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Ann Robinson's research reviews—27 January 2022

Ann Robinson *NHS GP and health writer and broadcaster*

How long are your telomeres and does it matter?

These protective DNA caps at the ends of most of our chromosomes shorten with each cell cycle. Leucocyte telomere length (LTL) is a biomarker for cell damage and can be seen as a mitotic clock, ticking away as we age. A cohort study using UK Biobank data from more than 450 000 people, and with a follow-up of over five million person-years, found that shorter baseline LTL was associated with a small increased mortality rate overall and an increase in some disease-specific mortalities such as deaths from cardiovascular and respiratory disease.¹ It's complicated, however: shorter LTL wasn't associated with an increase in total cancer-related deaths, although some cancers such as myeloid and oesophageal cancers were more prevalent. Smoking and alcohol consumption were associated with shorter LTL, but adjustment for both factors didn't change the overall results. This important study confirms the impression that LTL on its own is unlikely to become a meaningful marker for overall mortality.

Warning: screening can damage your health

Screening can damage your health if poorly targeted and ill conceived. This huge population-based ecological study of 12 million Taiwanese women, 95% of whom didn't smoke, found that promoting lung cancer screening (using low dose CT scanning) was associated with marked overdiagnosis and an apparent rise of 40% in five-year survival rates, which the authors say is spuriously high.² There was a sixfold increase in the incidence of early stage lung cancer (stages 0-I), but no change in the incidence of late stage (II-IV) or deaths from lung cancer. The inference is that lots more early lung cancers were picked up on screening—with all the attendant increase in testing, follow-up, cost, and anxiety for patients—but without any impact on mortality. Diagnosing cancers that are never going to cause death makes the five-year survival rate look good but has no real meaning. Offering screening to heavy smokers is likely to make more sense.

Artificial pancreas for young children with diabetes

The artificial pancreas is a game changer for people with type 1 diabetes, but is it safe for young children? An artificial pancreas is a hybrid closed loop system in which an algorithm automatically adjusts insulin delivery via a pump in response to a continuous glucose monitoring sensor that samples blood glucose levels. Sensor-augmented pump therapy isn't fully automated, but it can have features such as a low glucose suspend, in which the pump stops when an algorithm predicts that glucose levels are likely to fall to critically low levels. Closed loop systems improve glycaemic control and make the

management of diabetes easier for adults and older children: this small but well designed trial looked at whether 16 weeks of using a closed loop algorithm would be practical, safe, and effective in children aged 1-7 years old.³ The percentage of time spent within the target glucose range was 8.7 percentage points higher using the closed loop rather than standard care, with no difference in time spent in hypoglycaemia and one case of severe hypoglycaemia in the closed loop period. The positive results of this trial will be good news for young children who will have to live with diabetes for the rest of their lives.

Peanut allergy: avoid or treat?

Can children be cured of their peanut allergy? Currently, avoidance is advised, but it's easier said than done. A randomised US study found that initiating peanut oral immunotherapy before the age of 4 years was associated with increased desensitisation (a rise in the threshold of peanuts that can be tolerated, risk difference 69%) and remission (remaining able to tolerate peanut protein after discontinuation of immunotherapy, risk difference 19%) compared with those treated with placebo. Of those treated, 71% could safely eat 5000 mg peanut protein, equivalent to about 17 peanuts, after 2.5 years of immunotherapy. The younger the child was started on immunotherapy, the more likely they were to achieve remission, but, for most, full remission didn't last. Six months after stopping maintenance treatment, only one in five were still able to tolerate 5000 mg peanut protein, although three in five could safely manage small amounts (600 mg or about two peanuts). Almost everyone (98% of those given immunotherapy and 80% of those given placebo) had an adverse reaction, mostly mild. Nearly a fifth of those given immunotherapy needed at least one dose of adrenaline.

Boost for boosters

Almost two years after the start of the pandemic, covid-19 is still with us. As the national booster programme continues, this study asks a pertinent question: do three doses of an mRNA vaccine (Pfizer or Moderna) protect against symptomatic covid-19 with omicron and delta variants compared with not being vaccinated? This test-negative case-control study (a design which recruits people at a clinic who test positive for covid and compares them to controls who attend the same clinic but who test negative) found that, among more than 70 000 symptomatic people who attended US pharmacies for covid tests, there were far more unvaccinated than vaccinated people who tested positive (odds ratio 0.33 for omicron and 0.065 for delta) compared with controls. Two doses were less effective than three (adjusted odds ratio 0.34 for omicron, 0.16 for delta). Even being triple jabbed gives less protection against omicron than delta, but it's still a lot better than nothing (or

two doses). Further grist to our mill as we urge patients to get their booster.

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