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THE RELATIVE INCIDENCE OF FRACTURE NON-UNION IN A POPULATION OF 5.17 MILLION PEOPLE; AN EPIDEMIOLOGICAL STUDY.

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TITLE: THE RELATIVE INCIDENCE OF FRACTURE NON-UNION IN A POPULATION OF 5.17 MILLION PEOPLE; AN EPIDEMIOLOGICAL STUDY.

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No ethical approval was required for this research.

There was no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

The authors Miss L Mills and Prof. H Simpson have contributed to the paper regarding its design, data acquisition and analysis, both authors have been involved in the drafting and revising of the article and in the approval of the final version to be published.

TITLE: THE RELATIVE INCIDENCE OF FRACTURE NON-UNION IN A POPULATION OF 5.17 MILLION PEOPLE; A CROSS-SECTION EPIDEMIOLOGICAL STUDY.

Abstract

Objectives: In the UK there are approximately 850,000 new fractures seen each year. Rates of non-union of 5-10% of fractures have been suggested, the cost to the NHS of treating non-union has been reported to range between £7,000 and £79,000 per person yet there is little actual data available. The objective of this epidemiological study therefore is for the first time to report the rates of fracture non-union.

Design: A CROSS-SECTION EPIDEMIOLOGICAL STUDY

Setting: The population of Scotland

Participants: All patient admissions to hospital in Scotland are coded according to diagnosis. This data is collected by (and was obtained from) ISD Scotland. Those who have been coded for a bone non-union between 2005 and 2010 were included in the study. No patients were excluded. Population data was obtained from the Registrar General for Scotland.

Outcome measure: The number of fracture non-unions per 100,000 population of Scotland according to age, sex and anatomical distribution of non-union.

Results: 4895 non-unions were treated as inpatients in Scotland between 2005 and 2010, averaging 979 per year, with an overall incidence of 18.94 per 100,000 population per annum. The distribution according to gender was 57% male and 43% female. The overall peak incidence according to age was between 30 and 40 years. The mean population of Scotland between 2005-2010 was 5,169,140 people.

Conclusion: Fracture non-union in the population as a whole remains low at less than 20 per 100,000 population and peaks in the 4th decade of life. Further research is required to determine the risk of non-union per fracture according to age/ sex/ anatomical distribution.

TITLE: THE RELATIVE INCIDENCE OF FRACTURE NON-UNION IN A POPULATION OF 5.17 MILLION PEOPLE; A CROSS-SECTIONAL EPIDEMIOLOGICAL STUDY.

Aim

To perform an epidemiological study at a national population level to determine the number (and incidence) of non-union with respect to anatomical site, sex and age.

Introduction

The WHO recognize trauma as a major healthcare epidemic with over 16,000 people dying each day and injury accounting for 16% of the global burden of disease[1]. People in a low income setting are far more likely to suffer complications from traumatic injury than those in a high income setting; for instance Mock et al[2] report a 6 fold higher mortality rate (36% v 6%) in the severely injured between high and low income areas. Even within Europe there are major inequalities recognised in the provision of trauma care between Eastern and Western states with a 3.6 fold difference in injury related mortality between the high income and low/middle income countries[3]. For every trauma-associated death there are many more injured and for these injured individuals non-union of the fracture is one of the major causes of morbidity and creates a significant drain on a country's resources. However there is a paucity of data available regarding the incidence of non-union on a national scale.

In the UK there are approximately 850,000 new fractures seen each year (based on an incidence of fresh fractures of 13.8/1000/pa[4]) of which the majority heal without difficulty.

Rates of non-union of 5-10% of fractures have been suggested yet there is little available data for this figure. The cost to the NHS of treating non-union has been reported to range between £7,000 and £79,000 per person[5-8]. However, this does not take into account the morbidity and loss of earnings of the individual nor any long-term health burden, so the cost to society will be far greater than this.

Complex non-unions are best treated by a specialist limb reconstruction service. In order to plan the provision of these services, countries and health boards require data on the rates of non-union per head of population. In addition, in order to design prospective clinical research studies on non-union it is necessary to know the incidence so that realistic recruitment rates can be calculated.

The aim of this study therefore is for the first time to report the rates of fracture non-union of different anatomical regions for a large population, taking into account the age and sex distribution.

Method

Non-union data: Every patient that is admitted to hospital in Scotland is coded for a diagnosis on discharge using the ICD-10 classification by trained coders at each respective hospital. This data is collected by ISD Scotland (Information Services Division, a department within NHS Scotland) where all health data for Scotland is managed.

Information was obtained about all the non-unions admitted to hospital in Scotland from 2005 to 2010. Patients were coded as having a non-union if the responsible surgeon for that inpatient episode recorded the diagnosis of non-union in the patient notes or correspondence. All patients coded for non-union were included.

To assess the quality and consistency of hospital coding for non-union, we crosschecked the codes of 100 consecutive patients whom had been treated for NU as inpatients in Lothian over a similar time period. 97% had been coded for correctly.

Population data: The population data was obtained from the Registrar General for Scotland who publish an annual mid year population estimate with details of sex, age, council and health board.

Results

4895 non-unions were treated as inpatients in Scotland between 2005 and 2010, averaging 979 per year, with an overall incidence of 18.94 per 100,000 population per annum. The distribution according to gender was 57% male and 43% female. The overall peak incidence according to age was between 30 and 40 years. The mean population of Scotland between 2005-2010 was 5,169,140 people.

Table 1- Non-union numbers Scotland 2005- 2010

Site Location	0-14yrs	15-29yrs	30-44yrs	45-59yrs	60-74yrs	75yrs+	total
Shoulder Region (Clavicle & Scapula)	2	106	163	171	109	45	596
Upper Arm (Humerus)	10	41	93	184	228	178	734
Forearm (Radius & Ulna)	79	435	359	166	129	58	1226
Hand	3	120	65	37	13	3	241
Pelvis & Femur	7	38	76	114	169	175	579
Lower Leg (Patella, Tibia & Fibula)	35	137	189	168	94	49	672
Ankle & Foot	15	95	113	141	81	41	486
Axial skeleton	0	15	13	13	30	17	88
Multiple Sites	0	4	2	3	2	1	12
No Additional Detail	29	51	60	46	47	28	261
Total	180	1042	1133	1043	902	595	4895

Overall the actual numbers of non-unions treated were distributed fairly evenly across the ages from 15 to 75 years (table 1). The majority of non-unions occurred in the working aged population. However the incidence per capita demonstrated a different distribution. As expected less than 4% of

non-unions were accounted for by the paediatric population with 66% in the 15- 60 year olds and 30% in those older than 60 years.

5-year trend of non-union (table 2).

The mean incidence of NU over the 5 year period was 22.45 in males and 15.65 in females per 100,000 population per annum. The incidence of non-union in females has remained constant over the past 5 years. In males it has fallen, with a 9.3% drop in non-union numbers despite a rise in the male population, thus the non-union incidence has fallen by 10.5% either due to a fall in the fracture incidence or improvement in overall management and healing of fractures since 2005. Non-union incidence has remained consistently higher in the male compared to the female population although with the fall in numbers of non-union in male patients the gap has narrowed.

Table 2. A 5-year summary of non-union from 2005 to 2010

NU patient numbers				Incidence/ 100,000		
Year	Female	Male	Total	Female	Male	Total
2005/06	402	619	1021	15.18	25.07	19.95
2006/07	419	559	978	15.76	22.49	19.01
2007/08	420	576	996	15.74	23.04	19.27
2008/09	426	532	958	15.9	21.15	18.44
2009/10	421	521	942	15.64	20.59	18.04
5 year mean	417.6	561.4	979	15.65	22.45	18.94

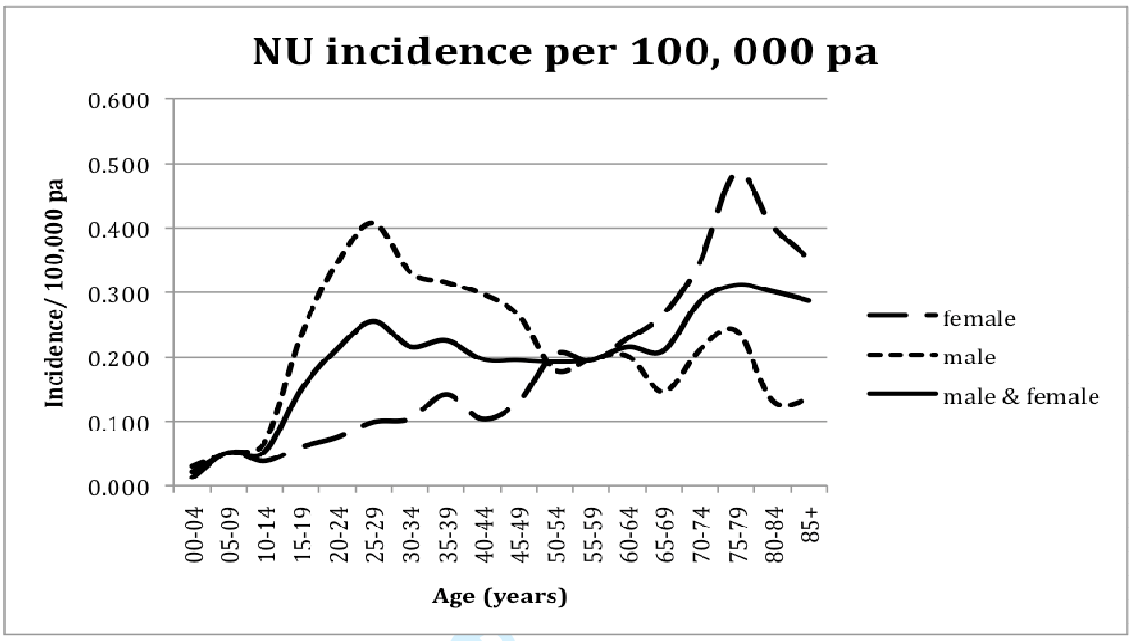
Distribution of non-union with age and sex

Graph 1 demonstrates that the pattern of non-union varied in three age groups; the paediatric population had a very low incidence (less than 5 per 100,000 per annum) followed by a sharp rise and a plateau which was observed in the 20- 70 year age group at around 20 NU per 100,000 population per year. A second rise and further plateau was observed in the elderly at about 28 per 100,000 per annum.

When the data was divided into the separate sexes a different pattern was evident. In the males there was a high peak in the early adult years (25-29 year olds), accounted for mostly by forearm non-union, followed by a gradual decline in incidence and a second small peak in the eight decade due to a rise in the incidence of humeral and femur/ pelvis non-unions. In the female population there was a consistently steady increase in NU incidence from childhood onwards with the female incidence over taking that of the males in the 50-60 year age group and peaking in the 75-79 year age group. Similar to the male population, this peak was predominantly due to an increased incidence of humeral and femoral/ pelvis non-unions.

This distribution of non-union reflected the bimodal (male) and unimodal (female) distribution of fresh fractures that has been reported with age and sex in adults[9].

Graph 1- Incidence of non-union with age and sex



Anatomical distribution of non-union

Table 3 and graphs 2a and b detail the incidence of non-union by site and age. Non-union occurred 60% more frequently in the upper than the lower limb. 5% of non-union patients coded had data unavailable regarding their specific anatomical site.

Notably the forearm had the highest NU rate overall, 2.5 times more common in males (6.68/ 100,000) than in females (2.79/ 100,000) with the majority of cases occurred in the younger population. The hand had one of the lowest rates of NU and these occurred predominantly in the young male patients (1.5/ 100,000) compared to females (0.4/ 100,000).

The humerus was the most frequent site of NU in females (3.54 per 100,000 population) and this became a greater problem with increasing age, representing the increasing number of osteopaenia related proximal humerus fractures in the elderly. The shoulder, which was predominantly the clavicle, was affected 50% more frequently in males but with a more even distribution across the ages.

In the lower limb, NU of the femur and pelvis was more common in females, the incidence increased from the sixth decade upwards following a similar trend to that of the humerus. The highest rate of non-union in the lower limb was seen in the male leg: Non-union of the tibia and

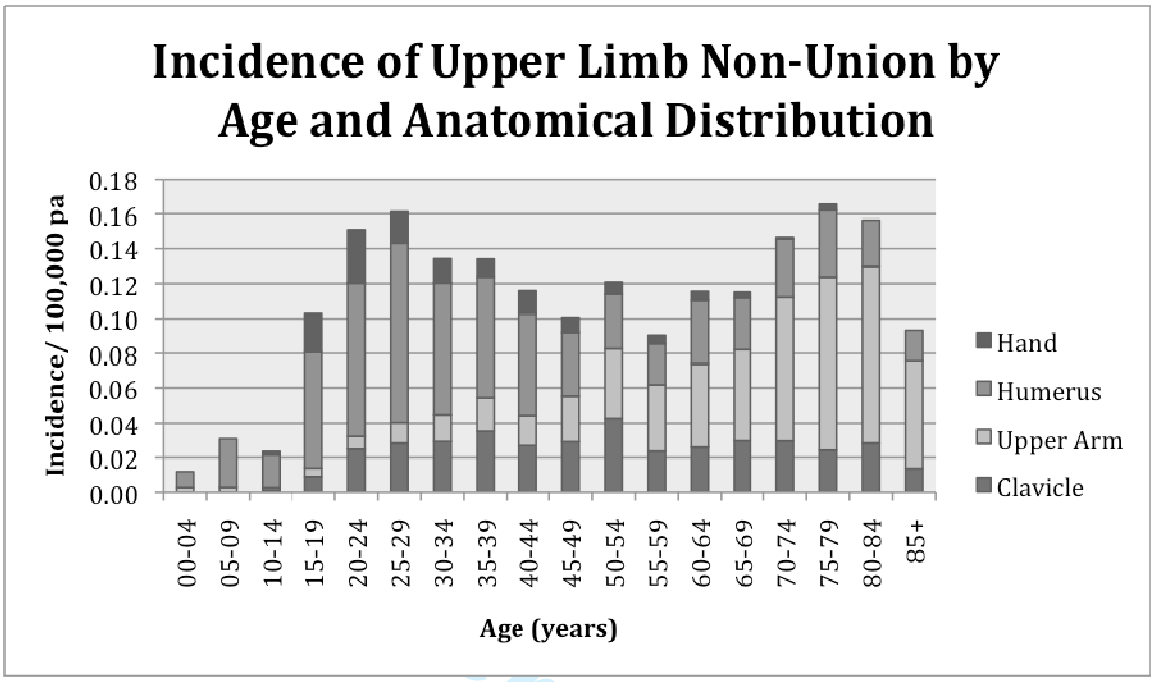
fibula was the second highest site of non-union overall, 70% more frequent than any other area of the lower limb and twice as common in males (3.4/ 100,000) than in females (1.8/100,000). NU of the foot and ankle was evenly distributed between the sexes and across the ages.

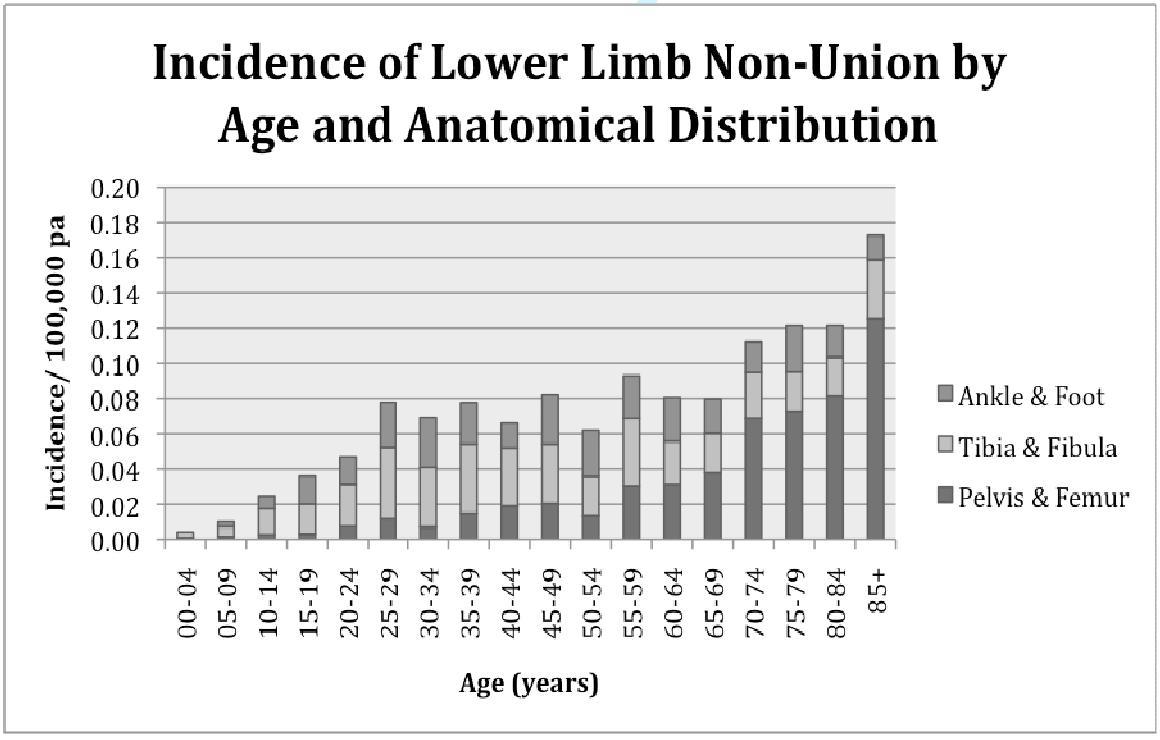
Non-union of multiple sites and the axial skeleton was very rare.

Table 3. Incidence of non-union by sex and anatomy

Site Location	Female incidence /100,000 pa	Male incidence /100,000 pa	Total incidence /100,000 pa
Shoulder Region (Clavicle)	1.87	2.77	2.31
Upper Arm (Humerus)	3.54	2.1	2.84
Forearm (Radius & Ulna)	2.79	6.83	4.74
Hand	0.4	1.5	0.93
Upper limb total	8.6	13.2	10.82
Pelvis & Femur	2.43	2.04	2.24
Lower Leg (Tibia & Fibula)	1.83	3.42	2.6
Ankle & Foot	1.77	2	1.88
Lower limb total	6.02	7.46	6.72
Multiple Sites	0.04	0.06	0.05
Axial skeleton	0.25	0.44	0.34
Total	15.65	22.45	18.94

Graph 2a & 2b- distribution of non-union by site and age, upper and lower limb





Discussion

The 5-year mean for non-union in Scotland (2005- 2010) was 18.9 per annum; 22.45 in males and 15.65 in females. Although there has been a decreasing trend in male incidence a longer period of analysis is necessary to draw any significance from it. The age /gender distribution followed a trend that was similar to the fracture pattern in the Edinburgh population[6] with a bimodal male and unimodal female distribution reflecting the larger number of fractures seen with higher energy injuries in the young males and the osteoporotic fractures in the elderly.

The most common site for non-union in males was the forearm and in females the humerus, with the upper limb having a 60% higher incidence of non-union than the lower limb likely in part due to the greater incidence of upper limb than lower limb fractures. In a recent epidemiology study the fracture incidence was 290/100,000 for forearms and 173/ 100,000 in the upper arm and shoulder compared to 199/100,000 in the pelvic/thigh region and 55/100,000 in the lower leg[4].

This study may under represent the numbers of NU, as in the elderly the potential for complications and the invasiveness of corrective surgery may outweigh the benefits of achieving union for the individual.

Previous estimates of fracture non-union have generally been derived from small cohorts of particular anatomical regions. The many study variables make comparison difficult although most studies of closed fracture injuries quote less than 15%[10] NU. Site specific studies have reported 1.54/ 100,000 pa in the clavicle[11], 1.1/ 100,000 pa in the diaphyseal humerus[12] and 1.89/ 100,000pa in closed tibial fractures[13]

At a population level the number of non-union is potentially affected by several different factors. These include the number of fractures, the nature of the injuries (for instance high energy open tibial fractures compared to closed low energy fractures[13]), the incidence of infection and importantly the access of the population to health care provision and adequacy of the initial fracture treatment. In addition, there will be intrinsic host factors such as diabetes and systemic agents such as non-steroidal anti-inflammatory drugs and smoking, which inhibit the repair process and would potentially, influence the incidence of non-union.

For health care planning and for clinical trial design, the absolute number of non-unions is required, particularly as there is an increasing need to evaluate current and proposed new treatments for non-union.

The ISD data used in this study records all hospital episodes. As almost all non-unions are treated operatively, the ISD data is a good reflection of the number of clinically symptomatic non-unions (as was confirmed by the validation of the ISD coding carried out in our unit). Therefore the data provided here gives realistic estimates for the number of non-unions that can be expected for each anatomical region in a given time, which will enable realistic recruitment rates to be calculated.

Our data gives an overall NU incidence in Scotland of 19 per 100,000 per annum. Clearly less than the 138/ 100,000 primary hip replacements[14] and 572/ 100,000 registered malignant neoplasms[15] but on a par with 19/ 100,000 revision hip replacements[14], and 13.5/ 100,000 on the renal transplant waiting list in Scotland in 2009.

An estimated 25% of non-unions are complex and require referral to a specialist unit dealing with limb reconstruction, such a unit with a catchment of 2 million would see approximately 100 non-union referrals per year. This compares to the 33 primary hip replacements performed per arthroplasty surgeon and 6.7 revision hips per 'revision' arthroplasty hip surgeon in Scotland in 2009[14].

Conclusion

There is very little data available in the literature regarding non-union in large numbers or populations. This study reports data which can be used as a baseline to compare against rates in other regions to assess the adequacies of trauma care provision. The pattern of non-union by age, sex and anatomical distribution in a 5.2 million Scottish population, is described with a young male bimodal and elderly female unimodal distribution and a higher incidence in the upper limb than lower limb.

Bibliography

1. Mock C, Lormand J.D., Goosen J., Joshipura M., Peden M. Guidelines for eesential trauma care. Geneva: World Health Organiziation, 2004.
2. Mock CN, Adzotor KE, Conklin E, Denno DM, Jurkovich GJ. Trauma outcomes in the rural developing world: comparison with an urban level I trauma center. *J Trauma* 1993;35(4):518-23.
3. Sethi D, Racioppi F, Baumgarten I, Bertollini R. Reducing inequalities from injuries in Europe. *Lancet* 2006;368(9554):2243-50.
4. Court-Brown C, Aitken SA, Forward D, O'Toole R. The Epidemiology of Adult Fractures. In: Bucholz RW, Court-Brown C, Heckman JD, Tornetta P, editors. *Rockwood and Green's fractures in adults*. 7 ed: Philidelphia, Lippincott Williams & Wilkins, 2010, 2009:53-84.
5. Dahabreh Z, Calori GM, Kanakaris NK, Nikolaou VS, Giannoudis PV. A cost analysis of treatment of tibial fracture nonunion by bone grafting or bone morphogenetic protein-7. *Int Orthop* 2009;33(5):1407-14.
6. Dahabreh Z, Dimitriou R, Giannoudis PV. Health economics: a cost analysis of treatment of persistent fracture non-unions using bone morphogenetic protein-7. *Injury* 2007;38(3):371-7.
7. Kanakaris NK, Giannoudis PV. The health economics of the treatment of long-bone non-unions. *Injury* 2007;38 Suppl 2:S77-84.
8. Patil S, Montgomery R. Management of complex tibial and femoral nonunion using the Ilizarov technique, and its cost implications. *J Bone Joint Surg Br* 2006;88(7):928-32.
9. Court-Brown CM, Caesar B. Epidemiology of adult fractures: A review. *Injury* 2006;37(8):691-7.
10. Tzioupis C, Giannoudis PV. Prevalence of long-bone non-unions. *Injury* 2007;38 Suppl 2:S3-9.
11. Robinson CM. Fractures of the clavicle in the adult. Epidemiology and classification. *J Bone Joint Surg Br* 1998;80(3):476-84.
12. Broadbent MR, Will E, McQueen MM. Prediction of outcome after humeral diaphyseal fracture. *Injury* 2010;41(6):572-7.
13. Court-Brown CM. Reamed intramedullary tibial nailing: an overview and analysis of 1106 cases. *J Orthop Trauma* 2004;18(2):96-101.
14. NoAuthorsListed. Scottish Arthroplasty Project Annual Report: www.arthro.scot.nhs.uk/Reports/Scottish_Arthroplasty_Project_Report_2009 2010.
15. NoAuthorListed. Cancer in Scotland (August 2011). In: Information Services Division NNSS, editor, 2011.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
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	2
Objectives	3	State specific objectives, including any pre-specified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	3
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	n/a
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	n/a
Bias	9	Describe any efforts to address potential sources of bias	n/a
Study size	10	Explain how the study size was arrived at	n/a
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	n/a
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
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	3
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	3
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	4
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	4
		(*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	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
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	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
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	1

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
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 www.strobe-statement.org.

The relative incidence of fracture non-union in the Scottish population (5.17 million), a 5 year epidemiological study.

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Secondary Subject Heading:	Health economics, Surgery, Public health
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Key words: non-union, nonunion, fracture, incidence, epidemiology, bone.

Word Count: 2100 excluding abstract and references

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No ethical approval was required for this research.

Funding

There was no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

Contributorship

The authors Miss L Mills and Prof. H Simpson have contributed to the paper regarding its design, data acquisition and analysis, both authors have been involved in the drafting and revising of the article and in the approval of the final version to be published.

Competing Interests

None

Data Sharing

There is no additional data available.

TITLE

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ABSTRACT

Objectives

In the UK there are approximately 850,000 new fractures seen each year. Rates of non-union of 5-10% of fractures have been suggested, the cost to the NHS of treating non-union has been reported to range between £7,000 and £79,000 per person yet there is little actual data available. The objective of this epidemiological study therefore is for the first time to report the rates of fracture non-union.

Design

A cross-sectional epidemiological study

Setting

The population of Scotland

Participants

All patient admissions to hospital in Scotland are coded according to diagnosis. This data is collected by (and was obtained from) ISD Scotland. Those who have been coded for a bone non-union between 2005 and 2010 were included in the study. No patients were excluded. Population data was obtained from the Registrar General for Scotland.

Outcome measure

The number of fracture non-unions per 100,000 population of Scotland according to age, sex and anatomical distribution of non-union.

Results

4895 non-unions were treated as inpatients in Scotland between 2005 and 2010, averaging 979 per year, with an overall incidence of 18.94 per 100,000 population per annum. The distribution according to gender was 57% male and 43% female. The overall peak incidence according to age was between 30 and 40 years. The mean population of Scotland between 2005-2010 was 5,169,140 people.

Conclusion

Fracture non-union in the population as a whole remains low at less than 20 per 100,000 population and peaks in the 4th decade of life. Further research is required to determine the risk of non-union per fracture according to age/ sex/ anatomical distribution.

ARTICLE SUMMARY

Article focus

- The cost of treating non-union is between £7,000 and £79,000 per case in the UK
- There is no population data in the literature regarding the rate of non-union; smaller site specific cohort studies suggest it to be a complication of fracture healing in up to 5-10% of cases
- This study aims to report for the first time the rates of fracture non-union of different anatomical regions for a large population, taking into account the age and sex distribution

Key messages

- There were almost 1000 non-unions treated in Scotland each year between 2005 and 2010 with an annual non-union incidence of 22.45 in males and 15.65 in females per 100,000 population per annum
- The age/ gender distribution was bimodal in males and unimodal in females reflecting the larger number of fractures seen with higher energy injuries in the young males and the osteoporotic fractures in the elderly
- Non-union was more frequent in the upper than the lower limb, likely reflecting the higher incidence of fractures in the upper limb compared to the lower limb

Strengths and limitations

- This is the first study of its kind in the literature to attempt to measure the incidence of non-union in the general population
- It is based upon a stable population of 5.17 million people
- It can be used as a baseline to compare healthcare systems and adequacy of trauma care provision elsewhere

- It may under represent the true incidence as it does not account for the asymptomatic non-unions (rare) which do not seek treatment or in those where the risks of surgery outweigh the benefits to the individual (also rare).
- Further research is required to look at the rate of non-union per fracture in a large population setting

TITLE: The relative incidence of fracture non-union in the Scottish population (5.17 million), a 5 year epidemiological study.

Aim

To perform an epidemiological study at a national population level to determine the number (and incidence) of non-union with respect to anatomical site, sex and age.

Introduction

The WHO recognize trauma as a major healthcare epidemic with over 16,000 people dying each day and injury accounting for 16% of the global burden of disease[1]. People in a low income setting are far more likely to suffer complications from traumatic injury than those in a high income setting; for instance Mock et al[2] report a 6 fold higher mortality rate (36% v 6%) in the severely injured between high and low income areas. Even within Europe there are major inequalities recognised in the provision of trauma care between Eastern and Western states with a 3.6 fold difference in injury related mortality between the high income and low/middle income countries[3]. For every trauma-associated death there are many more injured and for these injured individuals non-union of the fracture is one of the major causes of morbidity and creates a significant drain on a country's resources. However there is a paucity of data available regarding the incidence of non-union on a national scale.

In the UK there are approximately 850,000 new fractures seen each year (based on an incidence of fresh fractures of 13.8/1000/pa[4]) of which the majority heal without difficulty.

Rates of non-union of 5-10% of fractures have been suggested yet there is little available data for this figure. The cost to the NHS of treating non-union has been reported to range between £7,000 and £79,000 per person[5-8]. However, this does not take into account the morbidity and loss of earnings of the individual nor any long-term health burden, so the cost to society will be far greater than this.

Complex non-unions are best treated by a specialist limb reconstruction service. In order to plan the provision of these services, countries and health boards require data on the rates of non-union per head of population. In addition, in order to design prospective clinical research studies on non-union it is necessary to know the incidence so that realistic recruitment rates can be calculated.

The aim of this study therefore is for the first time to report the rates of fracture non-union of different anatomical regions for a large population, taking into account the age and sex distribution.

Method

Every patient in Scotland has a unique CHI (community health index) number. Every patient admitted into hospital in Scotland has a code attached to their CHI number when they are discharged. This individual code is derived from the ICD-10 classification and is specific for the diagnosis from that admission; it is generated by trained coders who are specialty specific in each health trust.

It is mandatory for NHS Scotland Information Services Department (ISD) to collect the all the ICD-10 data for all the hospitals in Scotland. The combination of the unique patient CHI number and ICD-10 data enables them to provide age, sex and hospital specific details for each patient treated for a non-union upon request.

Information was obtained regarding all non-unions admitted to hospital in Scotland from 2005-2010. Patients were coded as having a non-union if the responsible surgeon for that inpatient episode recorded the diagnosis of non-union in the patient notes or correspondence. All patients coded for non-union were included.

To assess the quality and consistency of hospital coding we checked the codes of 100 consecutive non-union patients whom had bent rated for NU as inpatients in Lothian over a similar time period. 97% had been correctly coded for, those that had not been had codes for malunion or osteomyelitis (which had been present in addition to the NU).

The population data for Scotland between 2005 and 2010 was obtained from the Registrar General for Scotland who publish an annual mid year population estimate with details of sex, age, council and health board.

Results

4895 non-unions were treated as inpatients in Scotland between 2005 and 2010, averaging 979 per year, with an overall incidence of 18.94 per 100,000 population per annum. The distribution according to gender was 57% male and 43% female. The overall peak incidence according to age was between 30 and 40 years. The mean population of Scotland between 2005-2010 was 5,169,140 people.

Table 1- Non-union numbers Scotland 2005- 2010

Site Location	0-14yrs	15-29yrs	30-44yrs	45-59yrs	60-74yrs	75yrs+	total
Shoulder Region (Clavicle & Scapula)	2	106	163	171	109	45	596
Upper Arm (Humerus)	10	41	93	184	228	178	734
Forearm (Radius & Ulna)	79	435	359	166	129	58	1226
Hand	3	120	65	37	13	3	241
Pelvis & Femur	7	38	76	114	169	175	579
Lower Leg (Patella, Tibia & Fibula)	35	137	189	168	94	49	672
Ankle & Foot	15	95	113	141	81	41	486
Axial skeleton	0	15	13	13	30	17	88
Multiple Sites	0	4	2	3	2	1	12
No Additional Detail	29	51	60	46	47	28	261
Total	180	1042	1133	1043	902	595	4895

Overall the actual numbers of non-unions treated were distributed fairly evenly across the ages from 15 to 75 years (table 1). The majority of non-unions occurred in the working aged population. However the incidence per capita demonstrated a different distribution. As expected less than 4% of

non-unions were accounted for by the paediatric population with 66% in the 15- 60 year olds and 30% in those older than 60 years.

5-year trend of non-union (table 2).

The mean incidence of NU over the 5 year period was 22.45 in males and 15.65 in females per 100,000 population per annum. The incidence of non-union in females has remained constant over the past 5 years. In males it has fallen, with a 9.3% drop in non-union numbers despite a rise in the male population, thus the non-union incidence has fallen by 10.5% either due to a fall in the fracture incidence or improvement in overall management and healing of fractures since 2005. Non-union incidence has remained consistently higher in the male compared to the female population although with the fall in numbers of non-union in male patients the gap has narrowed.

Table 2. A 5-year summary of non-union from 2005 to 2010

NU patient numbers				Incidence/ 100,000		
Year	Female	Male	Total	Female	Male	Total
2005/06	402	619	1021	15.18	25.07	19.95
2006/07	419	559	978	15.76	22.49	19.01
2007/08	420	576	996	15.74	23.04	19.27
2008/09	426	532	958	15.9	21.15	18.44
2009/10	421	521	942	15.64	20.59	18.04
5 year mean	417.6	561.4	979	15.65	22.45	18.94

Distribution of non-union with age and sex

Graph 1 demonstrates that the pattern of non-union varied in three age groups; the paediatric population had a very low incidence (less than 5 per 100,000 per annum) followed by a sharp rise and a plateau which was observed in the 20- 70 year age group at around 20 NU per 100,000 population per year. A second rise and further plateau was observed in the elderly at about 28 per 100,000 per annum.

When the data was divided into the separate sexes a different pattern was evident. In the males there was a high peak in the early adult years (25-29 year olds), accounted for mostly by forearm non-union, followed by a gradual decline in incidence and a second small peak in the eight decade due to a rise in the incidence of humeral and femur/ pelvis non-unions. In the female population there was a consistently steady increase in NU incidence from childhood onwards with the female incidence over taking that of the males in the 50-60 year age group and peaking in the 75-79 year age group. Similar to the male population, this peak was predominantly due to an increased incidence of humeral and femoral/ pelvis non-unions.

This distribution of non-union reflected the bimodal (male) and unimodal (female) distribution of fresh fractures that has been reported with age and sex in adults[9].

Anatomical distribution of non-union

Table 3 and graphs 2a and b detail the incidence of non-union by site and age. Non-union occurred 60% more frequently in the upper than the lower limb. 5% of non-union patients coded had data unavailable regarding their specific anatomical site.

Notably the forearm had the highest NU rate overall, 2.5 times more common in males (6.68/ 100,000) than in females (2.79/ 100,000) with the majority of cases occurred in the younger population. The hand had one of the lowest rates of NU and these occurred predominantly in the young male patients (1.5/ 100,000) compared to females (0.4/ 100,000).

The humerus was the most frequent site of NU in females (3.54 per 100,000 population) and this became a greater problem with increasing age, representing the increasing number of osteopaenia related proximal humerus fractures in the elderly. The shoulder, which was predominantly the clavicle, was affected 50% more frequently in males but with a more even distribution across the ages.

In the lower limb, NU of the femur and pelvis was more common in females, the incidence increased from the sixth decade upwards following a similar trend to that of the humerus. The highest rate of non-union in the lower limb was seen in the male leg: Non-union of the tibia and fibula was the second highest site of non-union overall, 70% more frequent than any other area of the lower limb and twice as common in males (3.4/ 100,000) than in females (1.8/100,000). NU of the foot and ankle was evenly distributed between the sexes and across the ages.

Non-union of multiple sites and the axial skeleton was very rare.

Table 3. Incidence of non-union by sex and anatomy

Site Location	Female incidence /100,000 pa	Male incidence /100,000 pa	Total incidence /100,000 pa
Shoulder Region (Clavicle)	1.87	2.77	2.31

Upper Arm (Humerus)	3.54	2.1	2.84
Forearm (Radius & Ulna)	2.79	6.83	4.74
Hand	0.4	1.5	0.93
Upper limb total	8.6	13.2	10.82
Pelvis & Femur	2.43	2.04	2.24
Lower Leg (Tibia & Fibula)	1.83	3.42	2.6
Ankle & Foot	1.77	2	1.88
Lower limb total	6.02	7.46	6.72
Multiple Sites	0.04	0.06	0.05
Axial skeleton	0.25	0.44	0.34
Total	15.65	22.45	18.94

Discussion

The 5-year mean for non-union in Scotland (2005- 2010) was 18.9 per 100,000 per annum; 22.45 in males and 15.65 in females. Although there has been a decreasing trend in male incidence a longer period of analysis is necessary to draw any significance from it. The age /gender distribution followed a trend that was similar to the fracture pattern in the Edinburgh population[6] with a bimodal male and unimodal female distribution reflecting the larger number of fractures seen with higher energy injuries in the young males and the osteoporotic fractures in the elderly.

The most common site for non-union in males was the forearm and in females the humerus, with the upper limb having a 60% higher incidence of non-union than the lower limb likely in part due to the greater incidence of upper limb than lower limb fractures. In a recent epidemiology study the fracture incidence was 290/100,000 for forearms and 173/ 100,000 in the upper arm and shoulder compared to 199/100,000 in the pelvic/thigh region and 55/100,000 in the lower leg[4].

This study may under represent the numbers of NU, as in the elderly the potential for complications and the invasiveness of corrective surgery may outweigh the benefits of achieving union for the individual.

Previous estimates of fracture non-union have generally been derived from small cohorts of particular anatomical regions. The many study variables make comparison difficult although most studies of closed fracture injuries quote less than 15%[10] NU. Site specific studies have reported 1.54/ 100,000 pa in the clavicle[11], 1.1/ 100,000 pa in the diaphyseal humerus[12] and 1.89/ 100,000pa in closed tibial fractures[13]

At a population level the number of non-union is potentially affected by several different factors. These include the number of fractures, the nature of the injuries (for instance high energy open tibial fractures compared to closed low energy fractures[13]), the incidence of infection and importantly the access of the population to health care provision and adequacy of the initial fracture treatment. In addition, there will be intrinsic host factors such as diabetes and systemic agents such as non-steroidal anti-inflammatory drugs and smoking, which inhibit the repair process and would potentially, influence the incidence of non-union.

For health care planning and for clinical trial design, the absolute number of non-unions is required, particularly as there is an increasing need to evaluate current and proposed new treatments for non-union.

The ISD data used in this study records all hospital episodes. As almost all non-unions are treated operatively, the ISD data is a good reflection of the number of clinically symptomatic non-unions (as was confirmed by the validation of the ISD coding carried out in our unit). Therefore the data provided here gives realistic estimates for the number of non-unions that can be expected for each anatomical region in a given time, which will enable realistic recruitment rates to be calculated.

Our data gives an overall NU incidence in Scotland of 19 per 100,000 per annum. Clearly less than the 138/ 100,000 primary hip replacements[14] and 572/ 100,000 registered malignant neoplasms[15] but on a par with 19/ 100,000 revision hip replacements[14], and 13.5/ 100,000 on the renal transplant waiting list in Scotland in 2009.

An estimated 25% of non-unions are complex and require referral to a specialist unit dealing with limb reconstruction, such a unit with a catchment of 2 million would see approximately 100 non-union referrals per year. This compares to the 33 primary hip replacements performed per arthroplasty surgeon and 6.7 revision hips per 'revision' arthroplasty hip surgeon in Scotland in 2009[14].

Conclusion

There is very little data available in the literature regarding non-union in large numbers or populations. This study reports data which can be used as a baseline to compare against rates in other regions to assess the adequacies of trauma care provision. The pattern of non-union by age, sex and anatomical distribution in a 5.2 million Scottish population, is described with a young male bimodal and elderly female unimodal distribution and a higher incidence in the upper limb than lower limb.

Bibliography

1. Mock C, Lormand J.D., Goosen J., et al. Guidelines for essential trauma care. Geneva: World Health Organiziation, 2004.

2. Mock CN, Adzotor KE, Conklin E, et al. Trauma outcomes in the rural developing world: comparison with an urban level I trauma center. J Trauma 1993;**35**(4):518-23

3. Sethi D, Racioppi F, Baumgarten I, et al. Reducing inequalities from injuries in Europe. Lancet 2006;**368**(9554):2243-50 doi: S0140-6736(06)68895-8 [pii] 10.1016/S0140-6736(06)68895-8[published Online First: Epub Date]|.

4. Court-Brown C, Aitken SA, Forward D, et al. The Epidemiology of Adult Fractures. In: Bucholz RW, Court-Brown C, Heckman JD, Tornetta P, eds. Rockwood and Green's fractures in adults. 7 ed: Philidelphia, Lippincott Williams & Wilkins, 2010, 2009:53-84.

5. Dahabreh Z, Calori GM, Kanakaris NK, et al. A cost analysis of treatment of tibial fracture nonunion by bone grafting or bone morphogenetic protein-7. Int Orthop 2009;**33**(5):1407-14 doi: 10.1007/s00264-008-0709-6[published Online First: Epub Date]|.

6. Dahabreh Z, Dimitriou R, Giannoudis PV. Health economics: a cost analysis of treatment of persistent fracture non-unions using bone morphogenetic protein-7. Injury 2007;**38**(3):371-7 doi: S0020-1383(06)00545-6 [pii] 10.1016/j.injury.2006.08.055[published Online First: Epub Date]|.

7. Kanakaris NK, Giannoudis PV. The health economics of the treatment of long-bone non-unions. Injury 2007;**38 Suppl 2**:S77-84 doi: S0020-1383(07)80012-X [pii][published Online First: Epub Date]|.

8. Patil S, Montgomery R. Management of complex tibial and femoral nonunion using the Ilizarov technique, and its cost implications. J Bone Joint Surg Br 2006;**88**(7):928-32 doi: 88-B/7/928 [pii] 10.1302/0301-620X.88B7.17639[published Online First: Epub Date]|.

9. Court-Brown CM, Caesar B. Epidemiology of adult fractures: A review. Injury 2006;**37**(8):691-7 doi: S0020-1383(06)00323-8 [pii] 10.1016/j.injury.2006.04.130[published Online First: Epub Date]|.

10. Tzioupis C, Giannoudis PV. Prevalence of long-bone non-unions. Injury 2007;**38 Suppl 2**:S3-9 doi: S0020-1383(07)80003-9 [pii][published Online First: Epub Date]|.

11. Robinson CM. Fractures of the clavicle in the adult. Epidemiology and classification. J Bone Joint Surg Br 1998;**80**(3):476-84

12. Broadbent MR, Will E, McQueen MM. Prediction of outcome after humeral diaphyseal fracture. Injury 2010;**41**(6):572-7 doi: S0020-1383(09)00505-1 [pii] 10.1016/j.injury.2009.09.023[published Online First: Epub Date]|.

13. Court-Brown CM. Reamed intramedullary tibial nailing: an overview and analysis of 1106 cases. J Orthop Trauma 2004;**18**(2):96-101 doi: 00005131-200402000-00007 [pii][published Online First: Epub Date]|.

14. NoAuthorsListed. Scottish Arthroplasty Project Annual Report: www.arthro.scot.nhs.uk/Reports/Scottish_Arthroplasty_Project_Report_2009 2010.

15. NoAuthorListed. Cancer in Scotland (August 2011). In: Information Services Division NNSS, ed., 2011.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

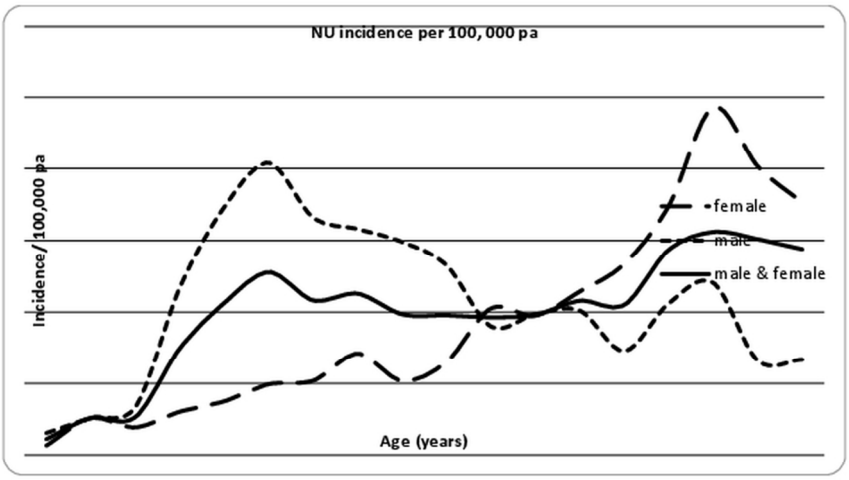
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
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	2
Objectives	3	State specific objectives, including any pre-specified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	2
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	n/a
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	n/a
Bias	9	Describe any efforts to address potential sources of bias	n/a
Study size	10	Explain how the study size was arrived at	n/a
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	n/a
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
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	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	5
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	5
		(*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	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	5-13
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	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-13
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	1

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
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 www.strobe-statement.org.

Graph 1- Incidence of non-union with age and sex



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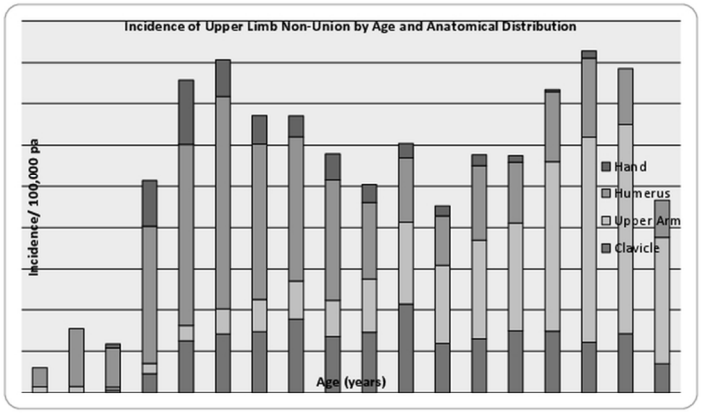
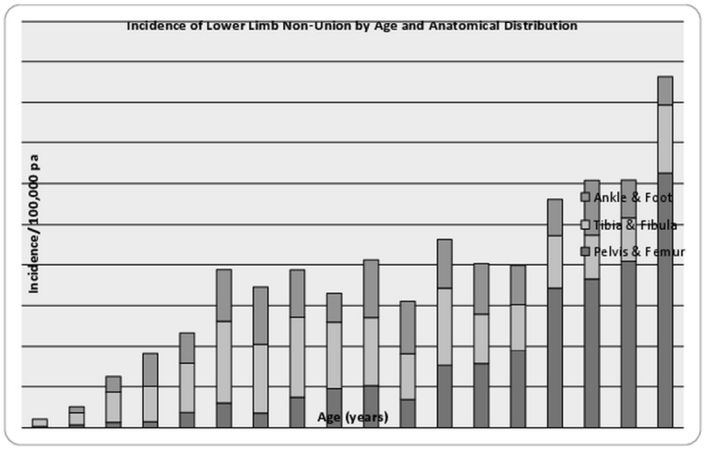
Graph 2a & 2b- distribution of non-union by site and age, upper and lower limb





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