

# Delayed diagnosis of Charcot foot: A systematic review and meta-analysis

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## Abstract

### Aims

This study aims to examine the duration of the delay in diagnosis, as well as the rate of delayed diagnosis in Charcot foot.

### Methods

We systematically reviewed articles published in Medline, SCOPUS and Cumulative Index of Nursing and Allied Health Literature (CINAHL) to identify articles discussing the delayed or misdiagnosis of Charcot foot. A meta-analysis was conducted to determine the average time from symptom onset to correct diagnosis (called “diagnostic delay duration”) and proportion of patients misdiagnosed prior to being correctly diagnosed (“delayed diagnosis rate”).

### Results

Our search identified 142 articles, 7 of which are included in this review. The review found that 53.2% of cases of Charcot osteoarthropathy experienced a delay in diagnosis (95% CI 28.9-77.4%). Overall, the duration of diagnostic delay was determined to be 86.9 days (95% CI 10.5-162.1).

### Conclusion

We found that patients with Charcot foot experienced prolonged times from symptom onset to correct diagnosis, and a majority of patients are misdiagnosed. These delays in diagnosis contribute to worse patient outcomes.

**Keywords (max 6):** Systematic review, Diabetes, Charcot osteoarthropathy, Delayed diagnosis, Diagnostic errors

**Highlights (optional)** 3-5 bullet points, 85 chars per bullet (including spaces)

- Charcot foot is a complication of longstanding diabetes
- This pathology is often misdiagnosed (53.2%), and this causes a delay in diagnosis
- On average, patients experience a delay in diagnosis of 12.4 weeks

## 1. Introduction

Charcot neuropathic osteoarthropathy, also referred to as neuropathic arthropathy, or neuroarthropathy, or Charcot foot, is a debilitating, destructive process that may be confused with other conditions. Although the exact pathogenesis is unclear, Charcot foot occurs in the context of peripheral neuropathy and metabolic abnormalities, most often occurring in patients with long-standing diabetes. In such patients minor trauma to the foot may trigger high levels of inflammatory cytokines, resulting in osteoarthropathy<sup>1</sup>.

Clinically, this often presents as an inflamed and swollen foot. This nonspecific presentation can easily be confused with other diabetic comorbidities such as cellulitis, deep vein thrombosis, gout, or osteomyelitis<sup>2</sup>, so high index suspicion is required to accurately diagnose Charcot foot in the acute phase (i.e., during Eichenholtz stage 0). The diagnosis of Charcot foot can be made with X-ray if fractures are present, or via MRI or bone technetium scan if X-rays are equivocal<sup>3</sup>.

The gold standard of treatment for those diagnosed with Charcot foot is total weight offloading early in the course of the disease, as total offloading may reduce need for reconstructive surgery<sup>4</sup>. Prompt diagnosis of Charcot foot is key to successful management, as delays in diagnosis may lead to further injury including ulceration, infection, and further fracture<sup>5,6</sup>.

Given the seriousness of the disease, the importance of early diagnosis, and the ease of confusion with other pathologies, we aimed in this systematic review to examine the rates of delayed diagnosis of Charcot foot, as well as to examine the duration of diagnostic delay.

## 2. Material and Methods

### **2.1 Search strategy**

A systematic review of the literature was conducted using Ovid-Medline, Scopus, and Cumulative Index to Nursing and Allied Health Literature (CINAHL). Articles published between January 2015 and August 2020 were identified by searching for Charcot foot plus either diagnostic delay or antibiotics (see [Supplemental Table 1](#) for full search terminology). This search strategy was designed to identify articles describing diagnostic delay, even if it this not their research objective of the article.

Abstracts of all articles were screened, and English language articles discussing the diagnostic process or classification of Charcot foot were included for the full-text review. Studies describing Charcot arthropathy of body parts other than the foot were excluded, as were articles aimed primarily at diseases other than diabetic Charcot foot (e.g., syphilitic arthritis, management of osteomyelitis, etc.). On full text review, articles were excluded if they did not present specific data on the rates of delayed diagnosis, reasons for misdiagnosis, or the time from symptom onset to correct diagnosis. However, all articles included in the full-text review, whether included in the final study or not, were searched for the purpose of obtaining additional references. Clinical trials, cohort studies, case-control studies, cross-sectional studies, and case-series were eligible for inclusion. Case reports, letters, expert opinions,

systematic reviews, and meta-analyses were excluded (although they were reviewed for sources).

## **2.2 Data items & collection**

Articles were summarized by J.T. & R.J. and independently reviewed by H.R. & G.K. for accuracy. The final data was reviewed and agreed upon by all authors. The year, country, number of patients, number of cases, study design, and inclusion/exclusion criteria were recorded for each study. Descriptive statistics for each study were also recorded, including average patient age, average duration of diabetes, proportion of patients who were male, proportion of patients with type II diabetes, and proportion of cases of Charcot foot that were preceded by trauma to the affected foot. For each study, we collected the following 3 outcomes: average time from symptom onset to correct diagnosis (called “diagnostic delay duration”), proportion of patients misdiagnosed prior to being correctly diagnosed (“delayed diagnosis rate”), and any previous diagnoses made before arriving to the correct diagnosis (“misdiagnosis reason”).

## **2.3 Synthesis of results**

Some studies evaluated cases of Charcot per foot (i.e., in patients with bilateral Charcot), so summary statistics for our 3 primary outcomes are presented per case of Charcot (instead of per patient), as is the history of trauma to the foot. All other variables reported are per patient, unless otherwise stated. In studies that reported the diagnostic delay time in months rather than day, we assumed each month has 30 days. In studies where the mean and/or standard deviation were missing for our outcomes, these values were imputed using the methodology outlined by Hozo et al<sup>7</sup>. In studies that reported results stratified by groups, the results presented here are aggregates for the entire study population. Due to the methodological heterogeneity of the studies included, the meta-analyses for diagnostic delay duration and delayed diagnosis rate were conducted using random-effects models.

We conducted two sensitivity analyses to account for potential bias in study designs or inclusion criteria. Specifically, we calculated the duration of diagnostic delay excluding Gill et al.<sup>8</sup> (because in that study patients were included only if they had diagnostic delay) and excluding Hingsammer et al.<sup>9</sup> (because of restrictive inclusion criteria). All analysis was conducted using the R software environment (version 3.6.3)<sup>10</sup>.

# **3. Results**

## **3.1 Study selection**

Our database searches identified 142 abstracts, 32 of which were duplicates. After screening of these articles, 43 articles were identified for full text review, which identified an additional 41 articles to be reviewed upon reviewing the references of the 43 previous full text reports. After review of these 84 articles, a total of 7 studies were included in the final analysis ([Figure 1](#)).

## **3.2 Characteristics of included studies**

All the studies included were retrospective chart reviews of patients eventually diagnosed with Charcot foot who were referred to specialty clinics for foot care. Three of the studies were case

series and detailed the presentation, diagnosis, and treatment of patients with Charcot foot. Two of these case series<sup>11,12</sup> presented the accounts of all of the patients with Charcot foot treated in their respective foot clinics, while the remaining case series<sup>8</sup> was limited exclusively to patients who experienced a delay in their diagnosis of Charcot foot.

The remaining four studies were either case-control or retrospective cohort studies. Because these four studies were aimed primarily at investigating outcomes other than diagnostic delay, they varied greatly in their exclusion criteria. Notably, Hingsammer et al.<sup>9</sup> and Chantelau<sup>13</sup> excluded patients with active ulcers or osteomyelitis from their studies, while Thewjitcharoen et al.<sup>14</sup>, Wukich et al.<sup>15</sup>, and the 4 case series studies did not.

### **3.3 Patient characteristics**

The 7 studies included a grand total of 257 cases of Charcot foot among 230 patients ([Table 1](#)). In the subset of studies that reported demographic data, the weighted average age of patients was 54.1 years old. A majority of patients were male (n = 118, 56.2%) and had type 2 diabetes (n=177, 82.4%). Most patients had a longstanding history of diabetes prior to diagnosis, with an average duration of 19.1 years among the 100 patients for which data was available. A history of trauma to the foot was reported in 37.9% of cases (n=89), though this figure varied greatly by study (range: 21.3 to 87.5%).

### **3.4 Delays in diagnosis and reasons**

Diagnostic delay was common across all studies, with over half of cases experiencing a delay in diagnosis (53.2%, 95% CI: 28.9 – 77.4%; [Figure 2](#); [Table 2](#)). Among the 5 studies which reported the duration from symptom onset to correct diagnosis, the overall duration of diagnostic delay was 86.9 days (95% CI: 28.0 –145.8; [Figure 3](#); [Table 1](#)). Because Gill et al. was a case series of 4 patients who had all experienced diagnostic delay, we performed a sensitivity analysis excluding Gill et al.<sup>8</sup> in our calculations of diagnostic delay duration and arrived at similar results (86.3 days; 95% CI: 10.5 – 162.1). We performed an additional sensitivity analysis excluding Hingsammer et al.<sup>9</sup> (due to the restrictive inclusion criteria), which increased the overall diagnostic delay duration to 106.5 days (95% CI: 48.8 – 164.2).

Charcot foot was most commonly mistaken for cellulitis or other skin infections, accounting for 34.1% (n=31) of delayed diagnoses ([Table 2](#)). Other common reasons for delay included fractures/sprains of the ankle (19.8%, n=18), deep venous thrombosis (14.3%, n=13), gout (11.0%, n=10), or arthritis (11.0%, n=10).

## 4. Discussion

In this systematic review, we found that over half of cases of Charcot foot were initially misdiagnosed (53.2%), and patients often experienced a long duration from symptom onset to correct diagnosis (86.9 days). Most commonly, Charcot foot was misdiagnosed as an infection (either of the skin or bone), other inflammatory conditions (e.g., gout or arthritis), fractures/sprains, or deep venous thrombosis.

The correct diagnosis of Charcot foot may be challenging, given its relatively low incidence compared to other inflammatory conditions in diabetic feet. The incidence of Charcot foot among all patients with diabetes has been estimated to range from 3-11 per 1000 patients per year<sup>5,16</sup>, although it may be prevalent in up to 7.5% of patients with diabetic neuropathy<sup>17</sup>. Thus, Charcot foot should be on the differential for all patients with long-standing diabetes with neuropathy presenting with an acutely inflamed and swollen foot.

Further, several other pathologies may be mistakenly diagnosed in patients with Charcot. Also, the presence of a foot ulcer on the affected limb presents a diagnostic challenge, as they are a substantial risk factor for both infection and Charcot foot. If the ulcer can be probed to the bone, this favors a diagnosis of osteomyelitis<sup>18</sup>. However, Charcot foot and infections are not mutually exclusive, and Thewjitcharoen et al. found that 48% of patients diagnosed with Charcot foot had a coexisting foot ulcer<sup>14</sup>. When in doubt about a possible diagnosis of Charcot foot, the patient's weight should be promptly offloaded from the affected foot and they should be referred to a foot/ankle specialist to minimize further injury<sup>2,6</sup>.

Given the serious consequences of delayed diagnosis, our finding of prolonged delays in diagnosis further highlights this need for a timely referral. Wukich et al. found that 14% of patients experienced a complication if the diagnosis was delayed by 4 weeks, and two thirds had complications by 8 weeks<sup>15</sup>. In our review we found that patients experienced an average delay of 12.4 weeks (95% CI: 4.0 – 20.9 weeks; [Table 1](#)), suggesting that many patients with Charcot foot may experience preventable complications due to delayed diagnoses.

While the studies in our review were generally moderate to high quality, some biases may exist, reinforcing the importance of reducing delay. Specifically, the retrospective cohorts / case control studies had shorter duration of diagnostic delay than the case series studies. This could reflect a selection bias occurring in the non-case series studies. For example, Hingsammer et al.<sup>9</sup> excluded 36% of their potential patients due to active skin ulcers or lesions and excluded another 17.5% of patients due to missing labs or a lack of MRI and X-rays. While this was certainly appropriate for the aims of their study, this likely biases our results to a lower duration of diagnostic delay (86.9 days in the main analysis vs 106.5 days when excluding Hingsammer et al.). This bias again highlights the need for improved diagnoses.

While a paucity of evidence makes it difficult to determine the true rate of misdiagnosis and delay in diagnosis of Charcot foot in diabetic patients, this systematic review nevertheless establishes that the misdiagnosis is very common and treatment is often delayed.

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### **Author Contributions**

All authors have approved the final manuscript. G.K. and H.R. have contributed equally.

#### **Per CRediT taxonomy:**

J.T. – Conceptualization, Investigation (data collection), Data curation, Writing – review & editing

R.J. – Conceptualization, Investigation (data collection), Writing – review & editing

G.K. – Methodology, Data curation, Validation, Writing the original draft, Writing – review & editing

H.R. – Methodology, Data curation, Validation, Formal analysis (supervised by D.J.), Writing the original draft, Writing – review & editing

D.J. – Conceptualization, Methodology, Writing – review & editing, Supervision

### **Declaration of Competing Interest**

The authors declare no conflict of interest.

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## Tables

**Table 1**

Author, Year	Design [Country]	Cases / patients	Age $\pm$ SD (years)	Male sex (%)	T2DM (%)	Years of diabetes	Trauma history (%)	Diagnostic delay duration $\pm$ SD [range]
Pakerinen et al., 2002 <sup>11</sup>	Case series [Finland]	36 cases 32 patients	NR	22 (68.8%)	19 (59.4%)	19.9	8 (22.2%)	203 $\pm$ 224 days [1 - 164 weeks]
Hingsammer et al., 2016 <sup>9</sup>	Retrospective cohort [Switzerland]	42 patients	48.2 $\pm$ 9.4	36 (85.7%)	42 (100%)	NR	12 (28.6%)	12 $\pm$ 11.5 days [2 - 48 days]
Gill et al., 2004 <sup>8</sup>	Case series [NR]	4 patients	52.0 $\pm$ 19.6	3 (75.0%)	2 (50%)	15.3	3 (75%)	97.5 $\pm$ 56.8 days [2 - 6 months]
Myerson et al., 1994 <sup>12</sup>	Case series [United States]	89 cases 68 patients	54	28 (41.2%)	NR	NR	19 (21.3%)	NR
Chantelau, 2005 <sup>13</sup>	Case-control [Germany]	24 patients	55.2 $\pm$ 10.9	13 (54.2%)	16 (66.7%)	20.7	12 (50.0%)	103.0 $\pm$ 73.3 days [0.5 - 12 months]
Thewjitcharoen et al., 2018 <sup>14</sup>	Retrospective cohort [Thailand]	40 patients	58.7 $\pm$ 10.2	16 (40.0%)	38 (95%)	18.0	35 (87.5%)	NR <sup>†</sup>
Wukich et al., 2011 <sup>15</sup>	Retrospective cohort [United States]	22 cases 20 patients	56.3	NR	NR	NR	NR	50.6 $\pm$ 34.0 days [NR]
<b>Weighted Totals</b>		257 cases 230 patients	54.1 years n = 198	118 / 210 (56.2%)	117 / 142 (82.4%)	19.1 years n = 100	89 / 235 (37.9%)	86.9 days (95% CI: 28 – 145.8) n = 128 cases

**Table 1 caption:** Study characteristics of included studies. The grand totals in the bottom row are weighted to the number of patients for all variables except trauma history, which is weighted to the number of cases. Diagnostic delay duration is the number of days from symptom onset until correct diagnosis of Charcot foot.

*Abbreviations:* T2DM = Type 2 diabetes mellitus; NR = Not reported

† Thewjitcharoen et al. did report a range of 2 - 12 months



**Table 2**

Author, Year	Delayed diagnosis cases (%)	Cellulitis	Osteomyelitis	DVT	Fracture or Sprain	Gout	Arthritis	No diagnosis	Other
Pakerinen et al., 2002 <sup>11</sup>	22 / 36 (61.1%)	10 <sup>a</sup>	- <sup>a</sup>	5	2	4	5	-	4 <sup>a</sup>
Hingsammer et al., 2016 <sup>9</sup>	11 / 42 (26.2%)	5	-	3	-	2	-	1 <sup>b</sup>	-
Gill et al., 2004 <sup>8</sup>	4 / 4 (100%)	1	-	2	1	1	-	-	-
Myerson et al., 1994 <sup>12</sup>	22 / 89 (24.7%)	5 <sup>c</sup>	-	-	2	2	2	9	2 <sup>d</sup>
Chantelau, 2005 <sup>13</sup>	19 / 24 (79.2%)	6	4	3	11	-	2 <sup>e</sup>	-	3 <sup>f</sup>
Thewjitcharoen et al., 2018 <sup>14</sup>	13 / 40 (32.5%)	4	5	-	2	1	1	-	-
Wukich et al., 2011 <sup>15</sup>	21 / 22 (95.5%)	NR	NR	NR	NR	NR	NR	NR	NR
<b>Totals</b>	53.2% (95% CI: 28.9 - 77.4%) <sup>g</sup>	31	9	13	18	10	10	10	9

**Table 2 caption:** Reasons for misdiagnosis of Charcot foot. The row-wise counts may not sum to 100% because patients could contribute to more than one category in some studies.

*Abbreviations:* DVT = Deep venous thrombosis; NR = Not reported

a Four patients in Pakerinen et al. had “unspecified inflammation / osteomyelitis / tumor”

b One patient “did not seek prior medical care”

c Five patients’ conditions were “attributed to infection”

d One patient was misdiagnosed with “venous insufficiency” and one patient was diagnosed with “a tumor”

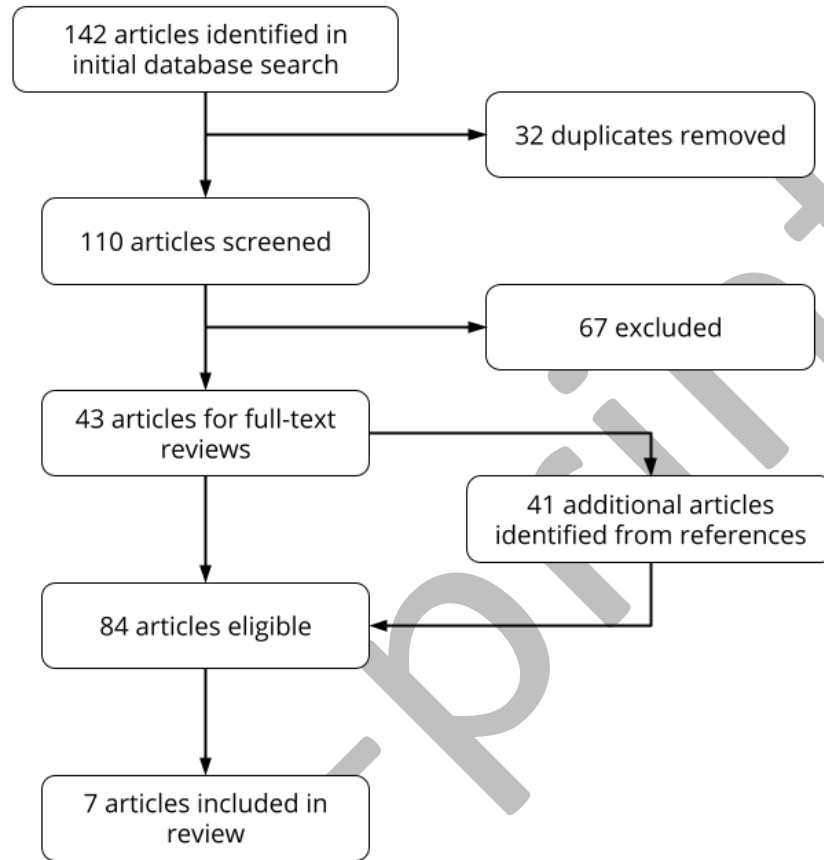
e Two patients were diagnosed with “rheumatoid arthritis” (vs osteoarthritis or arthritis)

f Three patients were diagnosed with “Sudeck atrophy” (also known as complex regional pain syndrome)

g The four cases from Gill et al. were excluded from this calculation because it was a case series of exclusively of patients with delayed diagnosis

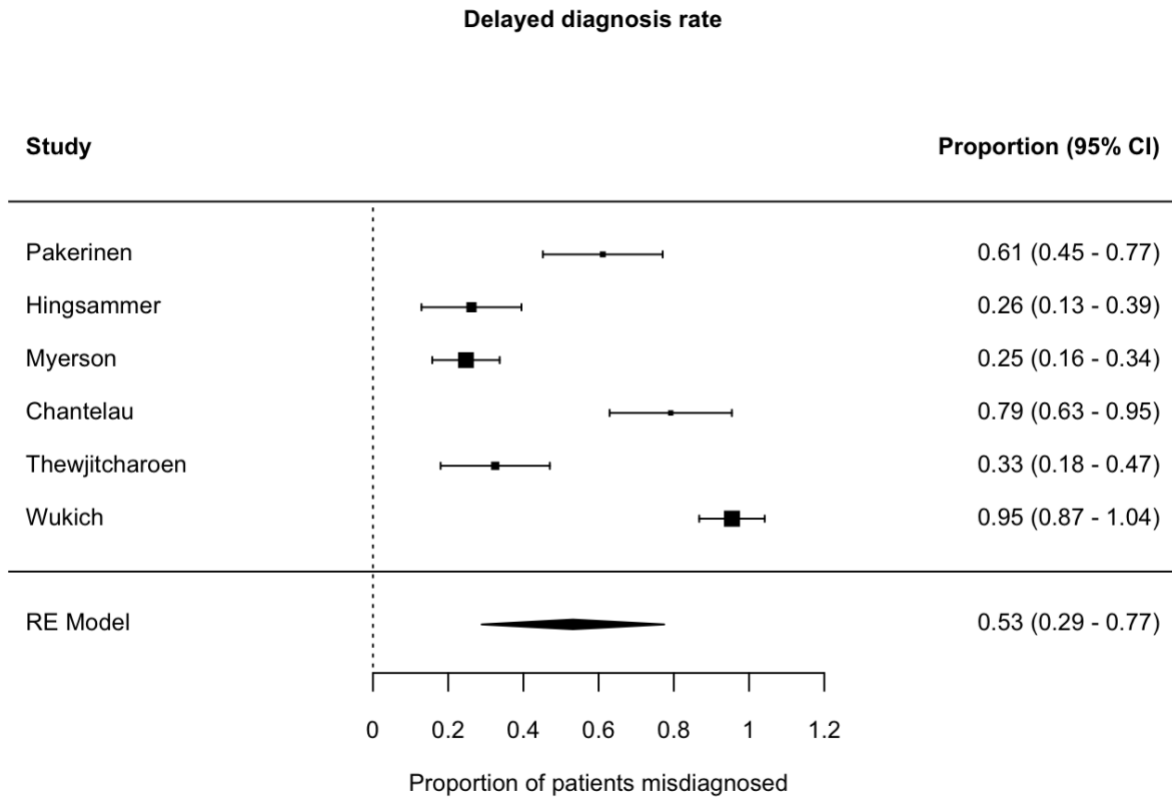
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Figures  
**Figure 1**



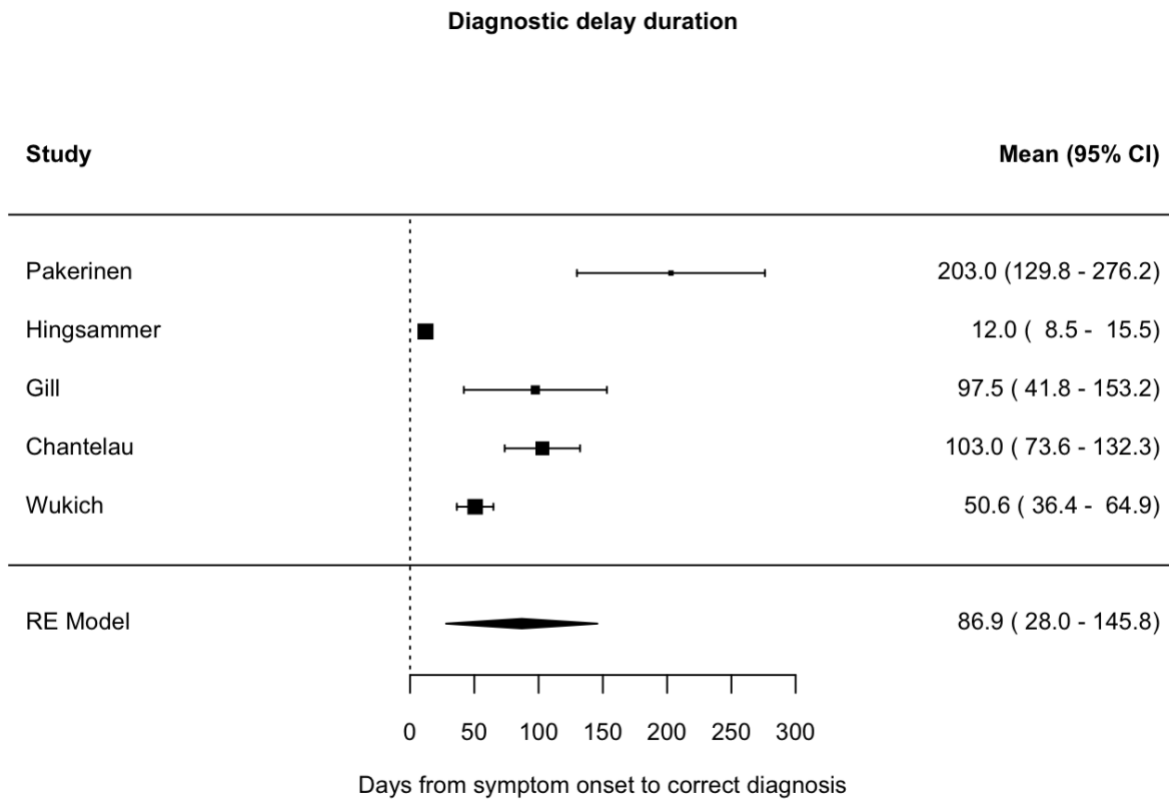
**Figure 1 caption:** Study flow diagram detailing study selection.

**Figure 2**



**Figure 2 caption:** Forest plot for the proportion of patients initially misdiagnosed. Point estimates are indicated by the squares with 95% confidence intervals (CI) represented by the error bars. Each square's size is proportional to the precision weight of the study in the meta-analysis. The black diamond at the bottom indicates the summary effect size in the random-effects model (RE model).

**Figure 3**



**Figure 3 caption:** Forest plot for the duration from symptom onset until correct diagnosis, in days. Point estimates are indicated by the squares with 95% confidence intervals (CI) represented by the error bars. Each square's size is proportional to the precision weight of the study in the meta-analysis. The black diamond at the bottom indicates the summary effect size in the random-effects model (RE model).

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## Supplemental material

### **Supplemental Table 1**

Query purpose	Query text
Charcot	(MH "Arthropathy, Neurogenic") OR "charcot neuropathic osteoarthropathy" OR "charcot foot" OR "charcot joint"
Diagnostic error	(MH "Diagnostic Errors+") OR "misdiagnosis" OR "incorrect diagnosis"
Antibiotics	(MH "Antibiotics+") OR ((anti-bacterial or anti bacterial or bacteriocid* or anti-mycobacterial or anti mycobacterial) N2 (agent* or compound*))
Full query	Charcot <b>AND</b> (Diagnostic error <b>OR</b> Antibiotics)

**Caption:** Outline of the search query used.

**Abbreviations:** MH = Medical Subject Headings; N2 finds the words if they are within two words of one another regardless of the order in which they appear