A116 · Discovering disease trajectories using genetic similarity

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Understanding trajectories among diseases poses real clinical value. For example, a disease associated with increased risk for developing another disease can help to justify early screening, provide insight into disease etiology, or point to drugs repurposing. We hypothesize that genetic similarity could be used to identify hidden relationships between diseases. For example, genetic similarity between irritable bowel syndrome (IBS) and lymphoma could point to subpopulation of lymphoma patients misdiagnosed with IBS, due to early abdominal pain symptoms. After building a database of genetic similarity scores among 177 common diseases, we develop a pipeline to assess matched comorbidity risk between prioritized disease pairs. This approach tests the association using 1:1 and coarsened exact matching approaches, matched on sex, age, and date. We include negative and positive controls to detect potential confounders in our relative risk (RR) estimation. In our pilot study of IBS and lymphoma, we obtained an estimated RR around 1.3-1.75 depending on the lymphoma occurrence window after the index date. We obtained ulcerative colitis (positive control) has ~5-6 RR, unfortunately, we also detected inflated RR among negative controls, i.e. cataract and fracture (~1.4). This inflation suggests the existence of unaccounted confounders. Our next step is to scale our pipeline across diseases that share genetic similarity. We implement high-dimensional score (hdPS) to address the hidden confounders. This work will allow us to put forward genetic similarity among diseases as a source of insight into disease trajectory, putting forward hidden early symptoms of diseases, causal factors, complications, or subtypes of diseases.

Discovering disease trajectories using genetic similarity

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