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Should Guidelines Be Developed to Indicate When Hyperthyroidism or Hypothyroidism Ought to Be Included on a Death Certificate?

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Goldacre MJ, Duncan ME. Death rates for acquired hypothyroidism and thyrotoxicosis in English populations (1979–2010): comparison of underlying cause and all certified causes. QJM, 2012;106: 229-235.

SUMMARY

Background

Death certificates contain the single condition judged to be the underlying cause of death, but may include other diseases considered to be contributory causes as well. The authors used a national English mortality database from 1995-2010, and also a smaller Oxford regional database dating back some 30 years, to calculate the annual age-standardized mortality rates for all cases in which hypothyroidism or hyperthyroidism was mentioned, either as the underlying cause or as a contributory cause. The codes and the rules for coding changed several times in the 1980s and coding also changed in 2001, which required a fairly complicated analysis of the results.

Methods

Robust data were obtained from the English national mortality database, which used the International Classification of Diseases, 9th Revision (ICD9) disease categories from 1995–2000, then switched to ICD10 categories from 2001 to 2010 (this change split the code for hypothyroidism, and removed the code for postsurgical and post irradiation hypothyroidism, putting them under "E89, Post procedural endocrine and metabolic complications and disorders, not otherwise classified"). The 2001–2010 English national data were also used to determine the 12 commonest "contributing factors" included on the certificates of patients who died of hyperthyroidism or hypothyroidism. The authors also determined the 12 commonest causes of death for all certificates that mentioned hyperthyroidism or hypothyroidism as a contributing factor. The data from the smaller Oxford region database that extended back as far as 1979 needed to be addressed in 4 different groups of years because of changes in codes and coding rules.

Age-standardized death rates were determined using age-specific death rates, in 5-year age groups, from the "European Standard Population." An "average annual percentage change" in mortality rate for all certificates containing any mention of hyper- or hypothyroidism was calculated by fitting regression models to the logarithms of the death rates. The significance of differences found between coding periods was assessed by Chi squared testing.

Results

The age-standardized English national data on certificates with any mention of hypothyroidism averaged over the 1995-2000 period did not differ significantly from that of the 2001-2010 period, whereas the percentage of deaths caused by hypothyroidism as a fraction of total mentions of hypothyroidism was actually higher in 2001-2010 than in the previous 1995-2000 period. Examination of the year-by-year graph of the age-standardized mortality rate confirmed the rise in certificates listing hypothyroidism as the underlying cause from 2001-2010, but - unlike the averaged data – showed that total mentions of hypothyroidism consistently and progressively fell from 1995 to 2000, and then consistently and progressively rose from 2001 to 2010. The Oxford

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regional mortality data were much more variable, but the graph of total mentions of hypothyroidism as well as of hypothyroidism as the cause of death trended downwards over the 1979-1995 period, and thereafter generally followed the national trends.

The percent of deaths caused by hyperthyroidism as a fraction of total mentions of hyperthyroidism did not change, based on the age-standardized English national data, averaged over the 1995–2000 period versus the 2001–2010 period. However the "average annual percentage change" in total mentions of hyperthyroidism did decrease significantly, the greatest decrease being in the age group of 65 to 74 years. Examination of the graph of the year-by-year age-standardized mortality rate revealed that total mentions of hyperthyroidism fell substantially and consistently, but that hyperthyroidism as the underlying cause of death also fell consistently. The graph of the Oxford regional graph showed that the total number of mentions of hyperthyroidism as well as deaths caused by hyperthyroidism fell, albeit erratically, from 1979 to 1995. Since 1995 they generally followed the national trends.

In the patients who died from hypothyroidism, the associated causes listed most commonly were, in descending order, pneumonia, followed by dementia, hypertension, chronic ischemic heart disease, atrial fibrillation and heart failure. In the patients who died from hyperthyroidism, the associated conditions most commonly listed also were pneumonia, followed by atrial fibrillation/flutter, hypertension, chronic ischemic heart disease and heart failure. On those death certificates listing hypothyroidism or hyperthyroidism as a contributing factor, the 6 commonest underlying causes of death were identical and in the same order: chronic ischemic heart disease, followed by stroke, myocardial infarction, COPD, dementia and heart failure.

Conclusions

In the Oxford region, particularly in the 1980s, mortality from both thyroid disorders fell, both when listed as a contributing factor and also when listed as the underlying cause of death. Over the past 15 years, the national data showed mortality from hyperthyroidism continued to fall, both as the underlying cause of death and also as the total number of mentions. Mortality from hypothyroidism listed as the cause of death was actually higher in 2001–2010 than in 1995–2000, which the authors attributed to the change in ICD coding of hypothyroidism as the underlying cause of death.

ANALYSIS AND COMMENTARY

The authors surmised that the decreases in thyroid-related mortality they found were likely due to improvements in the treatment of the thyroid conditions—stating that they were not aware of any evidence that the incidence of these thyroid conditions has declined over time; or that physicians have come to believe that fewer patients are dying from these disorders, but rather that the patients are merely dying with them; or that there was increasing reluctance to list these diseases as a cause of death.

We note that the marked improvement in the TSH assay over the period studied has made it embarrassingly clear that our record of maintaining a patient's TSH within the normal range is often less-than-perfect. When completing a death certificate, it is easy to overlook an earlier thyroid disorder if the thyroid function tests were normal at the time the patient died. True, there is evidence the therapy used to treat certain forms of hyperthyroidism has recently undergone change (1), but shifts in racial/ethnic make-up, dietary iodine levels (2) and

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smoking incidence (3) have been documented in the UK, and newer drugs like amiodarone may also have altered the incidence and/or severity of several causes of hyperthyroidism and/or hypothyroidism. Better assays for TSH and TSH-receptor antibodies were introduced, which have helped physicians recognize and treat more subtle diseases, like silent thyroiditis, and hyper- and hypothyroidism in elderly patients, who often lack classical symptoms. These improved assays have also instigated growing concern about morbidity and mortality in so-called subclinical hyperthyroidism and hypothyroidism. Finally, one should note that patients with autoimmune diatheses underlying Graves' and Hashimoto's disease can suffer later mortality due to "unrelated" autoimmune diseases.

Therefore, it might be more credible to ascribe at least some of the decrease in mortality to advances in the care of common disorders like pneumonia, dementia, hypertension, chronic ischemic heart disease, atrial fibrillation and heart failure. This would seem to be consistent with the authors' finding that total mentions of hyperthyroidism decreased the most in the 65-74 age group, in which these diseases may prove fatal. Disregarding the possible effects of thyroid disorders on pre-existing conditions, it is clear that thyroid disorders also can predispose to new medical conditions. Despite some methodological drawbacks, an increasing number of papers indicate that hyperthyroidism and hypothyroidism are associated with an increased risk of mortality, independent of any medical conditions present before the thyroid disorder was diagnosed (4,5). (The association between thyroid disorders and cardiovascular deaths seems to be more well-recognized, thus far, than deaths from osteoporotic hip fractures).

It is striking that less than 1% of patients with a diagnosis of hyperthyroidism or hypothyroidism have that diagnosis listed on their death certificates. (In the United Kingdom, the 2010 death rate was about 5 per 1000 for women and 7 per 1000 in men. A rough estimate of the annual incidence of primary hypothyroidism in women is about 4 per 1000 per year in surviving women and about 0.6 per 1000 in surviving men. The annual incidence of hyperthyroidism is about 1 per 1000 in women and 0. 15 per 1000 in men). The death certificates, on the other hand, mentioned hypothyroidism in only about 0.02 per 1000 women and 0.01 per 1000 in men , and mentioned hyperthyroidism in only about 0.004 per 1000 women and 0.001 per 1000 in men. Interestingly, the mortality rates for women were only 3 times those for men, although their prevalence in women is closer to 10-to-1. Despite the infrequency with which these disorders were mentioned in death records, a substantial fraction of patients with these thyroid diagnoses can have associated comorbidities, and presumably some die because of them. It is also striking that in the 2001–2010 period, 17% of the death certificates that mentioned hypothyroidism actually gave it as the underlying cause of death, and almost a quarter of all certificates that mentioned hyperthyroidism gave it as the underlying cause of death. This fraction of thyroid disorders as the direct cause of death, rather than as associated causes, seems high. What are the reasons for a physician to attribute a death directly to one of these thyroid conditions? An obvious reason would be deaths connected with thyroid storm/crisis or myxedema coma, but these are rare. Another reason could be fatal complications from treatment for the thyroid disorders (although the appropriate coding probably would fall under complications of surgery or of side effects of drugs or of radioiodine administration, while the thyroid disorder would probably be listed as an associated cause).

Unfortunately, death certificates cannot be used to determine the length of time between when the initial diagnosis of a thyroid disorder was made and the time death occurred, what therapies were given, or any associated laboratory or clinical information. Although concerns about privacy remain, the introduction of universal medical records would make it possible someday to devise guidelines for when

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thyroid disorders should be included on a death certificate as a possible associated cause. Should an associated thyroid disorder be included for all deaths from pneumonia, dementia, hypertension, chronic ischemic heart disease, atrial fibrillation and heart failure? Probably yes, if the death occurred within the first year after the thyroid disorder was diagnosed. But what about a patient who died of chronic ischemic heart disease at age 85 after having been "adequately treated" for hypothyroidism for 30 years? What if the hypothyroidism was due to ^{131}I therapy for Graves' disease: shouldn't hyperthyroidism also be included on the death certificate?

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