

## Abstract

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### Background

There is very little genetically informative research identifying true environmental risks for psychiatric conditions. These may be best explored in regions with diverse environmental exposures. The current study aimed to explore similarities and differences in such risks contributing to depression and fatigue.

### Methods

Home interviews assessed depression (lifetime-ever), fatigue and environmental exposures in 4,024 randomly selected twins from a population-based register in the Colombo district of Sri Lanka.

### Results

Early school leaving and standard of living showed environmentally-mediated effects on depression, in men. In women, life events were associated with depression partly through genetic pathways (however, the temporal order is consistent with life events being an outcome of depression, as well as the other way around). For fatigue, there were environmentally mediated effects (through early school leaving and life events) and strong suggestions of family-environmental influences.

### Conclusions

Compared to previous studies from higher-income countries, novel environmentally-mediated risk factors for depression and fatigue were identified in Sri Lanka. But as seen elsewhere, the association between life events and depression was partially genetically mediated in women. These results have implications for understanding environmental mechanisms around the world.