



decline in the body's DNA repair mechanisms.

Mutations over the lifespan can lead to loss of gene and cell function (Box 1). Premature ageing syndromes are often associated with deficiencies in DNA repair.<sup>8</sup>

**Chromosome shortening** - incomplete replication of chromosomes (Box 1) means that the end sections (telomeres) can be lost or damaged with each round of cell division. This happens faster when cells are under stress and can halt cell division (cell senescence).<sup>9,10</sup>

**Factors that bind to DNA** - ageing is associated with changes to epigenetic regulation across the genome (Box 1) which are linked to diseases such as Alzheimer's.<sup>11,12</sup> Epigenetic changes also accumulate

Metformin is a first line drug for the treatment of type 2 diabetes in the UK. Clinical data suggests metformin can increase healthy lifespan in laboratory animals.<sup>8</sup> Targeting Ageing with Metformin (TAME) is a US based human clinical trial of metformin, overseen by the Food and Drug Administration. It includes 3,000 individuals aged over 60 and will measure the time to occurrence of several age-related diseases.<sup>25</sup> TAME is the first time that a regulatory body will consider using mixed age-related diseases as outcomes in a clinical trial.

Rapamycin is approved as a treatment for cancer and to prevent the rejection of organ transplants. It promotes cellular processes such as metabolic stability and the removal of damaged cellular components.<sup>8</sup> An analogue of rapamycin, (everolimus) improved the efficacy of flu vaccinations in human individuals aged over 65.<sup>26</sup> The exact mechanisms remain unclear, but may involve replenishing the aged immune system. Researchers aim to test rapamycin, or safer analogues, against a range of ageing-related outcomes.

Research groups and commercial companies<sup>27,28</sup> are developing drugs (senolytics) that eliminate senescent cells.<sup>29,30</sup> Some cancer therapies (such as dasatinib and navitoclax) and food supplements (quercetin) have shown success in preclinical trials, removing senescent cells in different tissues and improving the health of ageing mice.<sup>31,32</sup> Researchers hope to begin clinical trials in humans soon.

### ***Challenges to implementation***

**Marketing pharmacological interventions against ageing will**

(CMO) suggests that more could be done to target pre-conception health.<sup>46</sup> Opportunities for giving women advice on preconception health include, for example, when individuals come into contact with health services to plan a pregnancy or obtain contraception.<sup>46</sup> Additionally 1 in 5 women are likely to be planning another pregnancy following the birth of a child; the CMO suggests that health checks for the mother and child could incorporate advice.<sup>46</sup> Greater levels of pre-conception health education in the curriculum may also be beneficial and reach many individuals over a wide-scale.<sup>46</sup>

### **Health during pregnancy**

Pregnancy is a time when women come into contact with health practitioners and promoting health at this time has the further benefit that two generations are targeted.<sup>46</sup> The government issues advice on diet, smoking cessation, alcohol intake and physical activity during pregnancy (see POSTnote 551). Despite this, many women experience excessive gestational weight gain

