
Continuous longitudinal monitoring using a standard method

Ronan J Canavan MB, MRCP
Diabetes Care Centre, James Cook University Hospital, Middlesborough, U.K.
Nigel C Unwin DM, FFPHM
Institute of Health and Society Newcastle University, Leech Building, The Medical School, Newcastle upon Tyne, U.K.

William F Kelly MD, FRCP
Diabetes Care Centre, James Cook University Hospital, Middlesborough, U.K.

Vincent M Connolly MD, FRCP
Diabetes Care Centre, James Cook University Hospital, Middlesborough, U.K.

Running Title: LEA incidence and better organized foot care

Corresponding Author:
Ronan J Canavan
Metabolic Unit
City Hospitals Sunderland
Kayll Road
Sunderland, SR4 7TP, UK

Received for publication 19 June 2007 and accepted in revised form 27 November 2007.

Copyright American Diabetes Association, Inc., 2007
ABSTRACT

Objective: There is a lack of continuous longitudinal population based lower extremity amputation (LEA) data in the UK. We present here accurate data on trends in diabetes related (DR)LEAs and non-DRLEAs in the South Tees area over a continuous 5 year period.

Research Design and Methods: All cases of LEA from 1st July 1995 to 30th June 2000 within the area were identified. Estimated ascertainment using capture-recapture analysis approached 100% for LEAs in the area. Data was collected longitudinally using the standard method of the Global Lower Extremity Amputation Study protocol.

Results: Over 5 years there were 454 LEAs (66.3% male) in the South Tees area, of which 223 were diabetes related (49.1%). Among persons with diabetes LEA rates went from 564.3 in the 1st year to 176.0 per 100,000 persons with diabetes in the 5th year. Over the same period non-DRLEAs increased from 12.3 to 22.8 per 100,000 persons without diabetes. The relative risk of a person with diabetes undergoing an LEA went from being 46 times that of a person without diabetes to 7.7 at the end of the 5 years. The biggest improvement in LEA incidence was seen in the reduction of repeat major DRLEAs.

Conclusion: Our data shows that in the South Tees area at a time when major non-DRLEA rates increased major DRLEA rates have fallen. These diverging trends mark a significant improvement in care for patients with diabetic foot disease as a result of better organized diabetes care.
Diabetic foot disease is a common complication of diabetes with major worldwide implications (1). Lower extremity amputation (LEA) remains an all too common outcome of this complication (2-5). A major LEA in a person with diabetes profoundly impacts on their independence and future health, (6,7). Financially major LEAs are expensive due to the need for multiple and extended hospitalizations (8).

Authors have reported regularly on LEA rates (5,10-16) but rarely using consistent methodologically (9). Interesting data from different studies is thus available but direct comparison is difficult.

To allow for more ready comparison of LEA rates between centers, the Global Lower Extremity Amputation Study (GLEAS) group through collaboration developed a standard protocol for LEA data collection (17). The GLEAS protocol describes a standard methodology that centers can use to arrive at population based diabetes related (DR) LEA and non-DRLEA rates for their own particular areas. An important point about the GLEAS protocol is that it allows for an estimation of ascertainment of all LEAs to be made so that the completeness of data collected can be assessed.

The South Tees area in the UK was part of the original 10 centre comparative study using the GLEAS protocol (18). Of the 4 UK centers that took part in the original GLEAS study the South Tees area was found to have by far the highest rate of major DRLEAs (20). In response to these findings the South Tees area reviewed and significantly altered its provision of diabetes foot care. An initiative called “Feet First” identified gaps in knowledge and practice of foot care in people with diabetes in the South Tees area. The team was restructured with diabetic foot care overseen by a named diabetologist (WFK) who developed the multidisciplinary team including an important community diabetic chiropody element along with establishing care pathways and protocols for managing diabetic foot problems. Following completion of GLEAS study and the implementation of these changes data was collected for a further 3 years in the South Tees area.

We present here data on trends in DRLEAs and non-DRLEAs in the South Tees area over a continuous 5-year period. There is a lack of continuous population based LEA data in the UK and this data to our knowledge is the longest and most thorough LEA longitudinal incidence study to date for the UK. The data is a real reflection of trends in LEAs in this community because of the thoroughness of the data collection, the use of valid local diabetes prevalence figures and because of high levels of ascertainment. It’s readily applicable as data has been collected using a standard methodology and it includes a non-diabetes comparator.

**RESEARCH DESIGN AND METHODS**

**Setting.** The South Tees area is an industrialized area in the North of England, bordered by the North Sea, the river Tees, and the North Yorkshire Moors. Middlesbrough is its main urban centre. At the 2001 census the South Tees area had a population of 273,987, which was predominantly white Caucasian (96.4%). It’s an area of high long-term unemployment. 7.0% of the population is greater than 75 years, below the average for England and Wales of 7.6% (21).

**Case definition.** Materials and methods as per GLEAS protocol have previously been published (18). LEA was defined as complete loss of any part of the lower limb for any reason, in the following anatomical planes: in the transverse anatomical plane proximal to, and including, the subtalar joint and in the frontal anatomical plane distal to the subtalar joint. A major LEA was defined as through or proximal to, the tarsometatarsal joint and a minor LEA as one distal to this joint. 1st LEA refers to the first event in any patient as it is felt that this
LEA incidence and better organized foot care

is the main event any service is trying most to prevent. A major LEA that is the 1st major LEA in a patient that occurs following an earlier minor LEA is a 1st major LEA. Subsequent events after a 1st major LEA are repeat events when a new level was attained at a later date including an LEA on the contra lateral limb. The GLEAS protocol records previous LEAs even if they occur prior to the study period. Repeat events were LEAs on a person who had had a previous LEA at any time but which was separate from the original event in time and the level at which it occurred. Patients undergoing amputation as a result of trauma alone were excluded.

**Data collection.** All cases of LEA from 1st July 1995 to 30th June 2000 within the South Tees area were identified. Four independent data sources (operating theatre records, limb fitting centre records, hospital discharge data and community diabetes register) were used to identify patients. LEAs were categorized as first and repeat, major and minor, diabetes related and non-diabetes related.

A standardized data extraction form was completed from patients’ medical records including age, sex, postcode, ethnicity, smoking habit, first or subsequent LEA, diabetes status, side of LEA, duration of diabetes, insulin treatment, level of LEA. LEA rates were calculated for sex, 20-year age bands, 1st, repeat, major, minor, for persons with and without diabetes. Completeness of the dataset was estimated using capture–recapture methodologies (22). Estimated ascertainment approached 100% for LEAs in the South Tees area. This estimate of ascertainment is based on identified cases matching the number of estimated cases along with narrow 95% confidence interval for estimated cases.

**Population.** The denominator populations for non-DRLEAs were 1996 midyear estimates based on 1991 UK census data less the population with diabetes. The South Tees area has a high quality community based diabetes register previously described (23). It is in operation since 1994 and identifies the local population known to have diabetes. Diabetes prevalence for each year was derived from the community diabetes register and was used to calculate DRLEA rates. An age standardized diabetes prevalence of 1.74% in 1994 for the South Tees area is in keeping with other comparable determinations of diabetes prevalence at the time (24,25). The World Health Organization (1993) defined European standard population was used for direct age standardization. (26)

**Statistics.** As the measured incidences are for a whole geographical population and not a sample of that population confidence intervals have not been calculated for incidence. Where shown 95% confidence intervals (CI) were calculated using the Confidence Interval Analysis program (27). A two side p< 0.05 was considered statistically significant.

**RESULTS**

Over 5 years there were 454 LEAs (66.3% male) in the South Tees area, of which 223 were diabetes related (49.1%). Most LEAs occur in the elderly with 73.6% in persons of 60 years and older. (70.4% DRLEA, 76.6% non-DRLEA, p>0.05). There was an excess of LEAs in males. Among person with diabetes the male to female ratio was 2.91 (CI 2.49-3.39), while among persons without diabetes it was half this with a male to female ratio of 1.41 (CI 1.18-1.66)). There was an excess of minor LEAs among persons with diabetes with the minor to major ratio DRLEAs 1.05 (CI 0.86-1.26) vs. non-DRLEAs 0.51 (CI 0.4-0.64)).

All LEAs (i.e. major, minor, 1st, repeat). Among persons with diabetes LEA rates went from 564.3 per 100,000 persons with diabetes in the 1st year to 176.0 per 100,000 persons with diabetes in the 5th year. For non-DRLEAs there was an increase from 12.3 to 22.8 per 100,000 persons without diabetes. The relative risk of a person with diabetes undergoing any LEA went from being 46 times that of a person without
diabetes at the start of the study to being only 7.7 times that of a person without diabetes at the end of the 5 years.

**DRLEAs.** Looking at LEAs among person with diabetes, major DRLEAs make up the main component of the improvement seen. 1st major and repeat major DRLEA rates fell in parallel (Figure 1). The downward trend was not consistent throughout the 5 years and in year 4 there was a rise in 1st and repeat major DRLEAs. Minor DRLEA rates didn’t significantly change over the five years. While going from 253.8 per 100,000 persons with diabetes in year 1 to 100.5 in year 5 this was offset by a peak in year 4 at 362.9.

**Non-DRLEAs.** There was a rise in major non-DRLEA rates over the 5 years. 1st major non-DRLEAs and repeat major non-DRLEA rates combined are shown (Figure 1). The rise in repeat major non-DRLEA rates is more significant than for 1st major non-DRLEAs (Table 1).

**Repeat LEAs.** Among person with diabetes the biggest improvement in LEA rates was seen in the repeat major events (Figure 1). Repeat minor DRLEA rates over the 5 years remained stable. The repeat major non-DRLEA rate more than tripled when comparing the 1st year to the 5th year of the study (Table 1). Repeat minor non-DRLEA rates over the 5 years increased significantly also.

DRLEA rates were high in the South Tees area at the start of the 5-year study period. In the South Tees area the relative risk for a person with diabetes undergoing a major LEA (either a 1st or repeat event combined) was 35.5 times that of a person without diabetes at the start of the study by the end of the 5 years the relative risk had fallen to 5.0.

**CONCLUSIONS**

Ultimately a person with diabetes should have an LEA risk approaching that of a person without diabetes. At the start of the 5 year study period the chance of a person with diabetes undergoing an LEA was 46.0 (CI 25.7-90.6) times that of a person without diabetes. The chance of a person with diabetes undergoing a major LEA was still 35.5 (CI 18.9-76.8) that of a person without diabetes. By the end the risk of a person with diabetes undergoing any LEA or a major LEA was down to 7.7 (CI 4.99-12.9) and 5.0 (CI 2.82-9.43) times that of person without diabetes.

The fall in DRLEAs overall has been achieved through a far greater reduction in major DRLEAs compared to minor DRLEAs. The significance of the fall in major DRLEAs is increased by the rise in major non DRLEA events particularly due to the rise in repeat major non-DRLEAs.

The variation in annual LEA rates in the later years of the study is interesting. It reflects the results seen in other studies that have shown a falling trend or stable trend with time but associated with large year to year variation in LEA incidence. (16,28). To smooth out year to year variation we calculated 3 year rolling averages. For combined (1st and repeat) major DRLEAs the 1st 3 year average was 211.2 per 100,000 persons with diabetes and the 3rd 3 year average was 160.5 per 100,000 persons with diabetes. For combined (1st and repeat) major non DRLEAs the change from the 1st to the 3rd 3 year average was from 10.2 to 11.9 per 100,000 persons without diabetes.

We were concerned to know if our very low DRLEA rates achieved in the 5th year of the study was maintained beyond the end of the study but to date have not been able to collect data in the same detail according to the GLEAS protocol. However hospital event statistics (HES) for the South Tees area show that while the low DRLEA rates for the 5th year of our study are the best achieved to date that the following years HES data (available up to 02/03) are the next lowest DRLEA rates. HES for non DRLEAs show that for the years after the end of our study that rates continue to rise.

**Likely explanations of results.** The principle change to diabetic foot care over the period studied was the establishment of a dedicated diabetic foot care team with a community based chiropody service. This
included establishment of care pathways and protocols for managing diabetic foot problems with input from a vascular and orthopedic surgeon, orthotist, diabetic chiropodists and a single diabetologist. Educational events to raise awareness of diabetes foot complications were organized.

Angioplasty practice over this period changed. More angioplasties per angiogram were done. The increased rate of angioplasties per angiogram was seen both in persons with and without diabetes but the rate of increase were greater among persons with diabetes. Hospital event statistics for the South Tees area show for persons with diabetes the ratio of femoral angioplasty to angiogram was 0.20 in 1997 and 0.42 in 2001. For patients without diabetes the ratio increased but not to the same extent going from 0.23 to 0.29 over the same period.

Another change in care for the population with diabetes immediately preceding and continuing through this period is the increased prescribing of medication aimed at modifying cardiovascular risk. This is seen in the increased prescribing of lipid lowering, antihypertensive and antiplatelet medication. The diabetes register between 1995 and 2001 shows the percentage of persons recorded to be on a statin, aspirin or an ACE inhibitor increased from 5.2% to 20.0% (p <0.001), from 21.7% to 32.6% (p <0.001) and from 14.5% to 37.5% (p <0.001) respectively (29).

Smoking in patients attending the hospital diabetes clinic over the same period has remained high. In 1995 20% of men and 19.3% of women were recorded as smokers while in 2001 it was 18.1% of men (p >0.05) and 19.8% of women (p >0.05)) (29). Smoking habits in the general population of North East England has changed little over the same period (30).

Diabetes prevalence changed significantly in the South Tees area as elsewhere over this period. We calculated DRLEA rates using a fixed denominator of the general population for major DRLEAs and for years 1 to 5 the rates were respectively 8.9, 10.6, 7.2, 10.5, and 3.8 per 100,000 general population. While the trend is less marked using this method the overall change is maintained with the trend for major DRLEAs still downward and the major non DRLEAs still increases significantly. However to use a flat denominator we feel would be incorrect as it doesn’t reflect the real change in cases of diabetes in the population (in year 1 there were 4,607 persons with diabetes and in year 5 there were 6,254 persons with diabetes in the South Tees area).

**Weak points of study.** Our data in common with all LEA studies can only suggest most likely reasons for the improvement seen across the whole South Tees population. It is not clear evidence for cause and effect. Also the extent or importance of each of the contributing factors can only be listed as most likely and the direction and amount contributed by different factors has not been quantified.

It’s not clear why there should be an increase in LEA rates among persons without diabetes. While all major non-DRLEA rates increased the main increase was seen in repeat major non-DRLEA events. At the start of the period repeats accounted for 1 in 5 major non-DRLEAs at the end of the 5 years repeats accounted for 2 in 5 major non-DRLEAs episodes. It’s known that variation in clinical decision making exists among surgeons considering LEA in cases that are borderline (31). The main change to the surgical structure over the period was the establishment of a regional vascular unit based at the South Tees area where previously it had been a local unit. However improvements in surgeon volume does not benefit lower extremity arterial surgery in terms of outcomes in the same way as other vascular procedures such as carotid endarterectomy and abdominal aortic aneurysm repair and may actually lead to an increase in procedure rates (32). We have not classified the etiology of the LEA in terms of ischaemic, neuroischaemic or neuropathic.
Strong points of study. We have used a number of methods to enhance the completeness and accuracy of our data. Our study is population based and therefore widely applicable. It uses multiple data sources and allows for the use of capture-recapture methods so that an estimate of ascertainment can be arrived at. Collection of data in a standard way and presentation of standardized rates means that our data is potentially comparable to a wide range of centers. The presentation alongside non-DRLEA rates emphasizes the improvement in major DRLEA rates and points to the importance of having non-DRLEA data included. By using direct diabetes prevalence data the accuracy of our data for this population is increased.

In this study estimate of ascertainment for LEAs approaches 100%. What the high level of ascertainment reflects is not a guarantee that all cases were identified as no method can do that but the trawl using this method was as thorough as possible and at worst only missed an occasional case.

We believe this study is important in a number of other ways. It is an accurate reflection of changes in LEA rates across a population rather than in a clinic itself. This study reaffirms the positive effect that a multi-disciplinary foot team approach has on reducing LEAs seen in a clinic setting (33). Our study shows the improvement is not just to the clinic population but also to the diabetic population served by the clinic also. The improvement in non-diabetes LEA data is further enhanced in the context of rising non-DRLEA rates. Without the comparison with non-DRLEA data the relative improvement in DRLEA incidence would have been lessened. This study is a natural extension of the GLEAS incidence study, following LEA rates over 5 years in one of the centers that took part in the original study. The robustness and standardization of the data allows for comparison with other studies.

The completeness of the study is based on it being a whole population study, estimation of ascertainment by capture-recapture methodologies, use of local valid diabetes population prevalence figures and comparison with the non-diabetes rate, using multiple data sources presented in a standardized way.

In conclusion our data shows that in the South Tees area at a time when major non-DRLEA rates increased major DRLEA rates have fallen. These diverging trends mark a significant improvement in care for patients with diabetic foot disease as a result of better organized diabetes care. Our study shows the importance of including a non-DRLEA comparison. A case control study would be an efficient approach to explore further the specific changes seen in our study.
REFERENCES

**TABLE 1. Annual incidence of major lower extremity amputation for persons with and without diabetes**

<table>
<thead>
<tr>
<th>Year</th>
<th>Diabetes related LEA – Major</th>
<th>Non diabetes related LEA - Major</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First</td>
<td>Repeat</td>
</tr>
<tr>
<td>1995-96</td>
<td>200.8</td>
<td>109.7</td>
</tr>
<tr>
<td>1996-97</td>
<td>117.2</td>
<td>72.9</td>
</tr>
<tr>
<td>1997-98</td>
<td>90.1</td>
<td>42.9</td>
</tr>
<tr>
<td>1998-99</td>
<td>177.1</td>
<td>95.8</td>
</tr>
<tr>
<td>1999-00</td>
<td>57.2</td>
<td>18.7</td>
</tr>
</tbody>
</table>

Figures are incidence per 100000 persons at risk
Figure 1–Year on year change in major lower extremity amputation rates for persons with diabetes (1st and repeat major DRLEAs shown separately and combined) and without diabetes (1st and repeat major non DRLEAs shown combined only)