



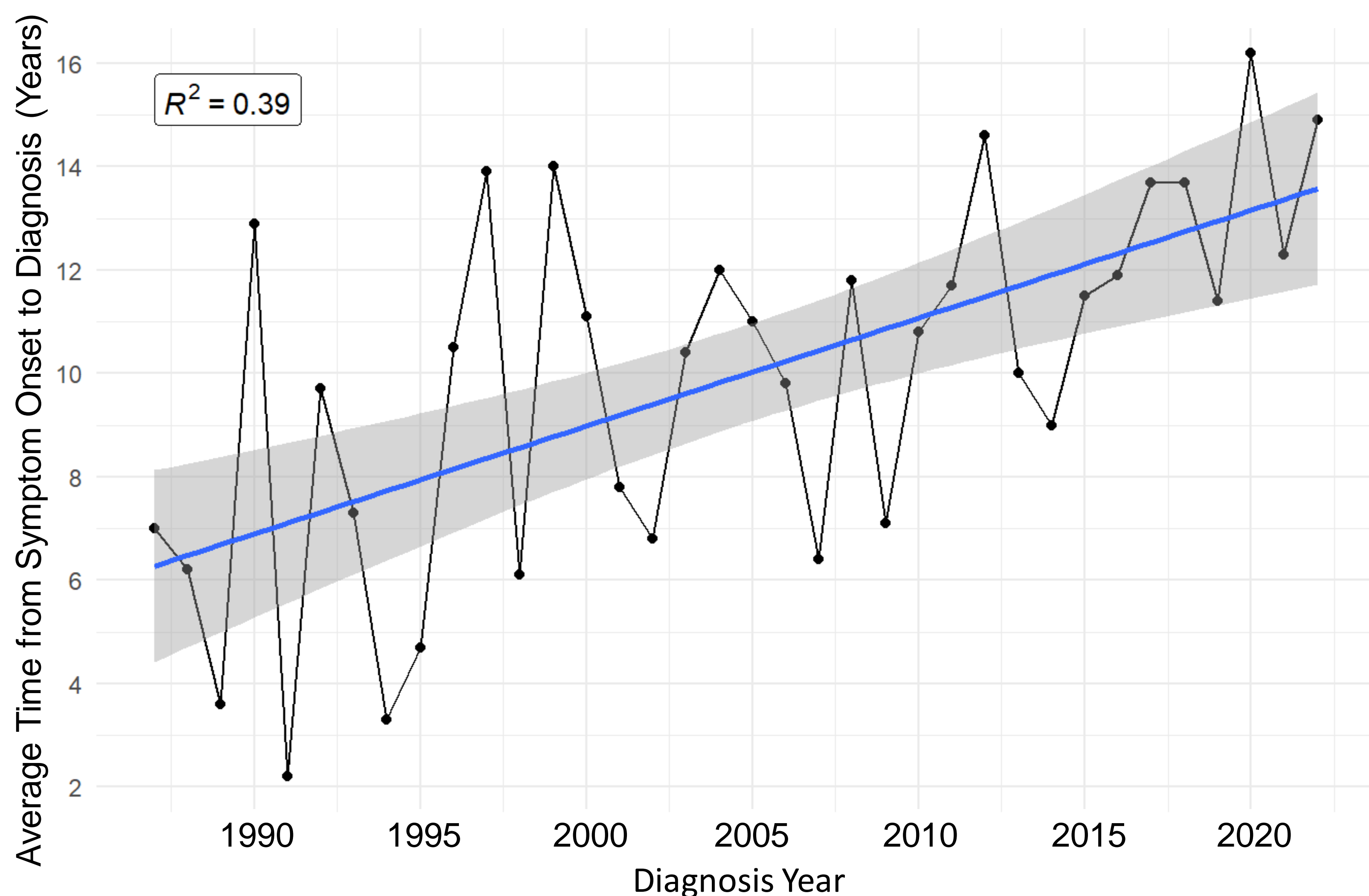
## BACKGROUND

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a chronic, complex, heterogenous disease that affects millions and lacks both diagnostics and treatments. Many physicians find it difficult to diagnose. Evidence suggests that ME/CFS is frequently misdiagnosed, with a lack of confidence and the absence of established diagnostic markers cited as primary reasons. We aim to assess whether the average time from symptom onset to a physician diagnosis has changed over time.

## METHODS

Participants of the You + ME Registry with a reported clinical diagnosis of ME/CFS from a healthcare provider (HCP) were included in this analysis. We calculated the average and median time from when participants reported that they first started to experience ME/CFS-related symptoms to the time that they were given an HCP diagnosis. To understand whether certain types of triggers are correlated with a shorter time-to-diagnosis, we assessed time-to-diagnosis according to self-reported triggering event.

**Figure 1:** Average time in years from symptom onset to ME/CFS diagnosis by diagnosis year



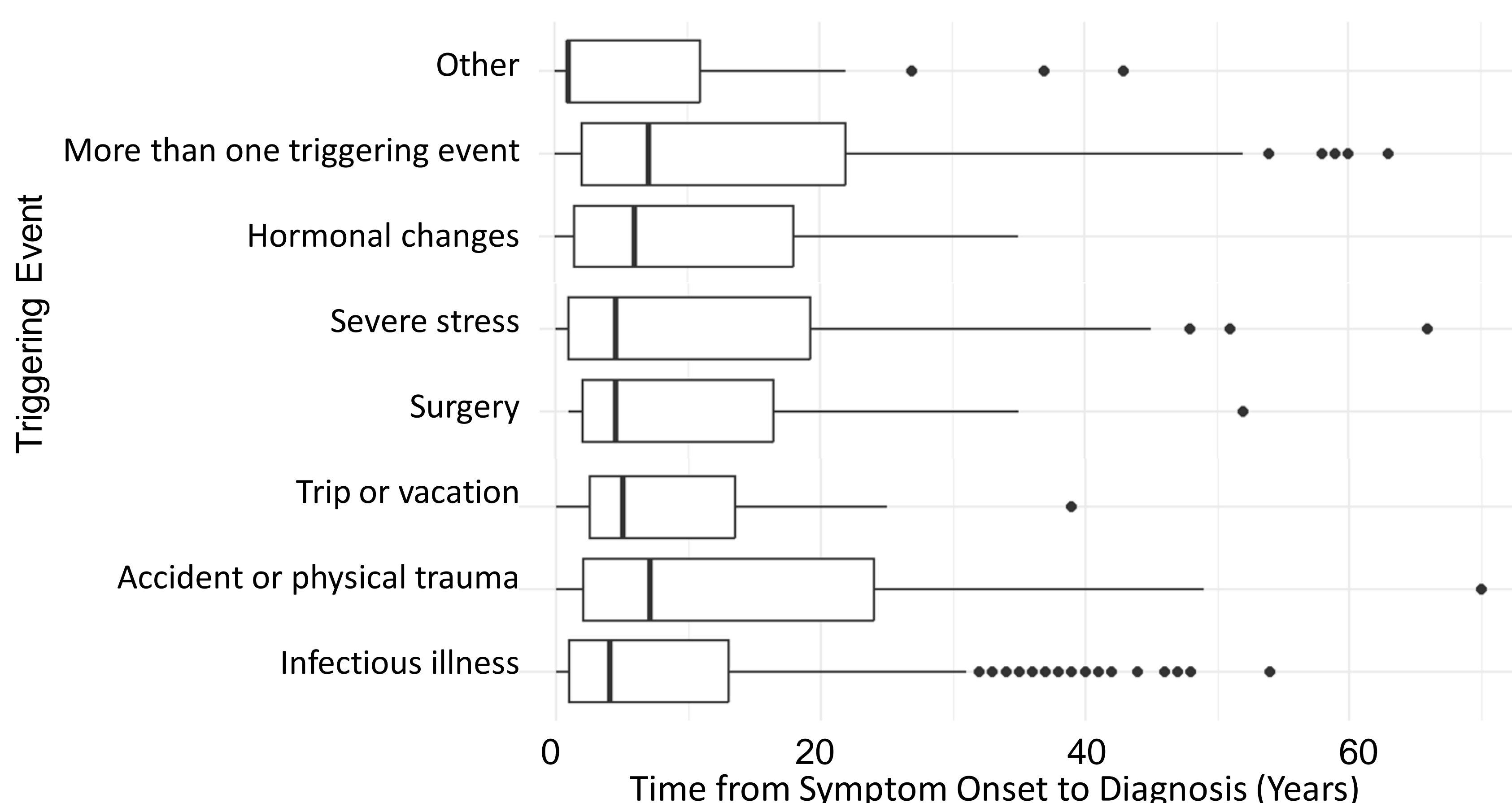
## RESULTS

Our results start in 1987, the first year that at least 10 registry participants were diagnosed, and end in 2022. In 1987, 20 participants were diagnosed with ME/CFS with an average of 7.0 years and a median of 1.5 years to diagnosis. In 2022, 76 participants were diagnosed with an average of 14.9 years and a median of 12.0 years to diagnosis. In 1991, we see the lowest average amount of time to diagnosis, with an average of 2.2 years and a median of 1.5 years. In 2020, we see the highest average amount of time to diagnosis, with an average of 16.2 years and a median of 12.0 years. Plotting the average time to diagnosis each year (Figure 1), we see an upward trend ( $R^2=0.39$ ) suggesting that time-to-diagnosis increased over the time period of study. When looking at the average time-to-diagnosis by triggering event (Table 1, Figure 2), participants reporting an infectious illness experienced the shortest time-to-diagnosis, while participants reporting an accident or physical trauma experienced the longest time-to-diagnosis. Most participants report more than one triggering event.

**Table 1:** Time from symptom onset to diagnosis by triggering event

Triggering Event	Average time from symptom onset to diagnosis (years)	Median time from symptom onset to diagnosis (years)	Number of participants
Infectious illness	9.0	4.0	391
Accident or physical trauma	15.7	7.0	17
Trip or vacation	10.4	5.0	11
Surgery	11.0	4.5	18
Severe stress	12.4	4.5	74
Hormonal changes	11.1	6.0	11
More than one triggering event	13.1	7.0	699
Other	7.2	1.0	41

**Figure 2:** Time from symptom onset to ME/CFS diagnosis by triggering event



## DISCUSSION

Counterintuitively, between 1987 and 2022, we saw an overall increase in the average time-to-diagnosis for You + ME ME/CFS Registry participants. We hypothesize that several factors might explain this unexpected result. The 1980s and 1990s were a period of dramatic healthcare transformation in the United States where most registrants reside. During this time, fee-for-service plans were commonly replaced by prepaid and other health plans that used primary care gatekeepers. Plans that rely on a gatekeeper to access specialty care naturally increase the time to diagnosis. Additionally, it's possible that selection bias took place in the Registry whereby people who were diagnosed in the 80s and 90s knew they had ME/CFS and were more likely to be recruited. Other factors could include the changing of ICD-9 and SNOMED codes over time, which made diagnosis more specific and restrictive; confusion from HCPs due to the newly developed and arguably vague CDC-1994/Fukuda case definition, as well as the Canadian Consensus Criteria in 2003 and the Institute of Medicine case definition in 2015; the use of the internet to better understand one's own symptoms and disease leading to self-diagnosis; initial attention in the mid-1980s from the medical communities and the general public that then turned into a dismissiveness of the disease in the 90s; high profile events like the Incline Village outbreak that meant people could reflect back and pinpoint any interaction with their HCP without actually receiving a diagnosis; and an impact from ME/CFS specialists retiring/dying in the last 5 years creating an increased demand on those few specialists that were left.