



*Accelerating research towards a cure for multiple sclerosis*

## Changes in longevity in persons with MS

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We spend countless hours pondering our time on earth. Hopefully by reflecting on the past, we appreciate the present, and look forward to tomorrow. There are so many questions a person with MS (PwMS) may have for medical professionals, amongst the first questions: “What’s my prognosis?”... “How much time do I have?” Having conversations on one’s mortality is not easy, and challenging, particularly when a disease is highly variable.



Nonetheless, these conversations have wonderful silver linings, directing our focus on the present and motivating us to invest in our legacies. For several decades, the life expectancy of PwMS were significantly lower than the general population, however, we have seen great improvements in recent years. This month there were three papers assessing mortality trends in PwMS, demonstrating further improvements<sup>1, 2, 3</sup>.

These studies are unique since they were truly population-based and captured their *source* populations. Whenever conducting a human study, we epidemiologists worry about the representativeness of our study sample and we work through a series of questions and steps when designing our studies and when we interpret our results. For a hypothetical study I may go through these stages: **Question:** What is the population I care to study or who is the *target* population I want my findings to inform/apply to? For me, I care about PwMS. **Question:** What is the *source* population? What population do I have access to? Well, I live in Cleveland, so PwMS in Cleveland. Thus, I may pursue collaborations with neurologists at a local hospital XYZ. My collaborators and I may approach all of the PwMS in their practices, and let's suppose 50% of the PwMS approached were willing to participate in my study. I conduct my study, I run my statistical models, and generate results. But before I can interpret my results, I work back through these questions. **Question:** Who was my study sample? Are they representative of all PwMS at hospital XYZ (why would someone not participate in a study? Are they too busy? Too sick?) **Next Question:** Are PwMS at hospital XYZ representative of all PwMS in Cleveland? (What type of insurance does this hospital accept? What neighborhood is it in? Are there reasons why the population at hospital XYZ might not reflect the rest of Cleveland? Am I capturing only the very sick by using a hospital?) **Next Question:** How do PwMS in Cleveland compare to PwMS from rest of Ohio, the Northeast USA, the USA, and the world? Thus, can I connect my *study* sample to my *source* sample and then to my *target* sample. Mind-bender right?! Fortunately, I can account for some of these gaps with statistical approaches, but not all. In the end these questions matter as they determine the validity of my study, and how broadly I can generalize my results.



Well, these three papers did an impressive job of capturing their *source* populations, since their *source* is also their *target* population. They also used data spanning many decades. The ***first study*** by Burkill et al, and published in *Neurology*<sup>1</sup> used multiple national Swedish registries, which

included detailed health information, to identify all Swedish persons with a diagnosis of MS between 1968 and 2012. For each PwMS identified, ten individuals without a diagnosis of MS but with the same age, gender, county of residence were also selected. The study was comprised of 29,617 PwMS and 296,164 controls. There were many findings, but the most interesting was the change in mortality over time. There was a 3.5 fold reduction in the risk of death in PwMS relative to the general population when comparing 1968-1980 to 2001-2012. This improvement in survival was not due to overall increases in longevity in the total population – thus the reduction in MS mortality was above and beyond expectation. The ***second study*** by Koch-Henriksen et al, and published in *Journal of Neurology, Neurosurgery & Psychiatry* used the Danish MS nationwide registry from 1950 to 1999, and linked to several other national health registries. 12,847 PwMS were identified and mortality was compared to known Danish mortality rates for the general population. The highlights of this paper were the results demonstrating between 1950-1959 to 1990-1999 there was a 5-fold reduction in lives lost to MS and survival for PwMS increased 15 years. The ***third study*** by Lunde et al, and published in *Journal of Neurology, Neurosurgery & Psychiatry* studied all PwMS in Hordaland County, Norway from 1953-2012. 1,388 PwMS were identified through thorough medical record evaluation and linkage to national Norwegian registries. The risk of death for PwMS compared to the general population reduced 3 fold from 1953-1974 to 1997-2012.

Collectively, these studies with exceptionally long study periods and complete sampling of their *source* population (thus, making generalizations easier to their *target* population) demonstrate significant improvements to survival in PwMS. We can only speculate as to the factors responsible for the reduction in mortality, as they were not the primary focus of these studies. Possible factors include: improvements in diagnosis – thus, PwMS are diagnosed earlier and therefore treated earlier; improvements in treatments for MS; improvements in treatments for other chronic and comorbid conditions (i.e. hypertension); changes in access to care; and changes in secular and societal trends (i.e. smoking habits). Considering disease modifying

therapies have only been available for two decades, and the dramatic improvements to clinical care in the last several years (reduction in diagnostic delays, improvements to symptom management, etc), I am optimistic life expectancy in PwMS, today or in the very near future, will be closely approaching (if not similar to) that of the general population!

1. <https://www.ncbi.nlm.nih.gov/pubmed/28687718>
2. <https://www.ncbi.nlm.nih.gov/pubmed/28705951>
3. <https://www.ncbi.nlm.nih.gov/pubmed/28365589>