A multi-polygenic score of clock resilience and its utility in predicting vulnerability to night work

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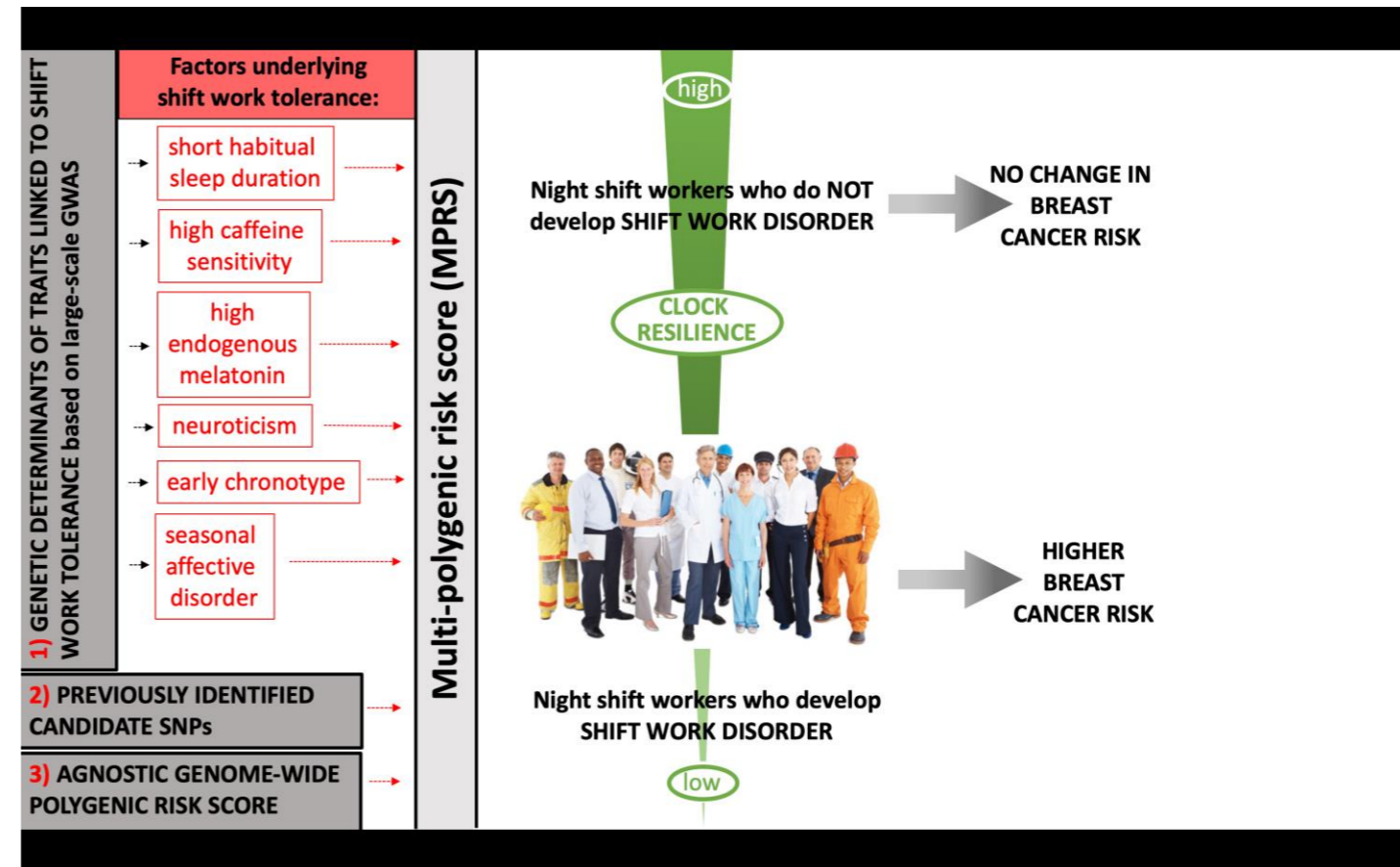
Background

Until almost two centuries ago, daylight, or natural light (i.e., the combination of any direct and indirect sunlight during the daytime), represented the primary source of light for humans. Daylight and darkness alternated in a predictable pattern that follows the solar cycle – synchronizing the circadian system and sleep/wake cycle in all living things to the 24-hour day. Edison's introduction of the electric light bulb in 1878, however, allowed for widespread adoption of artificial *light at night*, which challenged an ancient, evolutionary rhythm.

Night shift work represents one of the gravest and most complex perturbations of the circadian system, in the near term leading to a variety of symptoms, particularly insomnia, but also excessive sleepiness, difficulties concentrating, or lack of energy, that are commonly referred to as **'shift work disorder'**. Further, night workers experience modestly elevated risks of e.g., cardiovascular disease (CVD), type 2 diabetes, and depression.

Yet one of the most severe diseases linked with night shift work is a 60% (and higher, depending on the subtype) **increased risk of breast cancer**. Specifically, for breast cancer, which is the most common cancer among women worldwide, a large number of studies has accumulated, which in their totality imply that shift work is going to be recognized as a carcinogen for breast cancer based on sufficient evidence from human epidemiological studies: over 20 diverse study populations have examined the association between night shift work (which is typically defined as working at least 3 hours between midnight and 6am) and breast cancer risk, providing strong evidence that long-term night shift work is associated with significantly increased breast cancer risk. While for other cancer endpoints such as prostate and other particularly hormonal cancers evidence is also accumulating in support of heightened risk among night workers, a previous WHO classification from 2007 of **shift work as a probable carcinogen** was based on the much smaller body of literature available back then.

Schematic of the risk score concept

What is the genetic basis for shift work tolerance (SWT)?
Many traits have been linked to SWT in observational studies, among them are:

Use those and other traits to create and validate a clock resilience score for night work.

Hardiness — Languidity — Morningness — Neuroticism — Job Stress — Self esteem