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Statins are still safe and effective with long-term use! Several randomised trials have shown that lowering LDL cholesterol with statin use reduces vascular mortality and morbidity in a wide range of patients, without increasing the risk of non-vascular mortality or morbidity during 5 years of treatment. However, there is limited evidence about longer-term efficacy and safety (especially in relation to cancer risk) of statin treatment. A recent study assessed the effects of lowering LDL cholesterol on cause-specific mortality and major morbidity in an extended follow-up of the Heart Protection Study (HPS) (*Lancet 2011;378:2013-20*). The HPS study had randomly allocated 20,536 patients (40 - 80 years) at high risk of vascular and non-vascular outcomes to receive 40mg simvastatin or placebo with a mean "in-trial" follow up period of 5.3 years. The "post-trial" follow-up of surviving participants yielded a mean total duration of 11 years. During the in-trial period, follow-up occurred in study clinics at regular intervals, while post-trial follow-up information was obtained by annual questionnaires to surviving participants and from the participants' family doctors. The UK national registries for cancer and certified causes of death were also used to access information during the in-trial and post-trial periods. Results showed that **during the HPS in-trial period, there was an average LDL cholesterol reduction of 1 millimole/litre in patients allocated to simvastatin compared to those in the placebo group, with a proportionate decrease in major vascular events of 23%** (95% CI 19-28; $p < 0.0001$). After the first year there was a significant divergence each year between the groups. The reductions in vascular mortality and morbidity noted during the in-trial study persisted largely unchanged during follow-up in the post-trial study. In addition the absolute reduction in all-cause mortality that emerged with simvastatin allocation during the in-trial period persisted roughly unchanged after 11 years of follow-up. During the post-trial period, self reported statin use was similar in both groups. During the combined in-trial and post-trial periods, there were no significant differences recorded in cancer incidence at all sites or any particular site, or in mortality attributed to cancer or to non-vascular causes. There was no evidence of any adverse effect on non-vascular mortality in statin-allocated participants ≥ 70 years at baseline or those with pre-treatment cholesterol levels < 5 millimole/litre. The authors concluded that **prolonged follow-up of the HPS study showed that the 23% reduction in vascular mortality and morbidity persisted largely unchanged during the subsequent 6 years, despite similar LDL-cholesterol concentrations and statin use in both treatment groups. Reassuringly, no adverse effects on particular causes of non-vascular mortality or major morbidity (including site-specific cancers) were seen to emerge during prolonged follow-up.**

An accompanying editorial (*Lancet 2011;378:1980-81*) concludes that the results provide evidence that extended use of statins is safe with respect to possible risk of cancer and non-vascular mortality, even among elderly patients.



Wash your hands after peeling fruit!! A small randomised controlled trial assessed whether fruit handling results in a false blood glucose (BG) reading using capillary fingertip blood samples (CFBS) (*Diabetes Care March 2011; 34: 596-597*). Fasting CFBS were collected from healthy volunteers (n=10) 1 hour after they had peeled one of several kinds of fruit (orange, grape or kiwi), followed by no hand washing and no alcohol swab, hand washing with tap water, rubbing the fingertip with an alcohol swab once or 5 times. CFBS were obtained from the volunteers after no fruit handling to serve as controls. The results showed that the BG levels from CFBS obtained 1 hour after peeling fruit followed by hand washing were similar to those of the control results. However, **BG levels obtained after peeling fruit that was not followed by hand washing were statistically higher regardless of whether the fingertip was or was not rubbed once with an alcohol swab, while BG levels were statistically higher from participants who handled grape or kiwi after rubbing the fingertip with an alcohol swab 5 times.** The authors of the study concluded that the results indicate that hand washing with tap water after peeling fruit, rather than the use of an alcohol swab is very important for monitoring of BG levels using CFBS.



Most reproductive factors have no impact on risk of ovarian cancer.

In developed countries, ovarian cancer (CA) is the 6th most common malignancy and cause of cancer death in women. Parity and use of oral contraceptives (OCs) have been reported to reduce the risk of ovarian CA, but the impact of other reproductive factors is less clear. A recently published study (*Brit J Cancer 2011; 105: 1436-42*) evaluated the association between OC use and/or reproductive factors with the risk of ovarian CA using data from a large prospective study (European Prospective Investigation into Cancer and Nutrition). Approximately 370,000 women (age 35-70 years) were recruited in 10 countries and followed up for an average of 9 years. Incident ovarian CA cases were identified during the period of follow-up and the following information was collected in order to identify possible associations with ovarian CA risk: OC use data (age of first use, duration, type), age at menarche and menopause, numbers of full-term (FT) and incomplete pregnancies, age at time of first FT pregnancy, use of menopausal hormonal replacement therapy (HRT), information on breastfeeding, as well as lifestyle data (physical activity, smoking, BMI) and education status. Results identified 878 cases of ovarian CA during 2.9 million person-years of follow-up. **Compared with never users of OC, ever users had a significantly lower risk of ovarian CA and this was unaffected by adjustment for smoking, BMI, HRT, OC content, age at menarche, age at menopause and number of FT pregnancies.** The longer the duration of OC use, the greater the reduction in risk. In terms of parity, **women who had children had a 29% reduction in risk of ovarian CA** which was further reduced with each additional FT pregnancy (38% lower risk with ≥ 4 FT pregnancies). **Age at first FT pregnancy, ever having had an incomplete pregnancy, breastfeeding, age at menarche or menopausal status had no apparent effect on ovarian CA risk.** The authors note that the cumulative duration of breastfeeding was relatively short (upper level > 13 months), therefore the study couldn't rule out the possibility of a protective association with longer durations of use. Of interest, a **late age menopause was associated with significantly increased risk of ovarian CA risk** (46% increased risk for > 52 years vs. ≤ 45 years). The authors suggest that this may be due to the fact that these older women may mistake sub-clinical cancer bleeding for menses. The authors conclude that this study shows a strong protective association of OC use and parity with ovarian CA; however, apart from a higher risk with late age menopause (> 52 years), no association between risk of ovarian cancer and other reproductive factors was noted.



New safety advice for use of aliskiren. The Irish Medicines Board (IMB), in conjunction with the European Medicines Agency (EMA) has published a safety advisory concerning the use of aliskiren (Rasilez®), following the termination of the ALTITUDE study. Aliskiren is a renin inhibitor, which blocks the production of angiotensin I (and ultimately angiotensin II). It is currently licensed for the management of essential hypertension. The ALTITUDE study sought to

evaluate the potential benefits of aliskiren, added to standard care (which included an ACE inhibitor or angiotensin receptor blocker (ARB)), in reducing the risk of cardiovascular and renal events in $> 8,600$ patients with type 2 diabetes mellitus over a 4-year period. The study was terminated early, following review of preliminary interim analyses, which showed that study patients were unlikely to benefit from aliskiren; furthermore, there was a higher incidence of adverse events related to non-fatal stroke, renal complications, hyperkalaemia and hypotension in the aliskiren group.

All available data from the study and from all other sources are currently being reviewed by the EMA scientific committee (Committee for Human Medicinal Products) and the findings will be published when the review is completed. In the meantime, the following precautionary measures have been recommended for the use of aliskiren-containing medicines:

- Aliskiren-containing medicines should not be prescribed for diabetic patients, in combination with ACE inhibitors or ARBs.
- Doctors should review the treatment of patients taking aliskiren at a routine (non-urgent) appointment, and if patients are diabetic and are also taking ACE inhibitors or ARBs, aliskiren should be stopped and alternative treatments considered.
- Patients should not stop any of their treatments before speaking to their doctor, as discontinuation of anti-hypertensive medication can put them at risk.

Patients who have questions or concerns about their treatment should speak to their doctor or pharmacist at a routine appointment. Further information as well as a helpful Questions and Answers paper is available from: www.imb.ie and www.ema.europa.eu. The NMIC will publish updated findings from the CHMP review as soon as they are available.

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. This newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH. Tel: Direct Line (01) 473 0589 or 1850 727 727 Fax: (01) 473 0596 Email: nmic@stjames.ie