Effectiveness of Screening for Colorectal Cancer with FOBT in Finland

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Supplementary Appendix

In the estimation of the excess mortality rate ratio and its confidence interval, we followed van Leeuwen et al. (1 and 2). The two excess mortality rates are presented as \( m_i = e_i/n_i \), where \( i \) is the study arm (\( i = 1 \): screening arm and \( i = 2 \): control arm), \( e_i \) is arm-specific excess number of deaths and \( n_i \) is arm-specific number of observed person-years.

The excess number of deaths is the difference between the observed number \( d_i \) and the expected number \( d_i^* \) of deaths from any cause among the \( N_i \) CRC patients:

\[
e_i = d_i - d_i^*.
\]

Differences in the background mortality rates among attendees and non-attendees were taken into account by stratifying the patients in the screening arm according to their attendance status at diagnosis (\( N_{ip} \) patients had participated at least once before the diagnosis, and \( N_{in} \) patients had not participated). In the following formulae, subscript \( 1p \) denotes attendees and \( 1n \) denotes non-attendees. In the screening arm, the excess number \( e_1 \) of deaths is the sum of the excess number \( e_{1p} \) in attendees and the excess number \( e_{1n} \) in non-attendees, i.e.,

\[
e_1 = e_{1p} + e_{1n} = d_{1p} - d_{1p}^* + d_{1n} - d_{1n}^*.
\]

The expected numbers of deaths \( d_{1p}^*, d_{1n}^* \) and \( d_{2}^* \) are calculated based on the assumption that the patients would have the same mortality rates (stratified by sex, age, calendar year and study arm and, in the screening arm, also by attendance status) as persons who were not diagnosed with CRC in the randomized population.

The numbers of deaths \( d_i \) and \( d_i^* \) are mathematically related to the number \( N_i \) of CRC patients as

\[
d_i = N_i q_i \quad \text{and} \quad d_i^* = N_i q_i^*
\]

where \( q_i \) and \( q_i^* \) are the observed and the expected death proportions, respectively. In the estimation of the variance, neither \( d_i \) nor \( d_i^* \) can be regarded to be constant as they depend on \( N_i \), a Poisson-distributed random variable. The death proportion \( q_i \) is assumed to be a parameter of a binomial distribution with radix \( N_i \), and the expected death proportion \( q_i^* \) is regarded to be fixed as it is based on the large total number of deaths among persons who were not diagnosed with CRC in the randomized population.

Accounting for participation the excess mortality rate ratio can be written as

\[
\frac{m_1}{m_2} = \frac{d_{1p} - d_{1p}^* + d_{1n} - d_{1n}^*}{n_1} = \frac{N_{1p}(q_{1p} - q_{1p}^*) + N_{1n}(q_{1n} - q_{1n}^*)}{N_2(q_2 - q_2^*)} \frac{n_1}{n_1} = \frac{\text{num} \ n_2}{\text{den} \ n_1}.
\]

The 95% confidence interval for the excess mortality rate ratio was constructed on a logarithmic scale. The variance of the logarithm of the excess mortality rate ratio can be estimated by the delta method as
\[
\text{Var}(\log \left( \frac{m_1}{m_2} \right)) = \frac{\text{Var}(\text{num})}{(\text{num})^2} + \frac{\text{Var}(\text{den})}{(\text{den})^2}.
\]

The Var(num) and Var(den) can be estimated as
\[
\begin{align*}
\text{Var}(\text{num}) &= N_{1p} \left[ (q_{1p} - q_{1p})^2 + q_{1p}(1 - q_{1p}) \right] + N_{1n} \left[ (q_{1n} - q_{1n})^2 + q_{1n}(1 - q_{1n}) \right] \\
\text{Var}(\text{den}) &= N_{2} \left[ (q_2 - q_2)^2 + q_2(1 - q_2) \right]
\end{align*}
\]

Here, the Poisson assumption of \( N_i \), constancy assumption of \( q_i^* \), binomial assumption for \( q_i \), and the delta method for the variance of a product have been made use of.

References
