**Introduction**

In many advanced countries those aged over 70 years are the fastest growing demographic subgroup years and are responsible for a high proportion of the nation’s expenditure on health and social services. A significant proportion of the lifespan of the elderly is spent a poor quality of life resulting in an economic burden on younger generations and an urgent health challenge. As a result, there is an increasing imperative to delay the onset of chronic disease and disability and the requirement for costly institutional care.

Of the various pharmacological agents with a potential to reduce the burden of illness amongst the elderly , aspirin has been considered amongst the most promising. Despite limited evidence of its value in the older age group , a large number of older individuals have taken a regular dose of low-dose aspirin in the hope of delaying the onset of chronic disease and maintain good health.

But whenever drugs are prescribed for healthy people in a preventive mode the balance of benefits and risks is often a fine one, assessible only by large and prolonged clinical trials. And in the case of aspirin, whose likelihood of increasing bleeding is much greater in the elderly, it became increasingly untenable for millions to be taking a preventive agent when the balance of risks and benefits had not been established. This is the context in which the ASPREE trial was established

METHODOLOGY

The ASPREE RCT was funded by the US National Institute on Aging (NIA), National Cancer Institute (NCI) & the Australian National Health & Medical Research Council (NHMRC) to determine the balance of benefits and risks of aspirin therapy (100mg/day) when used for primary prevention amongst relatively healthy individuals aged 70yrs and above.

19,100 initially healthy US and Australians over 70 years of age (half taking aspirin and half an identical placebo) entered the trial between 2011 and 2014 and were followed for an average of 4.6 years. The study was double blind, so that neither the participants, nor the research staff knew which medication was being taken until after the results had been analysed.

Most prevention trials in the past have focussed on whether a drug is effective at preventing a single disease such as heart disease or stroke. However, amongst older people it is difficult to justify prescribing a preventive drug unless it leads to a clear prolongation of time spent in good health. ASPREE therefore focussed on whether low-dose aspirin prolonged survival free of physical disability or dementia. This endpoint also had the advantage of integrating the benefits and side-effects of aspirin, avoiding the need to have to make a judgement about whether preventing a certain number of events is better or worse than causing a certain number of serious side-effects.

RESULTS

The results of ASPREE were unexpected but also unambiguous. Essentially low-dose aspirin, when used for primary prevention in older adults did not extend healthy lifespan free of disability. It resulted in a significantly higher risk of major bleeding but did not result in a significantly lower risk of cardiovascular disease in comparison with placebo. More concerningly there was a higher death rate amongst aspirin users, largely attributed to an excess of deaths from a wide variety of solid cancers. Given the previous evidence that low-dose aspirin, albeit over a longer time-frame, was effective at reducing cancer incidence and mortality, this finding will require much more detailed investigation.

It must be emphasised that the participants in ASPREE were free of pre-existing heart disease or stroke; in this setting the evidence of benefit from low-dose aspirin is much better established.

Conclusions

The findings from ASPREE make it clear that low-dose aspirin is unlikely to prolong health or delay the onset of stroke or heart disease amongst otherwise healthy older people. On the other hand, in this age group it might do more harm than good. Of course, when the data is analysed in more detail there may be some classes of individual identified where the benefit outweighs the harm, however as no such subgroup has been identified.

ASPREE has shown yet again that when drugs are used to prevent disease, even a relatively small rate of serious adverse events may be enough to cause net harm. It is only be large carefully conducted clinical trials that such risks can be identified. The trial also conveys a strong message about the need for a better data about other drugs recommended for prevention in the elderly and the need to establish their balance of risks and benefits before they enter widespread use.