



Prevalence Rates of Myotonic Dystrophy Type 1 (DM1) in 9 Countries: A Systematic Literature Review and Meta-Analysis

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INTRODUCTION

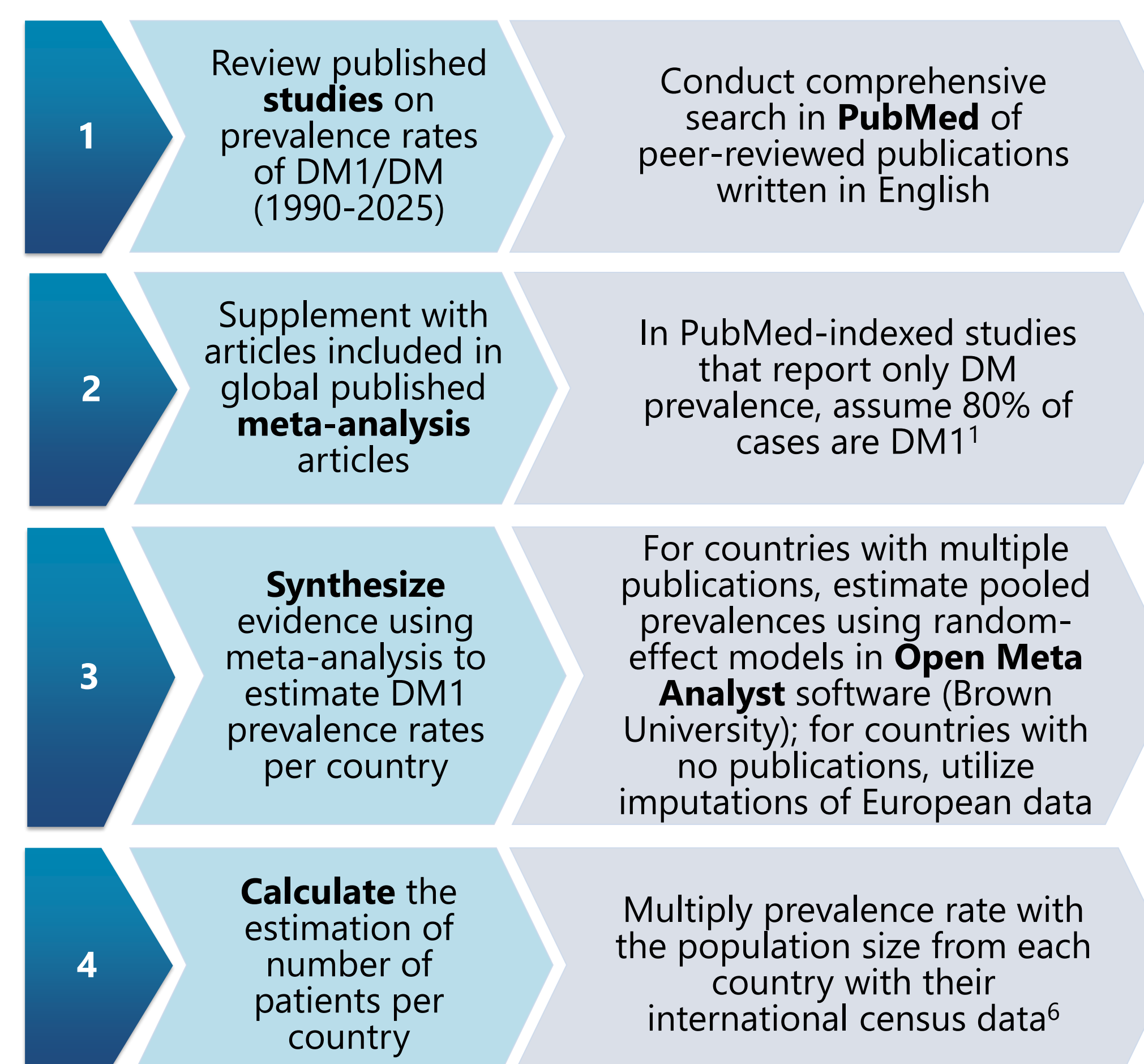
- Myotonic dystrophy type 1 (DM1) is a rare, inherited neuromuscular disease with no approved treatment
 - DM1 is a form of myotonic dystrophy and represents the majority (≈80%) of diagnoses¹
- Individuals with DM1 and caregivers may experience substantial decrement in health-related quality of life²
- Although myotonia is a hallmark symptom of the disease, DM1 is a multisystemic disease impacting cardiac, pulmonary, gastrointestinal, and ocular systems, among others
- Life expectancy for individuals with DM1 ranges from 48 to 55 years, showing a shortened lifespan vs the general population³
- Cardiac-related deaths are common among individuals with DM1, and respiratory failure is the leading cause of death in adult-onset DM1^{4,5}
- As a rare disease lacking approved disease-modifying therapies, the epidemiology of DM1 remains incompletely characterized

OBJECTIVE: To summarize and estimate the prevalence rates of DM1 in 9 countries (United Kingdom, Italy, Spain, Germany, France, Canada, the United States, Japan, and Israel) based on published literature

METHODS

- A systematic literature review and meta-analyses were performed (Figure 1)^{1,6}

Figure 1. Research Methodology

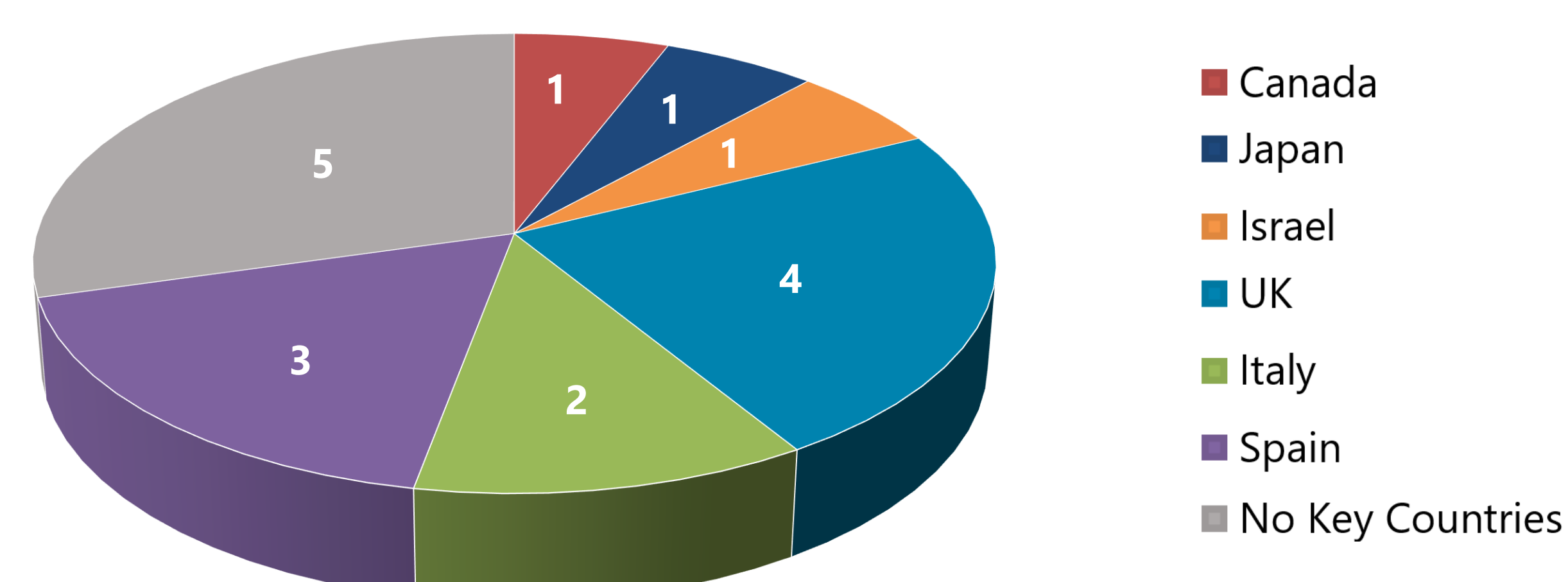


- The random-effect model was used for prevalence as the model had $I^2 > 25\%$, thereby indicating heterogeneity

RESULTS

- 18 country-specific studies and 2 meta-analyses were abstracted and summarized:
 - 4 (UK),⁷⁻¹⁰ 2 (Italy),^{11,12} 3 (Spain),¹³⁻¹⁵ 1 (Israel)¹⁶
 - Studies were identified for Norway, Sweden, Croatia, Serbia, and Finland, all of which were utilized for imputations (Figure 2)¹⁷⁻²¹
- Several key countries did not report DM1 prevalence rates (Figure 2)
 - There were no public data from articles in Germany and France, and there was an underestimation of patients in Japan
 - The United States only had a birth rate study²²; as this reported on incidence, it was excluded due to its lack of focus on prevalence

Figure 2. Studies per Country



- Reported prevalence rates of DM1 varied by region and country (Table 1)^{7-21,23}
- Some regions had significantly higher prevalence rates reported due to the founder effect (eg, Quebec, Canada; Navarre, Spain)^{15,24}

Table 1. Reported DM1 Prevalence Rates by Country

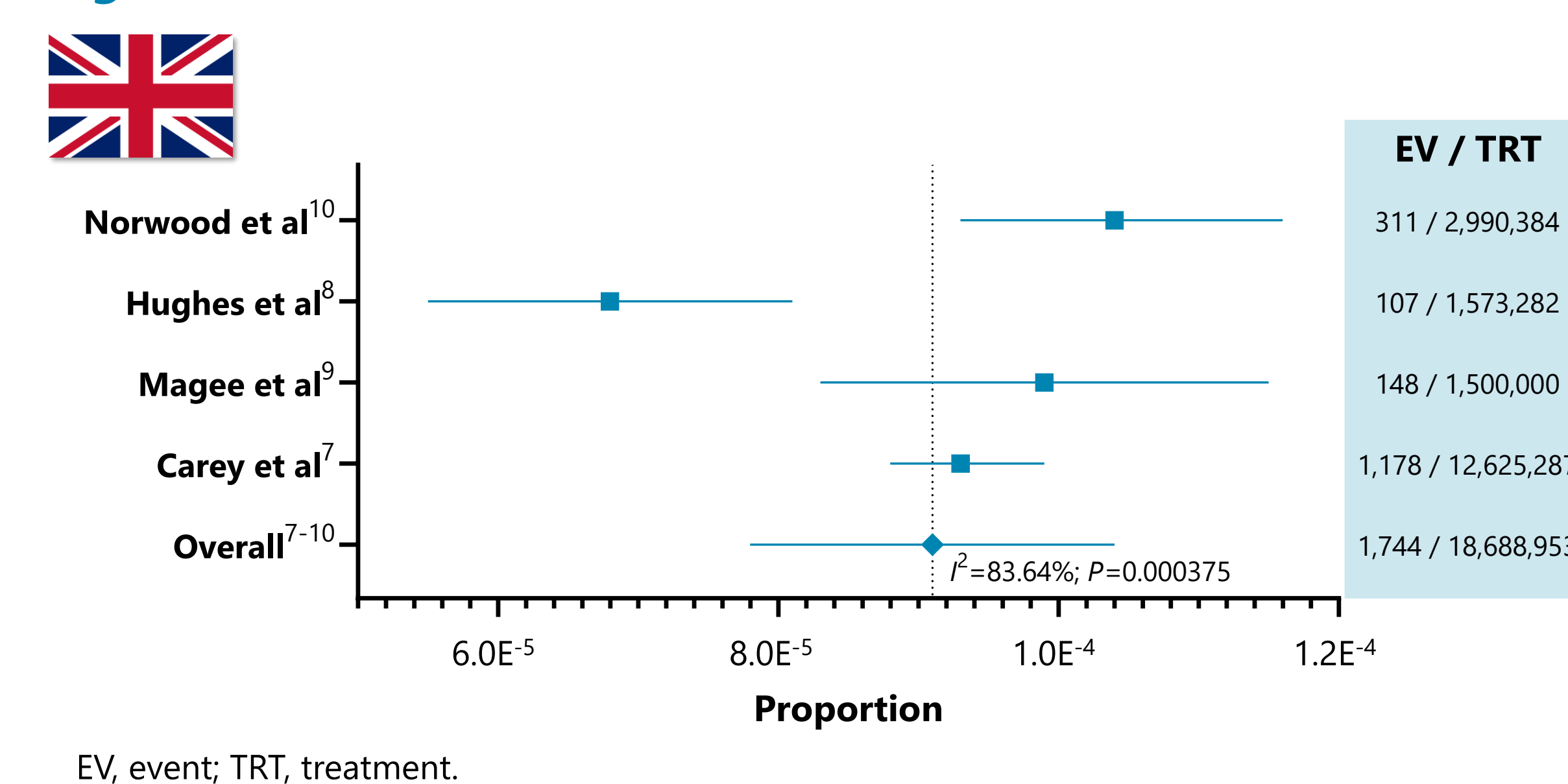
Country	Rate per 100,000
	10.4 ¹⁰
	8.4 (DM) ⁸
UK	12.0 (DM) ⁹
	9.9 (calculated DM1) ⁹
	9.37
	9.7 ¹²
Italy	9.3 (DM) ¹¹
	7.4 (calculated DM) ¹¹
	14.4 ¹³
	35.9 ¹⁵
Spain	26.5 (DM) ¹⁴
	21.2 (calculated DM1) ¹⁴
	9.1 (DM) ²³
Japan	7.3 (calculated DM1) ²³
	15.7 (DM) ¹⁶
Israel	12.6 (calculated DM1) ¹⁶
Canada	158.0 ²⁴
Norway	10.8 ¹⁷
Sweden	17.8 ¹⁸
	16.1 (DM) ¹⁹
Croatia	12.9 (calculated DM1) ¹⁹
Serbia	6.3 ²⁰
Finland	36.3 ²¹

DM, myotonic dystrophy; DM1, myotonic dystrophy type 1.

- For countries with no available data, imputations were used with the European articles meeting study criteria, including 5 articles not from key countries that were included in European global meta-analysis articles
- Imputations were performed for Germany, France, Canada, the United States, and Japan
 - Canada had evidence of the founder effect in the Saguenay-Lac-Saint-Jean, QB, region, with the highest prevalence rate in the world (158/100,000)^{24,25}
 - The effect did not apply to the entire country, and European data were used to impute the estimated prevalence rate
- One Japanese study met study criteria²³; however, based on its region in Okinawa, a smaller region in the south, it was not determined to be representative of the DM1 rate in Japan
 - Japan's prevalence rate was supplemented with the European meta-analysis

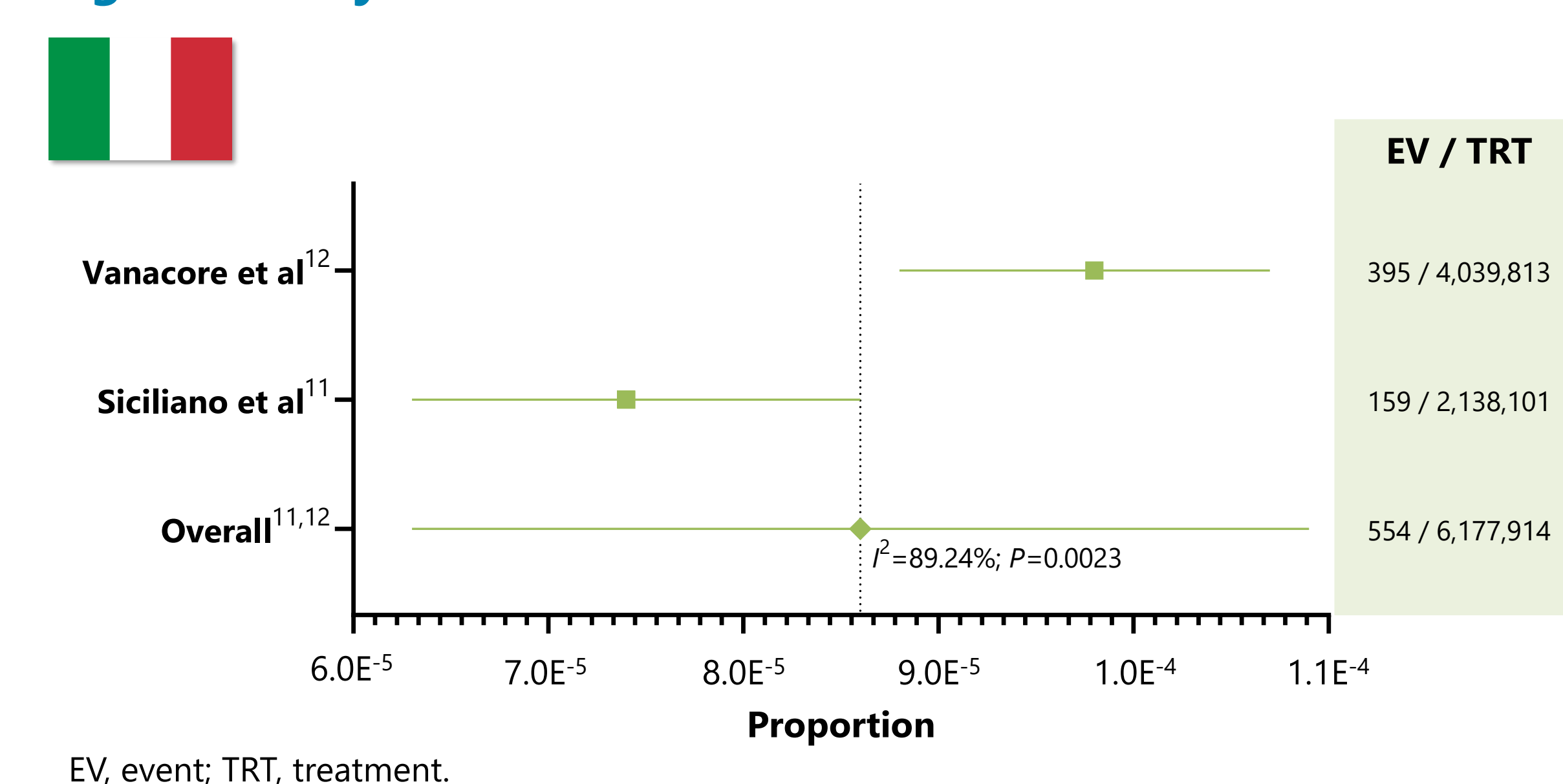
- The estimated overall prevalence rate in the United Kingdom was 9.1/100,000 (95% CI: 7.8-10.4) (Figure 3)⁷⁻¹⁰

Figure 3. UK Prevalence Rate



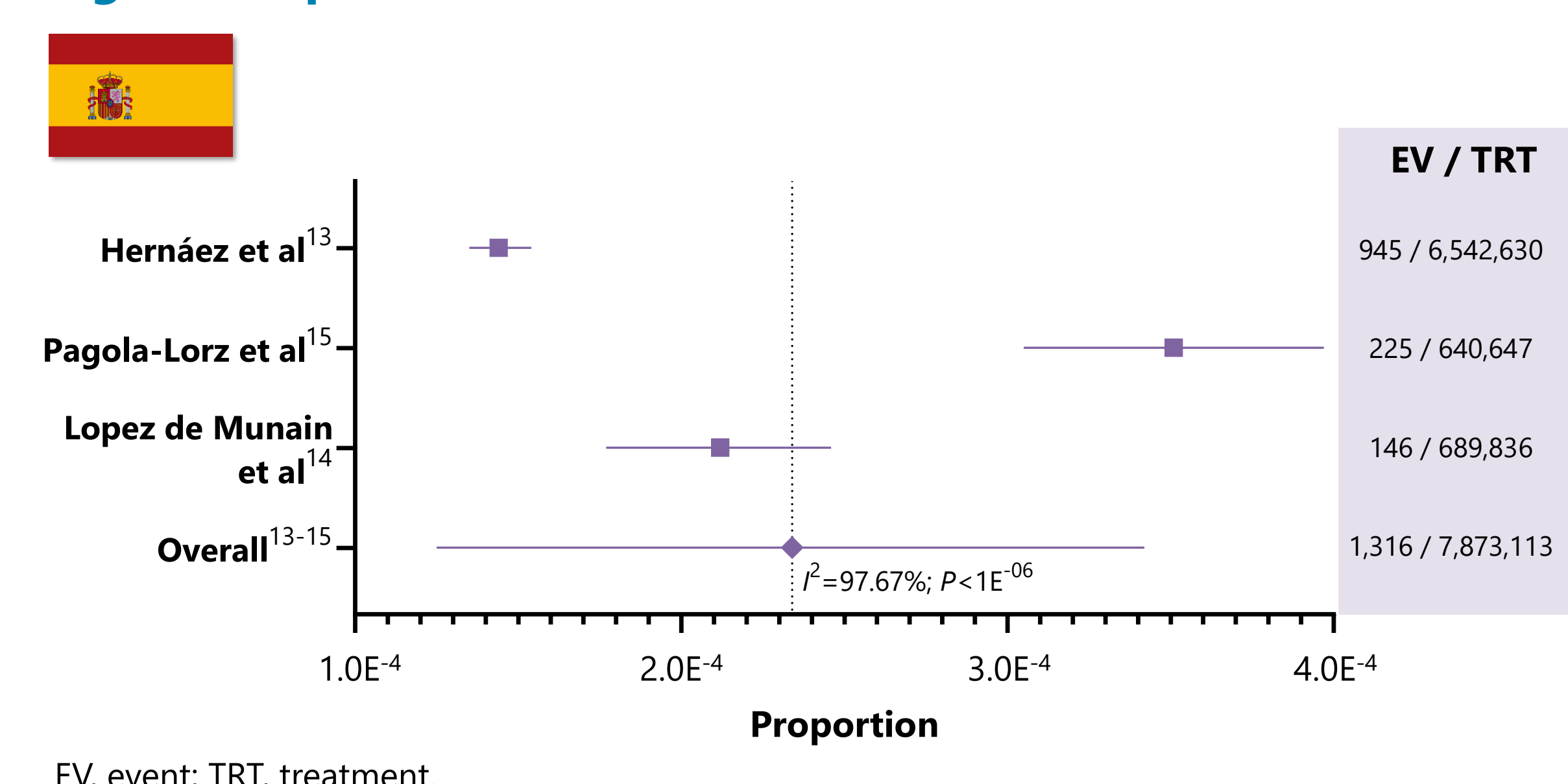
- The estimated overall prevalence rate in Italy was 8.6/100,000 (95% CI: 6.3-10.9) (Figure 4)^{10,11}

Figure 4. Italy Prevalence Rate



- The estimated overall prevalence rate in Spain was 23.4/100,000 (95% CI: 12.5-34.2) (Figure 5)¹³⁻¹⁵

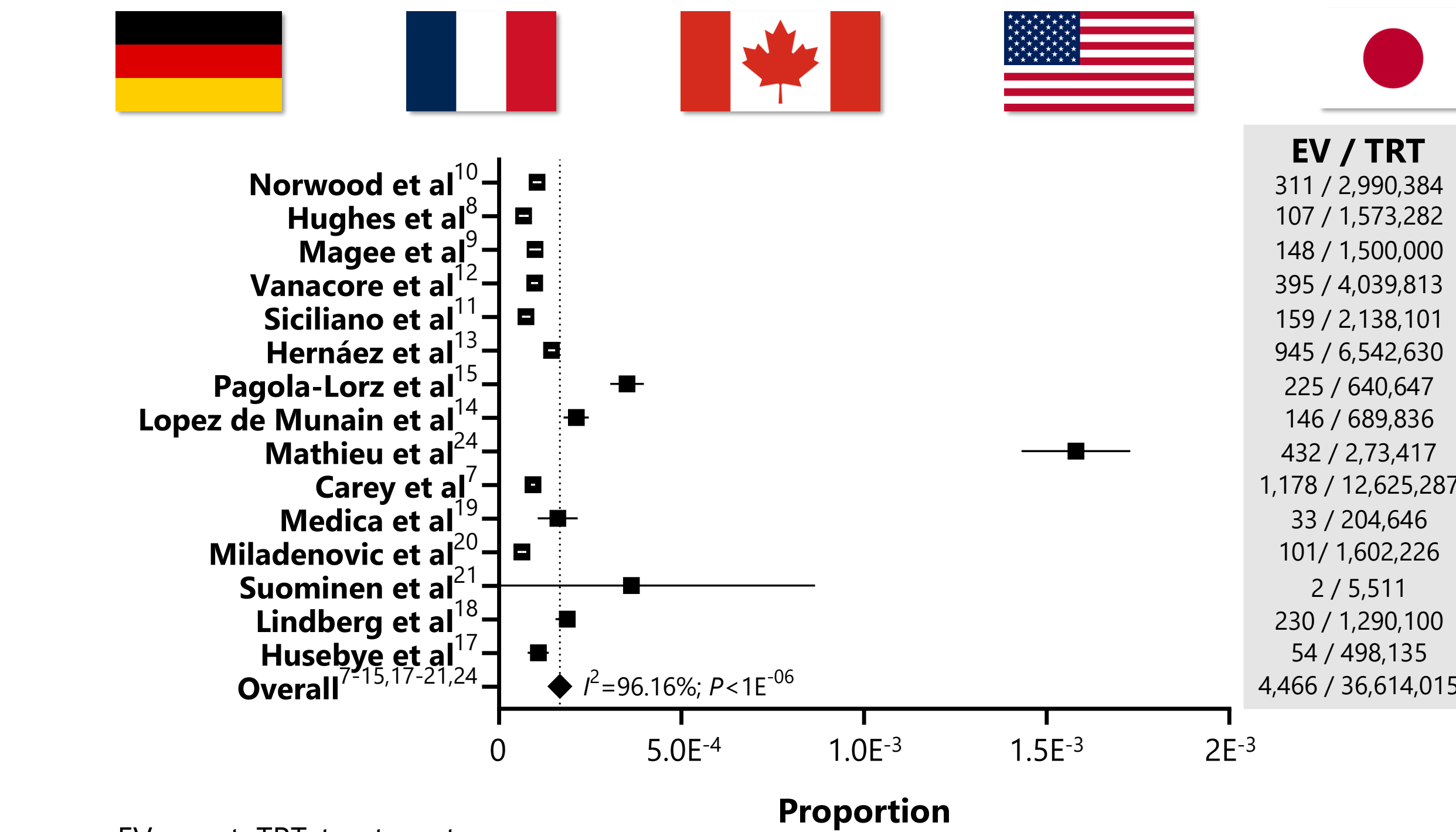
Figure 5. Spain Prevalence Rate



- The estimated prevalence rate for Spain was higher than those observed in Italy and the United Kingdom

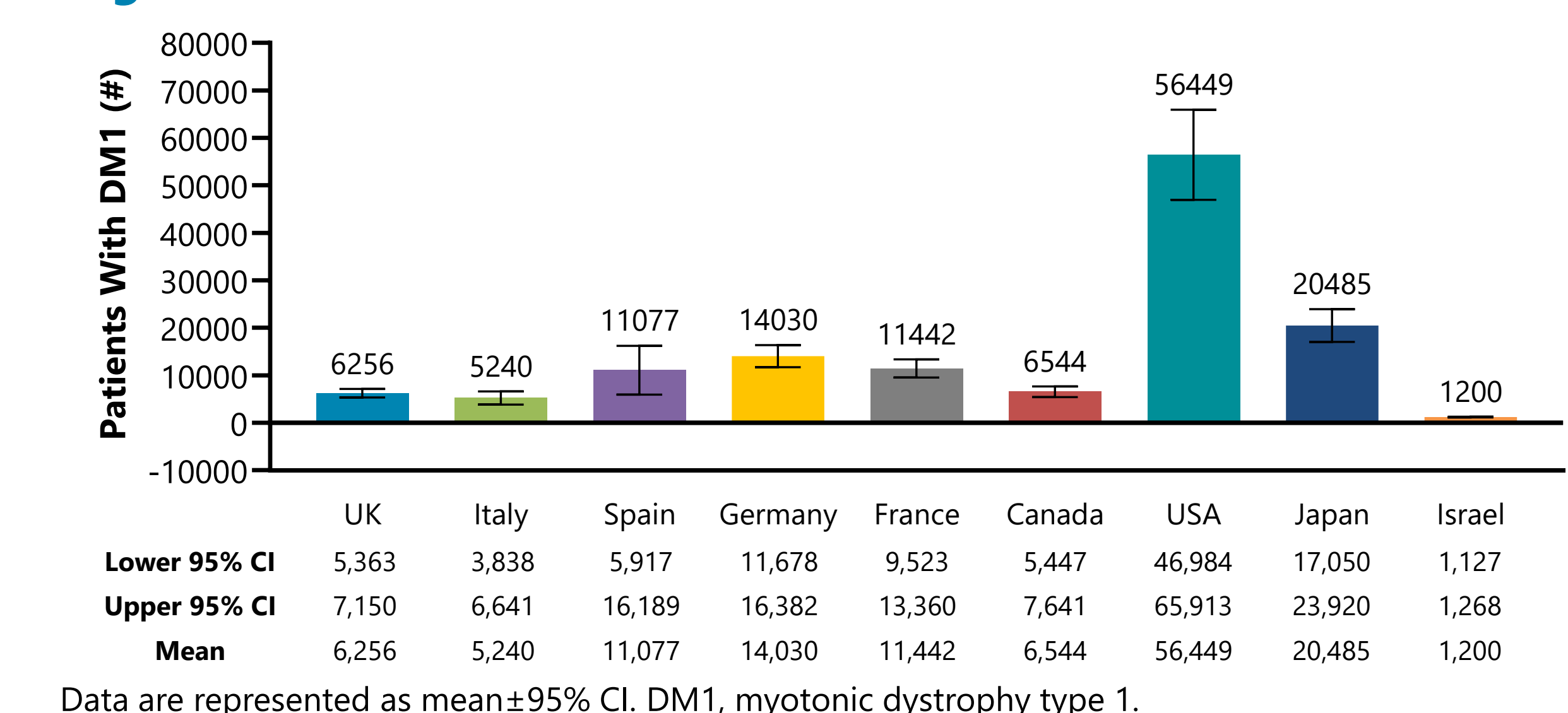
- Estimated overall prevalence rate for Germany, France, Canada, the United States, and Japan was 16.7/100,000 (95% CI: 13.9-19.5) (Figure 6)^{7-15,17-21,24}

Figure 6. Germany, France, Canada, United States, and Japan Prevalence Rates



- The United States had the largest estimated number of patients (56,449); conversely, Israel had the smallest number (1,200) (Figure 7)

Figure 7. Estimated Numbers of Patients With DM1



Data are represented as mean±95% CI. DM1, myotonic dystrophy type 1.

LIMITATIONS

- Only English-language literature was searched, and the study was limited to 9 countries
- Additional scenario analyses should be conducted following different imputation methods and with different assumptions

CONCLUSIONS

- Data on DM1 prevalence rates are sparse and highly heterogeneous across countries/regions
- All articles meeting inclusion criteria reported combined adult and pediatric cases
 - Future research with more detailed estimation separating pediatric from adult cases is needed
- Additional studies leveraging databases or modeling methods need to be conducted to better estimate accurate DM1 prevalence rates

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DISCLOSURES

SR, ZC: Employees of Avidity Biosciences, A Novartis Company.

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