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The study by Pourmemari et al.<sup>1</sup> provides a comprehensive assessment of the annual incidence, prevalence and risk factors for carpal tunnel release (CTR) in Finland. The study demonstrates once again that CTR (and by inference, underlying carpal tunnel syndrome (CTS)) is common, and also confirms many of the risk factors that have been identified in previous studies, such as age, female sex, obesity and certain underlying medical conditions. Nevertheless, the study also raises (directly or indirectly) a number of persistent and challenging questions that are common in the CTS/CTR literature.

Despite CTS being the most common nerve entrapment disorder and CTR one of the most common surgical procedures, it is surprisingly difficult to come up with an accurate estimate of the incidence or prevalence of CTS.<sup>2 3 4 5</sup> CTS is a clinical syndrome without a clear gold standard to use in establishing the diagnosis. The clinical symptoms are often not classic in their presentation, and verification with nerve conduction testing or ultrasound imaging do not have the high sensitivity and specificity that is desirable. <sup>2 6 7</sup> Part of the problem with confirming CTS with electrophysiology or imaging is the lack of a gold standard and part of the issue stems from a changing awareness of CTS from a time of under diagnosis to perhaps over diagnosis and/or earlier recognition.

The use of carpal tunnel release surgery as a diagnostic standard, as done in the accompanying manuscript by Pourmemari et al.<sup>1</sup>, creates a gold standard that is objective but does not necessarily clarify the incidence or prevalence of the underlying diagnosis of CTS. The rate of surgical intervention varies regionally (both between and within the countries) and has changed over time as well. The surgical rates in the United Sates are reported as 3-4 times higher than in Germany or Canada.<sup>8</sup> Other studies have reported rates in the US that are comparable to those in Europe.<sup>4</sup> Rates of surgery for CTS

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were found to vary among regions by 3.5-fold in the State of Maine. (5) Rates of surgery for CTS in France were found to vary regionally by a factor of 5.<sup>9</sup>

It is not clear what influences the decision to have CTR. The only randomized control trial that looked at surgery versus conservative care (splinting) found that surgical intervention was more effective.<sup>10</sup> In our experience, many clinicians use these findings to justify surgery as a first line, early intervention for CTS. At the same time the study did demonstrate the effectiveness of splinting in 65% of patients so many adopted a conservative approach as the first line of intervention, with surgery being considered only in those patients failing a trial of conservative care. The Gerritsen paper<sup>10</sup> was done prior to the widespread use of steroid injections as another non-surgical option. There have been several randomized controlled studies comparing CTR and steroid injection demonstrating that the steroid injection can be as effective as CTR although the procedure may need to be repeated. <sup>11 12</sup> What is frequently ignored in the discussion is the recurrence rate of symptoms after CTR which can be as high when there is long term follow-up.<sup>13 14</sup>

The demographic profile of the Finnish study population is strikingly different than the profile of the US population in terms of some important risk factors for CTS. It has been long recognized that obesity is a risk factor for CTS and more profoundly for focal prolongation of the median nerve latency across the wrist (median mononeuropathy) regardless of symptoms.<sup>15 16 17</sup> This is particularly striking in view of the impact of obesity on other sensory nerves. All other sensory nerves demonstrate improved function with obesity but the median sensory latency across the wrist is more prolonged with increasing levels of obesity and there is a strong dose effect.<sup>15 18</sup>

The percentage of obese subjects (BMI≥30) in the Finland study was 22% compared with an estimated rate of 38% in the US.<sup>19</sup> The hazard ratio (HR) for obesity was 1.6 in the current study and ranges from 2-4 in studies in the US. The lower rate of obesity in Finland likely impacts the incidence rate of CTS and

would certainly lead to a higher estimate of CTS incidence in the US. Similarly diabetes is an established risk factor for CTS in many studies, and although the current study did not find it to be a significant risk factor, the trend in this study was in the same direction and may be an issue of the statistical power of the current study due to the relatively low rate of diabetes in the sample. In the current study from Finland, the rate of diabetes was 5.5 % compared to an estimated 12.2% in the US.<sup>20</sup> The HR for diabetes has been estimated to be 2-3 for most US studies. The much higher rates of obesity and diabetes in the US would suggest a much higher rate of incident CTS in the US compared to the rates in Finland.

The influence of gender was confirmed by the current study and has been estimated to be as high as a 3 to 4 fold increase for women. This relationship varies depending upon the population under study. Several work-related CTS studies demonstrate a much less pronounced influence among active workers.<sup>17 21</sup> In the work-related CTS studies the relative risk is 1.2 for women and may reflect a younger cohort. It is primarily older women that have the highest risk, which may be related to post-menopausal hormonal changes. The present study reported that "lifetime prevalence" of CTR peaked at ages 50-59, which is somewhat strange since lifetime prevalence of irreversible conditions should typically increase monotonically with increasing age. The authors suggest that the decline in lifetime prevalence among those age 60 and older may be due to survivorship bias and recall bias.

Of the risk factors that influence incidence of CTS, many differ when comparing results from Finland and the United States whereas some are concordant. The influence of age, gender and occupational risk factors are similar while obesity, diabetes and rate of surgical intervention vary widely. We must be careful when reviewing the current literature regarding incidence and prevalence rates from differing studies. There are only a few true population-based studies of the incidence/prevalence of CTS (or CTR,) and the Pourmemari et al.<sup>1</sup> study is an important addition to the literature. Some population based

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studies are regional within a county such as the Gelfman study<sup>4</sup> based upon Olmstead County in Minnesota, which can reflect regional differences in obesity, surgical rates, occupational risks and age stratification. It has been noted that CTS is more common in the elderly and that the rate of surgical intervention for CTS also increases in the elderly.<sup>4</sup> Occupational risks also vary widely between countries and have regional differences within countries. The relative risk for CTS in the US for high force/high repetition jobs was estimated at 15 fold in the 1980s but now is closer to a 2 fold increase in high risk jobs (compared to low force/low repetition jobs).<sup>22 23</sup> This likely reflects the ergonomic changes in the US workplace to eliminate or modify very high risk jobs and distribute the ergonomic risk factors more evenly across the assembly line. The relative risk for CTS is still very high in certain job categories and some low and middle income countries, similar to the high relative risk noted by Silverstein et al. in the US 30 years ago.<sup>24</sup>

With these issues in mind, we need more population-based studies to better understand the true incidence/prevalence of CTS in the US as well as across the globe. The use of a standardized clinical definition or as in the current article, a surgical decision as a surrogate for the clinical entity, needs to be used consistently across studies.

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