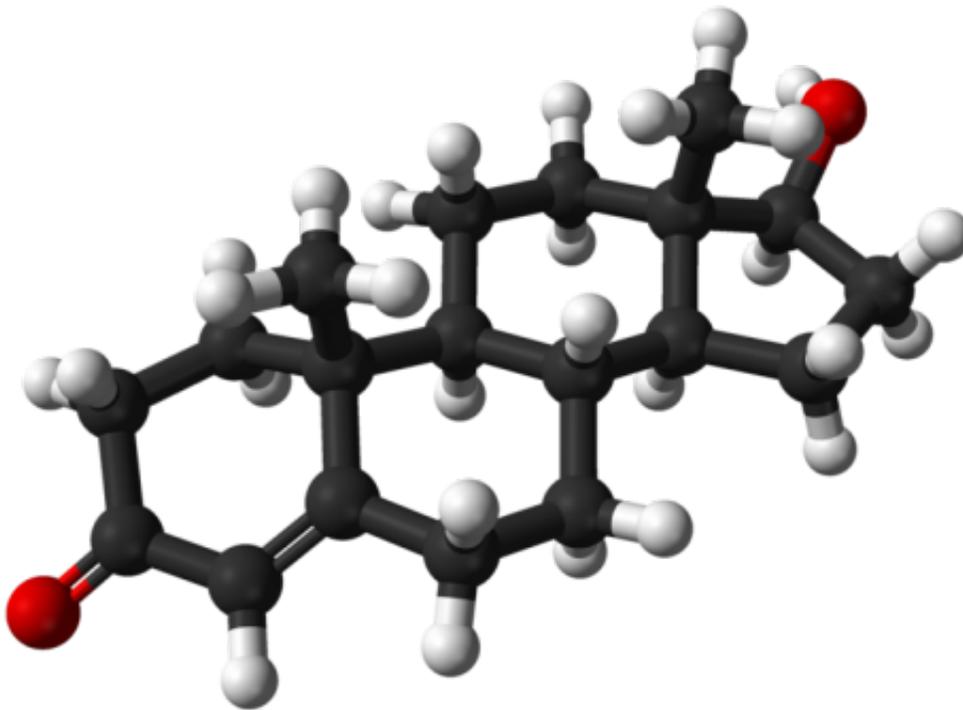


Testosterone levels affect risk of metabolic disease and cancers

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Ball-and-stick model of the testosterone molecule, $C_{19}H_{28}O_2$, as found in the crystal structure of testosterone monohydrate. Credit: Ben Mills/Wikipedia

Having genetically higher testosterone levels increases the risk of metabolic diseases such as type 2 diabetes in women, while reducing the risk in men. Higher testosterone levels also increase the risks of breast and endometrial cancers in women, and prostate cancer in men.

The findings come from the largest study to date on the genetic regulation of sex hormone levels, published today in *Nature Medicine* and led by researchers from the Medical Research Council (MRC) Epidemiology Unit at the University of Cambridge and the University of Exeter. Despite finding a strong genetic component to circulating testosterone levels in men and women, the authors found that the [genetic factors](#) involved were very different between the sexes.

The team used genome wide association studies (GWAS) in 425,097 UK Biobank participants to identify 2,571 genetic variations associated with differences in the levels of the sex hormone testosterone and its binding protein sex-hormone binding globulin (SHGB).

The researchers verified their genetic analyses in additional studies, including the EPIC-Norfolk study and Twins UK, and found a high level of agreement with their results in UK Biobank.

The team next used an approach called Mendelian randomisation, which uses naturally occurring genetic differences to understand whether known associations between testosterone levels and disease are causal rather than correlative. They found that in women, genetically higher testosterone increases the risks of type 2 diabetes by 37 per cent, and polycystic ovary syndrome (PCOS) by 51 per cent. However, they also found that having higher testosterone levels reduces T2D risk in men by 14 per cent. Additionally, they found that genetically higher testosterone levels increased the risks of breast and endometrial cancers in women, and prostate [cancer](#) in men.

Dr. John Perry from the MRC Epidemiology Unit at the University of Cambridge, and joint senior author on the paper, says:

"Our findings that genetically higher testosterone levels increase the risk of PCOS in women is important in understanding the role of testosterone

in the origin of this common disorder, rather than simply being a consequence of this condition."

"Likewise, in men testosterone-reducing therapies are widely used to treat prostate cancer, but until now it was uncertain whether lower [testosterone levels](#) are also protective against developing [prostate cancer](#). Our findings show how genetic techniques such as Mendelian randomisation are useful in understanding of the risks and benefits of hormone therapies."

Dr. Katherine Ruth, of the University of Exeter, one of the lead authors of the paper, added:

"Our findings provide unique insights into the disease impacts of testosterone. In particular they emphasise the importance of considering men and [women](#) separately in studies, as we saw opposite effects for testosterone on diabetes. Caution is needed in using our results to justify use of testosterone supplements, until we can do similar studies of [testosterone](#) with other diseases, especially cardiovascular disease."

More information: Using human genetics to understand the disease impacts of testosterone in men and women, *Nature Medicine* (2020). [DOI: 10.1038/s41591-020-0751-5](https://doi.org/10.1038/s41591-020-0751-5) , [nature.com/articles/s41591-020-0751-5](https://www.nature.com/articles/s41591-020-0751-5)

Provided by University of Cambridge

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