

### **How advances in epidemiology are influencing older adult psychiatry**

Natalie Shoham MSc is a Clinical Training Fellow at University College London and psychiatric registrar in Camden and Islington NHS Foundation Trust, UK.

Natalie.shoham.16@ucl.ac.uk

Claudia Cooper PhD is a professor of psychiatry of older age at University College London and honorary consultant psychiatrist in Camden and Islington NHS Foundation Trust, UK.

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## ABSTRACT:

Lilford and Hughes describe common epidemiological terms and summarise the evidence regarding the epidemiology of psychiatric illness in older adults. They outline research findings regarding conditions that particularly affect older people, including dementia and delirium, as well as illnesses that occur throughout the lifespan. They provide a reminder that 'association does not equal causation' but that, given the practical barriers to conducting trials, observational data remain key to understanding the determinants of illness. They can also provide insights into preventative and treatment strategies. We outline three areas in which observational studies are the primary source of evidence: very long-term impact of lifestyle change and medical treatments; evaluating effects of potentially harmful conditions where randomisation would be unethical, and evaluating health inequalities.

## MAIN TEXT:

One advantage of epidemiological studies is the potential for very long-term follow-up, relative to the short duration of most Randomised Controlled Trials (RCTs). Even three-year RCTs cost millions, so evaluating how lifestyle changes affect disease over decades needs a different approach. The recent positive public health message that up to one third of dementia cases might be preventable if lifestyle risk factors were comprehensively addressed was based on epidemiological evidence (Livingston et al 2017). Epidemiological findings such as these have led to public health innovations – especially when there is a very low risk of potential harms yet considerable potential benefits to introducing new strategies or advice. They have also informed successful trials of intensive lifestyle and behaviour change interventions aimed at reducing the incidence of dementia (Ngandu et al., 2015). Large-scale epidemiological research also provides a unique opportunity to evaluate geographic and temporal differences in disease incidence and prevalence. For example, that the prevalence of dementia is decreasing in higher income countries is falling could not be discovered through any other study design (Lilford and Hughes, this article).

As Lilford and Hughes describe, there are many situations where it would be unethical to conduct an RCT. We cannot randomly select and expose a group of people to low educational attainment, or poor diabetic or antihypertensive care, to see if they are at higher risk of developing Alzheimer's disease. New Mendelian Randomisation techniques may help. Mendelian Randomisation has been used to explore the association between Alzheimer's dementia and a variety of traits. One example is predicted educational attainment (Larsson et al., 2017). In this study, Single Nucleotide Polymorphism (SNP) variants identified through genetic studies as being associated with educational attainment were used as proxies for the exposure (predicted educational attainment). SNPs are clearly allocated to the individual before the outcome (Alzheimer's disease) has chance to develop. We can therefore be certain of their temporal relationship with the outcome. Additionally, SNPs are not influenced by other traits, and so confounding should not explain any association between them and the development of Alzheimer's disease. This means that by using SNPs as a tool to represent the exposure, the authors could be more confident in using observational data to attribute causality (Davies et al., 2018, Larsson et al., 2017). Mendelian Randomisation studies are not without limitations and as with other study designs, need to be interpreted with caution. They are only suitable when an identifiable and well-understood genetic basis for the exposure variable exists. Another problem is that since SNPs are only a proxy measure for the exposure and may individually confer very small effect on it, extremely large samples can be required to detect an association. Mendelian Randomisation studies do however represent an exciting recent development in the field of epidemiology.

Observational studies can observe impacts of disease and take up of treatments over whole populations, rather than in the minority of people who volunteer to take part in RCTs (Cooper et al., 2014). Even the most successful treatments only work if people take them, and in every area of medicine there are inequalities in access to good quality care. For example, an observational study using data from GP medical records reported that people from Black ethnic groups who are living in the UK are more likely to develop dementia than people from white ethnic groups, but they are less likely to receive a timely diagnosis (Pham et al., 2018). Knowing this can guide public health strategies to reduce health inequalities. Of note, preliminary evidence that certain medications may influence dementia risk identified in observational studies is not always replicated in randomised controlled trials (Scharf et al, 2007). This remains a challenge for observational studies.

Lilford and Hughes' review describes functional illnesses in later life, highlighting that they can occur at different rates in older compared to younger adults. Epidemiological studies can explore not only differences in prevalence but also differences in risk factors at different points in the lifespan, as well as mechanisms. There is evidence that genetic susceptibility differs between late-onset and early-onset depression (Power et al., 2017), and that late-onset depression may have a greater inflammatory component (Rozing et al., 2019). It has been proposed that first-episode psychosis in old-age can be a marker of underlying neurodegeneration (Van Assche et al., 2017). Prevalence of risk factors may also differ by age group. For example, hearing loss appears to be associated with both dementia and schizophrenia, and sensory impairments occur more commonly in older people (Lilford and Hughes, this issue).

Lilford and Hughes' helpful review highlights the importance of epidemiology to the mental health care of older adults. With the ever-increasing opportunities of big data for larger and more sophisticated observational studies, epidemiological data will continue to be a cornerstone of psychiatric research.

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