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Project summary:
This is an observational prospective cohort study to assess whether the incidence of new onset diabetes is increased with the use of statin drugs; when compared to blood pressure drugs, and to a control group. The importance is indicated from previous experience with unwanted increased rate of cardiovascular events due to new onset diabetes with use of certain antihypertensives (1, 2). We will look at patients with first prescription of statin drugs and assess the proportion of users who develop diabetes in 6 years. We will compare this with groups of patients with first prescription of drugs for high blood pressure (high diabetes risk control group), and patients with prescription for diclofenac (normal control group). We will use prescription data held electronically in the New Zealand Health Information Service’ (NZHIS) Pharmaceutical Collection.

Background:
In modern cardiovascular risk management, statin drugs are popular and beneficial adjuncts for prevention of primary and secondary cardiovascular events. All forms of pharmacotherapy have side effects. Common to statin drugs are increases in liver transaminases, muscle aches, cognition impairment and rhabdomyolysis, albeit rare. However, there is now new evidence to suggest that statin drugs could have drug class effect in causing diabetes in previously non-diabetic individuals (3). Statin induced diabetes was first observed in the JUPITER trial (4) with relation to rosvastatin use in non-diabetic subjects. It was reported by physicians involved in the trial as a secondary outcome and concluded that more evidence is needed to confirm the observed effect. Following that, multiple meta-analyses correlated an overall 9% increased risk of diabetes with statin use with newer evidence showing association with pravastatin and rosuvastatin use (5-8). The meta-analyses, should be interpreted with caution as diabetes is often not the primary outcome in the trials analysed. Recent evidence indicates the risk of new onset diabetes with statin use could also be dose dependent (9). These drugs may still have an overall cardiovascular benefit nonetheless (10). One of the difficulties in assessing the extent of the risk is that patients of higher cardiovascular risk also carry an increased risk of developing diabetes. In order that the risks and benefits of these drugs to be properly considered by patients and doctors, decisions whether to use them, it is very important to understand the extend of this risk in already high risk patients as development of diabetes further increases cardiovascular risk and carries its own morbidity, reducing lifespan and quality of life.

Objective
To assess comparative rates of diabetes development in patients in primary care population started on statin drugs; by comparing them with rates of diabetes development in patients also at high risk of cardiovascular disease started on blood pressure medications but not on statins, and with normal control group.

Methodology:
We will look at patients with first prescription of statin drugs and assess the proportion of users who develop diabetes in the subsequent 6 years. We will compare these rates in patients with first prescription of drugs for high blood pressure (high diabetes risk control group) and patients with prescriptions for diclofenac (normal control group). We will use
electronic prescription data from the New Zealand Health Information Service’ (NZHIS) Pharmaceutical Collection.

Study Design: Prospective cohort study using routinely collected data

Study population: New Zealanders between ages 40 and 60, who are commenced on either on statin drugs, or on antihypertensives (high risk control group), or diclofenac (low risk control group) in the year 2005.

Exclusion: Patients who previously have diabetes, glucose intolerance, polycystic ovarian syndrome, and those who are already on metformin, thiazides and corticosteroids (all known to increase diabetes risk).

Follow up: Cohort will be followed up for 6 years.

Outcome measure: First prescription of metformin.

Analysis: Proportions compared between statin started, antihypertensives known to have increased diabetes risk (thiazides and beta-blocker), antihypertensives known to have no increased diabetic risk (ACE-inhibitors, ARBs, calcium channel blockers) and diclofenac.

Ethical considerations:
No ethics committee is required by the National Ethics Advisory Committee, New Zealand as stated in the Ethical Guidelines for Observational Studies: Observational Research, Audits and Related Activities, NEAC, December 2006.

Pegasus Health has a method for anonymously electronically extracting and linking these data from the New Zealand Health Information Service’ (NZHIS) Pharmaceutical Collection. Data will be de-identified at the point of extraction from the clinical record. Collection of such data will be stored in de-identified manner. This study has been approved for support by the Pegasus Health Research, Audit and Evaluation committee.

References: