

Menopause in the spotlight: important research and clinical advances



Despite directly affecting around half of the global population during their lifetime, menopause research has been chronically underfunded, with clinical care lagging behind other fields. Over the past few years, this picture has started to shift.

Menopause (the cessation of menstruation) usually occurs between the ages of 45 and 55 years, and is preceded by a transition period termed perimenopause, which is when symptoms usually start to appear. The experience of menopause is highly individual and so the treatment plan also needs to be tailored. However, until a few years ago, treatment options were very limited, particularly for patients for whom hormone-based treatments are contraindicated.

The general media has focused attention on menopause in the past few years, with campaigns spearheaded by celebrities and backed by charities, patient groups and experts in the field. As a result, many patients are better equipped to seek the care they require and to advocate for their needs. In parallel, dedicated researchers have been working to better understand menopause and to develop new therapies. This issue features two articles on different aspects of menopause research and clinical care, highlighting some of these advances. In one Review, Martha Hickey et al.¹ outline our latest understanding of the risk factors for severe menopausal vasomotor symptoms (hot flushes and night sweats), as well as how they can be managed. In another Review, Víctor Navarro and colleagues² outline the research path that led to the approval of neurokinin 3 receptor antagonists for the treatment of vasomotor symptoms.

A wide range of symptoms are associated with menopause, including vasomotor symptoms, psychological effects (such as anxiety and depression) and genitourinary symptoms. In the post-menopause period, individuals also have increased risk of cardiovascular disease and osteoporosis (with associated risks of fractures). All of these factors represent a considerable clinical burden on the individual, as well as on healthcare systems when not managed well. Menopause also has broader socio-economic effects, with potential effects on engagement with employment and the ability to participate in wider society. In addition to the detrimental effects on individuals, menopause is therefore a major public health issue.

As outlined by Hickey et al., research from the past few years has made major advances in determining the broad range of factors that can affect an individual's risk of experiencing severe vasomotor symptoms during menopause.

These have been shown to range from adverse childhood experiences to dietary factors and smoking habits. Up to 80% of people going through menopause will experience vasomotor symptoms, generally over a period of 4–7 years (although some experience them for more than a decade). Hickey et al. report that the duration and severity of vasomotor symptoms is also affected by race, ethnicity and socio-economic background. The authors also outline the available treatments, which include menopause hormone therapies, non-hormonal pharmaceuticals (such as oxybutynin and neurokinin 3 receptor antagonists) and non-pharmacological options (such as cognitive behaviour therapy).

Navarro and colleagues provide a deep dive into the neurobiological pathways that underlie vasomotor symptoms and outline how these advances in basic research were translated into clinical care. We now understand that KNDy neurons (which express kisspeptin, neurokinin B and dynorphin) in the hypothalamus trigger vasomotor symptoms as a result of neurokinin B signalling to thermoregulatory neurons in the median preoptic area that express neurokinin 3 receptor. During menopause, the fall in oestrogen levels can cause hyperactivation of KNDy neurons, leading to high levels of neurokinin B release and inappropriate activation of the heat dissipation response. Once this pathway was established as a cause of vasomotor symptoms, researchers were able to develop antagonists that specifically target neurokinin 3 receptor, and fezolinetant and elinzanetant have both been approved for use in moderate-to-severe vasomotor symptoms in the past few years. This is a hugely important treatment advance, as it represents a targeted treatment option and one that can generally be taken by those for whom traditional hormone-based treatments are not an option (such as people who have had breast cancer).

Of course, as exciting as these advances are, there are still research gaps. More research is needed to expand the treatment options for all symptoms of menopause, including both pharmacological and non-pharmacological treatments. Furthermore, Navarro and colleagues point out that more research is needed into the effects of neurokinin 3 receptor antagonists, as well as trials that directly compare these new drugs with menopause hormone therapy. Advances are also needed to support personalized and stratified care. As Hickey et al. point out, improved models for predicting individual risk of each symptom of menopause (and the probable severity) are needed, as well as more clinical trials focused on the perimenopause period.

Menopause is an important issue for the research and clinical communities, as well as for broader society.

“...the two Reviews in this issue highlight important advances, but more work is needed to provide high quality care to the millions of people across the globe affected by menopause”

Affected individuals have been underserved for too long; the two Reviews in this issue highlight important advances, but more work is needed to provide high quality care to the millions of people across the globe affected by menopause.

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References

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