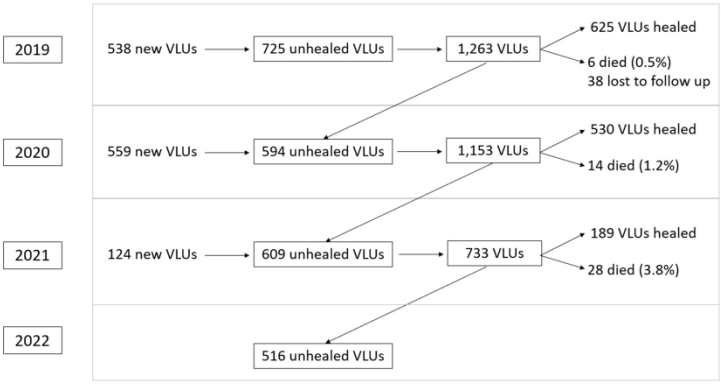

Figure 1

338x190mm (336 x 336 DPI)

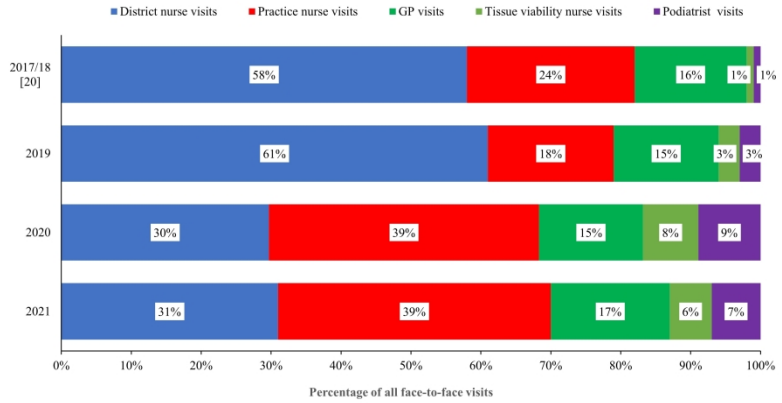

Figure 2

338x190mm (336 x 336 DPI)

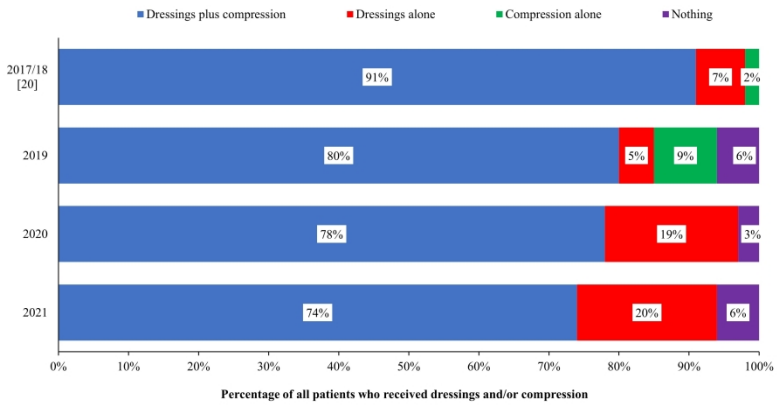

Figure 3

338x190mm (336 x 336 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3,4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8,9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	33
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	26
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	28

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	28 N/A N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	29,31,32
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.