A Meta-Analysis of the Epidemiology of Giant Cell Arteritis Across Time and Space

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Research article

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Abstract

Introduction: Giant cell arteritis (GCA) is the most common large vessel vasculitis in those over age 50 years. This meta-analysis examined the geographical and temporal distribution of the incidence, prevalence and mortality of GCA.

Methods: A systematic review was conducted using EMBASE, Scopus and PubMed from their inceptions until 2019. Studies were included if they reported at least 50 or more GCA patients and defined the location and time frame. Articles on mortality were included and standardized mortality ratio (SMR) was extracted where possible. Mean pooled prevalence, incidence, and SMR were calculated using a random effects model. Linear regression was used to explore correlations between latitude and incidence, prevalence, and mortality.

Results: Of the 3569 citations identified, 107 were included. The pooled incidence of GCA was 10.00 [9.22, 10.78] cases per 100,000 people over 50 years old. This incidence was highest in Scandinavia 21.57 [18.90, 24.23], followed by North and South America 10.89 [8.78, 13.00], Europe 7.26 [6.05, 8.47], and Oceania 7.85 [-1.48, 17.19]. Pooled prevalence was 51.74 [42.04, 61.43] cases per 100,000 people over age 50. Annual mortality was 20.44 [17.84, 23.03] deaths/1000. Mortality generally decreased over the years of publication (p=0.0008). Latitude correlated significantly with incidence (p=0.0011), but not with prevalence, or mortality.

Conclusions: GCA incidence varies nearly 3-fold between regions and is highest in Scandinavia but not significantly. Mortality may be improving over time.

Key Messages
1. Certain regions have a disproportionate burden of giant cell arteritis (GCA), and the mechanism is not fully understood.
2. Latitude influences the distribution of some autoimmune conditions, however, not GCA.
3. Despite increasing average age of GCA, increasing GCA rates were not found.

Introduction

Giant cell arteritis (GCA) is a polygenic immune-mediated disease of unknown etiology that occurs in individuals aged 50 years and older [1]. It is thought to be caused by exaggerated immune responses to vascular endothelial injury with lymphocyte proliferation and giant cell formation. These responses lead to luminal narrowing and disruption of the internal elastic lamina, which limit blood flow cause end organ ischemia [2]. Common symptoms include headache, scalp tenderness, jaw claudication, and visual loss. GCA is classified using the 1990 ACR criteria, and though a histological diagnosis is preferred, a positive temporal artery biopsy (TAB) is not mandated [4]. Diagnoses may be confirmed without a positive biopsy and imaging is sometimes used such as temporal artery ultrasound.
GCA is the most common systemic vasculitis in adults and is closely associated with polymyalgia rheumatica (PMR); approximately 40–60% of patients with GCA have PMR while 15–20% of those with PMR develop GCA symptoms [3].

The epidemiology of GCA has been extensively studied. The average age of diagnosis has increased from 75 in the 1950s to 79 in the 2000s [5]. GCA has also more common in females at a ratio of 2.5:1 [6] [1]. Incidence has consistently been found to be highest in Scandinavia and lowest in Asian countries [1]. Some autoimmune disorders such as multiple sclerosis have shown latitude-associated trends [7]. GCA may be increased in northern latitudes. Seasonal and temporal clustering of incident GCA have been reported, perhaps due to viral triggers, however this relationship remains unclear [1].

As the population continues to age, the incidence, prevalence and mortality of GCA are expected to increase. Considering the significant morbidity associated with GCA from blindness, aortic defects, and treatment, a better understanding of the changing epidemiology is needed.

The last major epidemiological meta-analysis of GCA was published in 2008 [18]. Our study aimed to provide a comprehensive update on the global geographic and temporal trends for incidence, prevalence, and mortality in GCA, and examine its potential connection with latitude.

Methods

Study selection

A systematic review of the literature was performed to identify studies examining the incidence, prevalence or mortality of GCA. EMBase, Scopus, and PubMed were searched from their inceptions until February 2019. Our search strategy is reported in the Supplementary Table 1. Studies were included if they were written in English, presented a cohort or cross-sectional data on more than 50 patients with GCA and reported on population, location and/or time-frame parameters. Articles on mortality were included as a rate, and if they provided an age and gender matched population (Standardized Mortality Ratio), that was also extracted. Review articles, case-control studies and case series were excluded. Study quality was assessed by using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

Data Extraction and Analysis

The following data were extracted from each study: year of publication, study country, total number of GCA cases, years of cohort, number of deaths, incidence, prevalence, and mortality rate. Mortality rate was standardized across cohorts to deaths per 1000 people per year. The website www.latlong.net was used to determine the latitude of the population location (city or region) examined in each included article. Forest plots were generated using Revman5.3 to determine the pooled incidence, prevalence, and mortality using Wilson's score method. The 95% confidence intervals were generated using a random effects model to account for differences in variance and quality between studies. Tau squared statistics
were used to evaluate heterogeneity between studies. Publication bias was assessed using funnel plots, which were also generated on Revman5.3. Linear regression was used to evaluate temporal and geographic differences using SPSS26 where p < 0.05 was significant.

**Results**

**Search Results**

The search identified 5426 articles of which 107 were included for analysis (Fig. 1). There were 3578 duplicates between databases and 1741 did not meet eligibility criteria. Table 1 provides the information on the studies extracted and the incidence, prevalence and mortality from each paper. The study quality as measured by the STROBE instrument is found in Table 1. Publication bias was negligible according to funnel plots (Supplementary Fig. 1).
| Epidemiological Study Category | First Author (citation) | Year | Location   | STROBE | Total patients | Rate  |
|-------------------------------|------------------------|------|------------|--------|----------------|-------|
| Mortality                    | Andersson R            | 1986 | Sweden     | 20     | 90             | 29.17 |
| Mortality                    | Baslund B              | 2014 | Denmark    | 21     | 1787           | 26.3  |
| Mortality                    | Belvedere LM           | 2016 | Italy      | -      | 280            | 21.84 |
| Mortality                    | Bengtsson BA           | 1981 | Sweden     | 17     | 90             | 28.89 |
| Mortality                    | Bisgard C              | 1991 | Denmark    | 18     | 34             | 40.72 |
| Mortality                    | Boesen P               | 1987 | Denmark    | 18     | 46             | 27.17 |
| Mortality                    | Brekke LK              | 2015 | Norway     | -      | 820            | 13.51 |
| Mortality                    | Brekke LK              | 2016 | Norway     | -      | 820            | 13.81 |
| Mortality                    | Catanoso M             | 2014 | Italy      | -      | 285            | 15.59 |
| Mortality                    | Catanoso M             | 2017 | Italy      | 19     | 285            | 16.76 |
| Mortality                    | Crow R                 | 2009 | USA        | 21     | 44             | 34.09 |
| Mortality                    | Diamantopoulos AP      | 2014 | Norway     | 22     | 212            | 18.87 |
| Mortality                    | Graham E               | 1981 | UK         | 18     | 90             | 35.56 |
| Mortality                    | Gran JT                | 2001 | Norway     | 20     | 338            | 20.41 |
| Mortality                    | Hachulla E             | 2001 | France     | 19     | 133            | 17.13 |
| Mortality                    | Hernandez-Rodriguez J  | 2002 | Spain      | 19     | 75             | 12.38 |
| Mortality                    | Huston KA              | 1978 | USA        | 21     | 42             | 20    |
| Mortality                    | Khalifa M              | 2009 | Tunisia    | 20     | 96             | 2.45  |
| Mortality                    | Knorring J             | 1979 | Finland    | 15     | 53             | 15.09 |
| Mortality                    | Kobayashi S            | 2003 | Japan      | 21     | 66             | 45.45 |
| Mortality                    | Labarca C              | 2015 | USA        | 21     | 286            | 16.08 |
| Mortality                    | Lie JT                 | 1995 | USA        | 19     | 72             | 10    |
| Mortality                    | Lin L                  | 2018 | UK         | 22     | 9778           | 14.58 |
| Mortality                    | Macchioni P            | 2018 | Italy      | 22     | 281            | 7.94  |
| Epidemiological Study Category | First Author (citation) | Year | Location | STROBE | Total patients | Rate |
|-------------------------------|-------------------------|------|----------|---------|----------------|------|
| Mortality                     | Matteson EL             | 1996 | USA      | 20      | 214            | 19.08|
| Mortality                     | Mohammad A              | 2011 | Sweden   | 22      | 792            | 24.38|
| Mortality                     | Mohammad AJ             | 2015 | Sweden   | 22      | 840            | 25.55|
| Mortality                     | Moinet F                | 2017 | Martinique | -     | 40             | 6    |
| Mortality                     | Ninan J                 | 2011 | Australia | 20    | 225            | 22.54|
| Mortality                     | Nordborg E              | 1989 | Sweden   | 20      | 284            | 28.87|
| Mortality                     | Pamuk ON                | 2009 | Turkey   | 21      | 19             | 35.09|
| Mortality                     | Pierluigi M             | 2016 | Italy    | -       | 280            | 16.33|
| Mortality                     | Pierluigi M             | 2018 | Italy    | 21      | 285            | 21.84|
| Mortality                     | Rajala S                | 1993 | Finland  | 19      | 66             | 22.73|
| Mortality                     | Tam S                   | 2008 | Hong Kong | 21    | 19             | 52.63|
| Mortality                     | Whitfeild AG            | 1963 | UK       | 10      | 72             | 13.89|
| Mortality                     | Yates M                 | 2013 | UK       | 21      | 119            | 21.01|
| Prevalence                    | Boesen P                | 1987 | Denmark  | 18      | 46             | 135  |
| Prevalence                    | Catanosono M            | 2017 | Italy    | 20      | 285            | 87.9 |
| Prevalence                    | Crowson CS              | 2016 | USA      | 20      | 248            | 204  |
| Prevalence                    | Herlyn K                | 2014 | Germany  | 20      | 150            | 44   |
| Prevalence                    | Khalifa M               | 2009 | Tunisia  | 18      | 96             | 7    |
| Prevalence                    | Kobayashi S             | 2003 | Japan    | 20      | 66             | 1.47 |
| Prevalence                    | Martinez PJM            | 2016 | Argentina | -     | 90             | 120  |
| Prevalence                    | Pamuk ON                | 2009 | Turkey   | 20      | 19             | 20   |
| Prevalence                    | Romero-Gomez C          | 2015 | Spain    | 21      | 29             | 12.2 |
| Incidence                     | Khalifa M               | 2009 | Tunisia  | 20      | 96             | 7    |
| Incidence                     | Richier Q               | 2018 | France   | -       | 60             | 2.33 |
| Incidence                     | Tam                     | 2008 | Hong Kong | 19    | 47             | 0.34 |
| Incidence                     | Jonasson F              | 1979 | UK       | -       | 136            | 4.2  |
| Incidence                     | Salvarani C             | 1991 | Italy    | 20      | 43             | 6.9  |
| Epidemiological Study Category | First Author (citation) | Year | Location       | STROBE | Total patients | Rate |
|-------------------------------|-------------------------|------|----------------|--------|----------------|------|
| Incidence                     | Gonzalez-Gay MA         | 1992 | Spain          | 20     | 255            | 6    |
| Incidence                     | Rajala SA               | 1993 | Finland        | 20     | 66             | 7.2  |
| Incidence                     | Gonzalez-Gay MA         | 1997 | Spain          | 21     | 93             | 9.38 |
| Incidence                     | Gonzalez-Gay MA         | 1999 | Spain          | 20     | 110            | 14.1 |
| Incidence                     | Gonzalez-Gay MA         | 2001 | Spain          | 20     | 161            | 10.24|
| Incidence                     | Schmidt D               | 2001 |                | 20     | 99             | 2.07 |
| Incidence                     | Gonzalez-Gay MA         | 2003 | Spain          | 20     | 210            | 9.75 |
| Incidence                     | Bustamante ME           | 2004 | Spain          | 21     | 55             | 4.1  |
| Incidence                     | Dadonine J              | 2005 | Lithuania      | 18     | 11             | 0.72 |
| Incidence                     | Smeeth L                | 2006 | UK             | 20     | 3928           | 8.42 |
| Incidence                     | Gonzalez-Gay MA         | 2007 | Spain          | 19     | 255            | 10.13|
| Incidence                     | Yates M                 | 2013 | UK             | 21     | 119            | 6.8  |
| Incidence                     | Catanoso M              | 2014 | Italy          | 21     | 285            | 3.3  |
| Incidence                     | Potocnik N              | 2014 | Slovenia       | -      | 97             | 8.7  |
| Incidence                     | Mollan SP               | 2015 | UK             | 17     | 7864           | 4.31 |
| Incidence                     | Petri H                 | 2015 | UK             | 20     | 4671           | 11.2 |
| Incidence                     | Romero-Gomez C          | 2015 | Spain          | 21     | 29             | 2.2  |
| Incidence                     | Elfving P               | 2016 | Finland        | 20     | 8              | 7.5  |
| Incidence                     | Catanoso M              | 2017 | Italy          | 21     | 285            | 7.8  |
| Incidence                     | Devauchelle-Pensec V    | 2018 | France         | 21     | 241            | 8.5  |
| Incidence                     | Potocnik N              | 2018 | Slovenia       | -      | 169            | 10.5 |
| Incidence                     | Pucelji NP              | 2018 | Slovenia       | 21     | 169            | 8.7  |
| Incidence                     | Reinhold-Keller E       | 2000 | Germany (north)| 20     | 180            | 8.7  |
| Incidence                     | Reinhold-Keller E       | 2000 | Germany (south)| 20     | 180            | 9.4  |
| Incidence                     | Friedman G              | 1982 | Israel         | 20     | 46             | 0.49 |
| Incidence                     | Sonnenblick M           | 1994 | Israel         | 20     | 84             | 10.2 |
| Epidemiological Study Category | First Author (citation) | Year | Location | STROBE | Total patients | Rate  |
|-------------------------------|-------------------------|------|----------|--------|----------------|-------|
| Incidence                    | Bas-Lando M             | 2007 | Israel   | 19     | 206            | 11.3  |
| Incidence                    | Pamuk ON                | 2009 | Turkey   | 21     | 19             | 1.13  |
| Incidence                    | Nesher G                | 2016 | Israel   | 20     | 140            | 8.1   |
| Incidence                    | Huston KA               | 1978 | USA      | 21     | 42             | 11.7  |
| Incidence                    | Smith CA                | 1983 | USA      | 18     | 26             | 1.58  |
| Incidence                    | Machado EBV             | 1988 | USA      | 19     | 94             | 17    |
| Incidence                    | Salvarani C             | 1995 | USA      | 18     | 125            | 17.8  |
| Incidence                    | Salvarani C             | 2004 | USA      | 20     | 173            | 18.8  |
| Incidence                    | Ramstead C              | 2007 | Canada   | 19     | 141            | 9.4   |
| Incidence                    | Mader T                 | 2009 | USA      | 19     | 122            | 1.02  |
| Incidence                    | Udayakumar PD           | 2013 | USA      | -      | 39             | 19.25 |
| Incidence                    | Chandran AK             | 2015 | USA      | 21     | 74             | 19.8  |
| Incidence                    | Martinez PJM            | 2016 | Argentina | -     | 90             | 8.6   |
| Incidence                    | Ing EB                  | 2019 | Canada   | 21     | 35             | 4.9   |
| Incidence                    | Abdul-Rahan AM          | 2011 | New Zealand | 20 | 70             | 12.73 |
| Incidence                    | Dunstan E               | 2014 | Australia | -   | 314            | 3.2   |
| Incidence                    | Bengtsson BA            | 1981 | Sweden   | 18     | 126            | 28.6  |
| Incidence                    | Boesen P                | 1987 | Denmark  | 20     | 46             | 76.6  |
| Incidence                    | Nordborg E              | 1989 | Sweden   | 18     | 284            | 18.3  |
| Incidence                    | Baldursson O            | 1994 | Iceland  | 18     | 133            | 27    |
| Incidence                    | Gran JT                 | 1997 | Norway   | 20     | 66             | 29    |
| Incidence                    | Haugeberg G             | 1998 | Norway   | 20     | 42             | 27.9  |
| Incidence                    | Petursdottir V          | 1999 | Sweden   | 19     | 665            | 22.2  |
| Incidence                    | Haugeberg G             | 2003 | Norway   | 18     | 70             | 32.4  |
| Incidence                    | Nordborg C              | 2003 | Sweden   | 20     | 665            | 22.2  |
| Incidence                    | Mohammad A              | 2011 | Sweden   | -      | 840            | 11.3  |
## Epidemiological Study

| Category   | First Author (citation) | Year | Location | STROBE | Total patients | Rate  |
|------------|-------------------------|------|----------|--------|----------------|-------|
| Incidence  | Diamantopoulos AP       | 2014 | Norway   | -      | 135            | 17.2  |
| Incidence  | Brekke LK               | 2015 | Norway   | -      | 820            | 15.7  |
| Incidence  | Mohammad AJ             | 2015 | Sweden   | -      | 840            | 14.1  |
| Incidence  | Brekke LK               | 2017 | Norway   | -      | 881            | 16.8  |

### Incidence

Of the 107 studies, 61 studies reported on the incidence of GCA. Studies were sorted into several geographic areas and pooled incidence was calculated per 100,000 people over 50 years (Fig. 2). The included geographic areas from highest to lowest incidence [95% CI] were Scandinavia 21.57 [18.90, 24.23], North and South America 10.89 [8.78, 13.00], Oceania 7.85 [1.48, 17.19], Europe 7.26 [6.05, 8.47], Middle East 5.73 [4.20, 7.26], Africa 4.62 [0.05, 9.20], East Asia 0.34 [0.12, 0.56]. The highest incidence within the studies was in Denmark 76.6 [54.65, 98.55] and the lowest was in Hong Kong 0.34 [0.12, 0.56]. The global pooled incidence was 10 [9.22, 10.78] per 100,000 people over 50 years. Global incidence rates were visually plotted on a map (Supplementary Fig. 2).

Incidence was also assessed across publication years of publication using linear regression. Scandinavia had the largest decreasing incidence rate. Incidence fell 0.80 per 100,000 people per year, corresponding to a reduction of two-thirds between 1981 (42.3 per 100,000) and 2017 (13.4 per 100,000). Globally, pooled incidence decreased over time at a rate of 0.41 per 100,000 per year. Excluding Scandinavia, global pooled incidence decreased at a rate of 0.27 per 100,000 per year.

### Prevalence

A total of 9 studies reported on the prevalence of giant cell arteritis. The overall pooled prevalence was 51.74 [42.04, 61.43] cases per 100,000 people over 50 years (Fig. 3). The prevalence was stable across publication years of the studies using a linear fit model.

### Mortality

Thirty-seven articles included data on mortality. The overall pooled mortality rate is 20.44 [17.84, 23.03] cases per 1000 people over 50 years (Fig. 4). Highest mortality was in Hong Kong (52.63) with lowest in the USA (34.09). Across publication years, there was an overall decrease in mortality over time with a rate of 0.14 per 1000 people per year ((p = 0.00076).

### Latitude

Incidence, prevalence and longitude were plotted against absolute latitude and were assessed using linear regression (Fig. 5). The R squared value for incidence, prevalence and mortality was: 0.1657,
Our linear model only showed a significant correlation between latitude and incidence ($p = 0.0011$, beta = 0.489), not prevalence ($p = 0.33$) or mortality ($p = 0.92$).

**Discussion**

The incidence of GCA was threefold higher in Scandinavia relative to the rest of Europe and was 6 times higher in Scandinavia compared to East Asia. The high incidence rates of GCA in parts of North America may be explained by communities with Scandinavian ancestry, such as in Olmsted County, USA [14]. This could disproportionately elevate the overall incidence of GCA in North America, with a rate exceeding most regions (except Scandinavia). These findings are consistent with those previously reported [1, 11–13, 17–18].

The increased incidence of GCA in Scandinavian countries may be explained by genetic susceptibility. Patients with GCA have haplotype variation in certain MHC class II alleles, with a predominance of HLA DRB1*04 specifically. Polymorphisms in genes expressing inflammatory mediators such as TNF, adhesion molecules, and IL18 are sometimes implicated in GCA [1, 19]. In addition, rates could be higher in Scandinavia due to more advanced healthcare tracking systems [20]. Seasonal variations have also been reported, albeit with low statistical power [1]. It is also speculated that microorganisms may trigger infections and lead to immune-mediated hypersensitivity, although evidence for this remains controversial [8].

Our results found that there was only a statistically significant association between latitude and incidence, not prevalence or mortality. However, regional differences may exist due to variations in population concentration; urban populations tend to have higher incidence rates of GCA compared to rural regions [9]. This trend is possibly explained by proximity to medical centres with greater diagnostic capacity and higher surrounding patient concentrations [9].

With respect to temporal trends, incidence rates globally were found to generally decrease over time, with some regional differences. Specifically, North America, South America, and Europe had stable incidence rates over time, whereas rates in Scandinavia decreased. The downward trend in Scandinavia may be explained by changes in immigration. Immigration to Sweden has been steadily rising since 2008, reaching record high numbers in 2013 [10]. As of 2017, Statistics Sweden reported that around 2,439,007 or 24% of Swedish residents were foreign born [14]. Most of these immigrants originated from Asian and Middle Eastern countries, where rates of GCA are among the lowest [15]. Denmark and Norway similarly underwent increases in immigration, albeit with lower numbers [16]. The timeframe over which these increases in immigration occurred coincides with when the decreasing trends in incidence of GCA began (approximately 2011, according to our data). This trend is in sharp contrast with previous epidemiological studies published prior to 2011, which showed increasing incidence over time across Scandinavia and other parts of Europe [11–13].

We expect total numbers of cases to begin increasing in the future as the population ages.
Mortality in GCA was found to generally decrease over time, and showed no geographic variation. The decrease in mortality can likely be explained by overall increased longevity in the elderly, earlier diagnoses, increased surveillance, and earlier initiation of therapy as well as possibly the use of steroid sparing treatments such as methotrexate. We had insufficient data to analyze the SMR and cannot comment if the mortality relative to the age/gender matched population is changing. Controversy exists surrounding studies with an increased mortality in GCA [1, 11, 22–23, 25].

Our study is not without limitations. There is a lack of a standardized definition of GCA used consistently in the literature, resulting in the inclusion of heterogeneous data in our analysis. This inconsistency is evident in administrative databases, where the lack of a specific billing code for GCA can misclassify patients and either over- or underestimate data [24]. Another consequence is that inclusion criteria were inconsistently used in the study selection process. As previously mentioned, the 1990 ACR criteria does not mandate biopsy positive results. Thus, the majority of hospital-based studies included only biopsy proven cases, whereas most population or community-based studies included also clinical diagnoses. Therefore, data may be vary depending on which inclusion criteria was used. Non-English studies were also excluded. Finally, some studies on mortality combined data for both PMR and GCA, which would have falsely deflated the reported mortality rates since PMR has a lower mortality rate than GCA [26].

Conclusion
This meta-analysis describes current global pooled incidence, prevalence and mortality of GCA. Incidence rates vary significantly between regions and are highest in Scandinavia. Temporally, GCA incidence and mortality decreased, while prevalence remained stable. Latitude does not influence incidence, prevalence, or mortality in GCA.

Abbreviations
ACR – American college of rheumatology
GCA – Giant Cell Arteritis
PMR - polymyalgia rheumatica
SMR - standardized mortality ratio
STROBE - Strengthening the Reporting of Observational Studies in Epidemiology
TAB - temporal artery biopsy

Declarations
Author's Disclosures: Nothing to disclose.
Ethics/IRB approval: This was not necessary as this was a systematic review.

Ethics approval and consent to participate

Ethics approval was not required as this is a systematic review. Not applicable.

Consent for publication

This study contains no personal patient data. Not applicable.

Availability of data and materials

Raw data is presented in Table 1 and Supplementary table 1. Further information is available upon reasonable request.

Competing interests

None to declare

Funding

None to declare

Authors contributions

KL and DS were responsible for manuscript writing, data analysis, and experimental design. MT was responsible for statistical analysis and manuscript editing. JP was responsible for experimental design and manuscript editing.

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References

[1] E. Nordborg, C. Nordborg. Giant cell arteritis: epidemiological clues to its pathogenesis and an update on its treatment, *Rheumatology*, Volume 42, Issue 3, March 2003, Pages 413–421, https://doi.org/10.1093/rheumatology/keg116

[2] Piggott K, Bioussé V, Newman NJ, Goronzy JJ, Weyand CM. Vascular damage in giant cell arteritis. *Autoimmunity*. 2009;42(7):596-604. doi:10.1080/08916930903002495

[3] Charlton R. Optimal management of giant cell arteritis and polymyalgia rheumatica. *Ther Clin Risk Manag*. 2012;8:173-179. doi:10.2147/TCRM.S13088
[4] Baig IF, Pascoe AR, Kini A, Lee AG. Giant cell arteritis: early diagnosis is key. *Eye Brain*. 2019;11:1-12. Published 2019 Jan 17. doi:10.2147/EB.S170388

[5] Kermani TA, Schäfer VS, Crowson CS, et al. Increase in age at onset of giant cell arteritis: a population-based study. *Annals of the Rheumatic Diseases* 2010;69:780-781.

[6] Marília A. Dagostin and Rosa M.R. Pereira (January 28th 2020). Giant Cell Arteritis: Current Advances in Pathogenesis and Treatment [Online First], IntechOpen, DOI: 10.5772/intechopen.91018. Available from: https://www.intechopen.com/online-first/giant-cell-arteritis-current-advances-in-pathogenesis-and-treatment

[7] Alonso A, Hernán MA. Temporal trends in the incidence of multiple sclerosis: a systematic review. *Neurology*. 2008;71(2):129-135. doi:10.1212/01.wnl.0000316802.35974.34

[8] Weyand, C., Goronzy, J. Immune mechanisms in medium and large-vessel vasculitis. *Nat Rev Rheumatol* 9, 731–740 (2013). https://doi.org/10.1038/nrrheum.2013.161

[9] Brekke LK, Fevang BT, Myklebust G. Increased Incidence of Giant Cell Arteritis in Urban Areas?. *J Rheumatol*. 2019;46(3):327-328. doi:10.3899/jrheum.180714

https://www.ncbi.nlm.nih.gov/books/NBK459376/

[10] Andersson, R, Weinar, A. Integration policies : Sweden country report. *Migration Policy Centre, INTERACT Research Report, Country Reports*. Updated 2014.

Retrieved from Cadmus, European University Institute Research Repository, at: http://hdl.handle.net/1814/32656

[11] Gonzalez-Gay MA, Miranda-Filloy JA, Lopez-Diaz MJ, PerezAlvarez R, Gonzalez-Juanatey C, Sanchez-Andrade A, Martin J, Llorca J (2007) Giant cell arteritis in northwestern Spain: a 25-year epidemiologic study. Medicine (Baltimore) 86:61–68

[12] Petursdottir V, Johansson H, Nordborg E, Nordborg C (1999) The epidemiology of biopsy-positive giant cell arteritis: special reference to cyclic fluctuations. *Rheumatol (Oxf)* 38:1208–1212

[13] Nordborg C, Johansson H, Petursdottir V, Nordborg E (2003) The epidemiology of biopsy-positive giant cell arteritis: special reference to changes in the age of the population. *Rheumatol (Oxf)* 42:549–552

[14] Summary of Population Statistics 1960-2019. Statistics Sweden website. Updated March 19, 2020. Accessed May 27, 2020. https://www.scb.se/en/finding-statistics/statistics-by-subject-area/population/population-composition/population-statistics/pong/tables-and-graphs/yearly-statistics-the-whole-country/summary-of-population-statistics/
[15] Foreign citizens by country of citizenship, age and sex. Year 1973-2019. Statistics Sweden website. Accessed May 27, 2020.

http://www.statistikdatabasen.scb.se/pxweb/en/ssd/START__BE__BE0101__BE0101F/UtlmedbR/?rxid=b83e5bbd-958a-4655-aa40-486ba2ca09a3

[16] Moore, H. Immigration in Denmark and Norway: Protecting Culture or Protecting Rights? Scandinavian Studies, 2010;82(3), 355-364. Retrieved May 28, 2020, from www.jstor.org/stable/25769037

[17] Richard A. Watts, 2. Epidemiology of giant cell arteritis: a critical review, Rheumatology, Volume 53, Issue suppl_2, July 2014, Pages i1–i2, https://doi.org/10.1093/rheumatology/keu183

[18] Lee JL, Naguwa SM, Cheema GS, Gershwin ME. The geo-epidemiology of temporal (giant cell) arteritis. Clin Rev Allergy Immunol. 2008;35(1-2):88-95. doi:10.1007/s12016-008-8075-0

[19] Palomino-Morales RJ, Vazquez-Rodriguez TR, Torres O, et al. Association between IL-18 gene polymorphisms and biopsy-proven giant cell arteritis. Arthritis Res Ther. 2010;12(2):R51. doi:10.1186/ar2962

[20] Brown, P. Chapter 1: Citizen-Science Alliances and Health Social Movements. In: Brown, P, Toxic Exposures: Contested Illnesses and the Environmental Health Movement. New York: Columbia University Press, 2007: 5.

[21] Vyvey M. Steroids as pain relief adjuvants. Can Fam Physician. 2010;56(12):1295-e415.

[22] Ben-Shabat N, Tiosano S, Shovman O, et al. Mortality among patients with giant-cell arteritis: A large-scale population-based cohort study [published online ahead of print, 2019 Dec 15]. J Rheumatol. 2019;jrheum.190927. doi:10.3899/jrheum.190927

[23] Bisgård C, Sloth H, Keiding N, Juel K. Excess mortality in giant cell arteritis. J Intern Med. 1991;230(2):119-123. doi:10.1111/j.1365-2796.1991.tb00418.x

[24] Lillian Bara, Janet E Pope, Priscila Pequeno, Farah E Saxena, Mary Bell, Derek Haaland, Jessica Widdifield, Incidence and prevalence of giant cell arteritis in Ontario, Canada, Rheumatology, , keaa095, https://doi.org/10.1093/rheumatology/keaa095

[25] Crow RW, Katz BJ, Warner JE, et al. Giant cell arteritis and mortality. J Gerontol A Biol Sci Med Sci. 2009;64(3):365-369. doi:10.1093/gerona/gln030

[26] Uddhammar A, Eriksson A-L, Nyström L, et al. Increased mortality due to cardiovascular disease in patients with giant cell arteritis in northern Sweden. J Rheumatol. 2002;29(4):737–42.