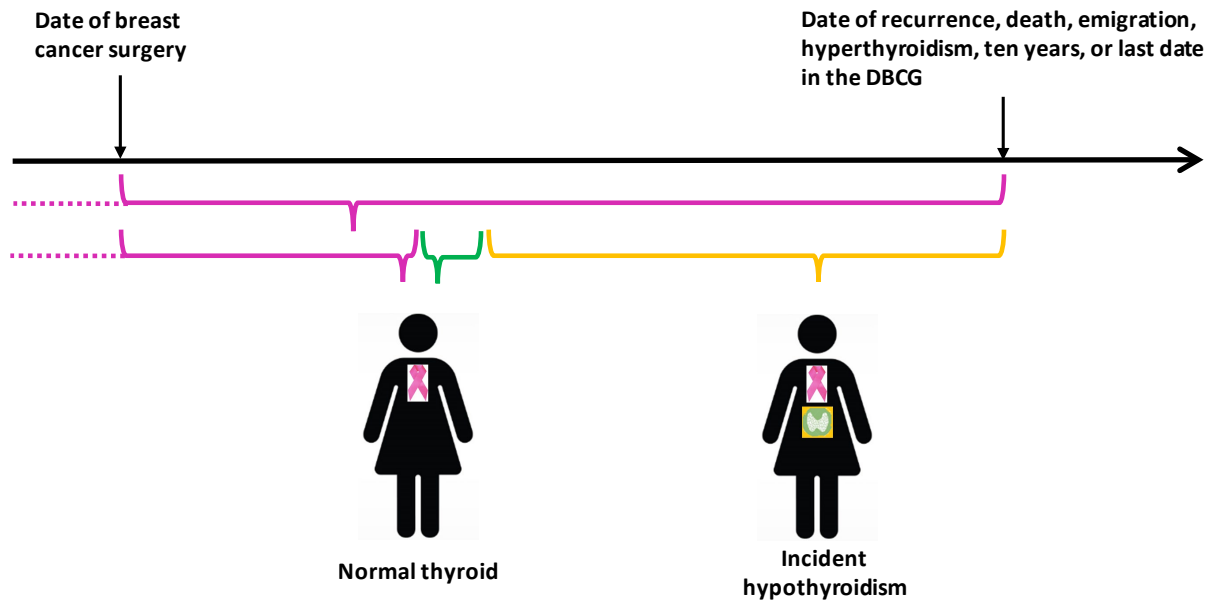


ADDITIONAL FILE 1: Time lagging exposure

In the Figure below, we illustrate the person-time lag and how this operationalized in the incident model.

The **pink line** represents person-time for women with no redeemed prescriptions and/or no hospital diagnosis code for hypothyroidism. This person-time is deemed unexposed and accordingly allocated "normal thyroid function". The **green line** and **yellow line** represent women with a hospital diagnosis code for hypothyroidism or redeemed levothyroxine prescription at some time during the study period. The **green line** starts at the date of hospital code or second redeemed prescription and lasts for one year. During this first year after hypothyroidism diagnosis code or prescription, the person-time is allocated to the "normal thyroid function" (therefore unexposed) to minimize reverse causation. The one-year lag means that after the end of this first year, the patient with a hypothyroidism diagnosis code or prescription then starts to contribute exposed person-time in the models. This method is recommended in pharmacoepidemiological studies to avoid immortal person-time bias [1].



References:

1. Suissa S: **Immortal time bias in pharmaco-epidemiology**. *American journal of epidemiology* 2008, **167**(4):492-499.