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Multiple Imputation: Application to a Global Avian Influenza Registry

Potential adverse events of interest were identified from the claims using ICD-9 codes, patients were followed from the index date until the first occurrence of the event of interest, end of 1-year follow-up period, or discontinuation from the health plan. The incidence rate (IR) and 95% confidence interval (CI) for each adverse event during a 1-year follow-up period were estimated.

**Results:** A total of 4,732 treated and 26,763 non-treated CHC patients were identified during the study period. Treated CHC patients have more patients with comorbidities such as hypertension, malignancy (non liver-biliary) and depression at baseline. The most common adverse event in treated CHC patients was hematologic abnormalities (IR: 17.7/100 person-years; 95% CI: 16.4–19.1). Other common adverse events were skin disorders (IR: 15.8/100 person-years; 95% CI: 14.6–17.1), GI toxicity (IR: 10.7/100 person-years; 95% CI: 9.7–11.7), and hepatic abnormalities (IR: 8.5/100 person-years; 95% CI: 7.6–9.4). Common adverse events in non-treated CHC patients were hepatic abnormalities (IR: 28.8/100 person-years; 95% CI: 28.1–29.5), and GI toxicity (IR: 10.5/100 person-years; 95% CI: 10.1–10.9).

**Conclusions:** Data from this study provides a comprehensive picture of the CHC patient profile in the real world medical care.

440. **Multiple Imputation: Application to a Global Avian Influenza Registry**

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**Background:** The avian flu registry collects data on cases of this highly pathogenic disease from across the globe for the purpose of understanding clinical presentation and treatment effectiveness. Due to the observational study design, information in source documents varies widely, resulting in substantial missing data. The number of cases available for an analysis of time-to-treatment and mortality was substantially reduced because of missing date values.

**Objectives:** Apply multiple imputation (MI) methods in a complex setting to reduce potential bias and improve the precision of estimates originally produced by complete-case (CC) analysis.

**Methods:** The Registry is a retrospective study containing laboratory-confirmed cases of influenza A/H5N1 infection from clinical records, published case series, and administrative reports in 12 countries. Key analyses (n = 282) compare outcomes in (a) patients who initiated treatment with the antiviral oseltamivir in 5 symptom-to-treatment time intervals with (b) patients who were eligible but did not initiate treatment in each interval. PROC MI (SAS 9.2) was used to impute exposures for 61 patients who were missing a critical date. Predictors included country, sex, symptoms, facility type, viral exposure and outcome. Risk ratios (RR) and 95% confidence intervals (CI) from the CC analysis were compared with MI results. The sensitivity of the RR was examined with respect to the coding of treatment status (binary vs. categorical) and rounding during imputation.

**Results:** Adjustments to SAS imputation procedures were required, including singular coding of each imputation iteration and timing constraint based on results from previous imputations, and manual calculation of summary estimates from each imputed dataset. CC vs. MI estimates were 4.17 (2.65, 6.55) vs. 3.02 (2.01, 4.55) for 0–2 days and 1.77 (1.11, 2.83) vs 1.87 (1.41, 2.48) for 3–5 days. Neither sensitivity analysis appreciably changed the RR.

**Conclusions:** MI results were generally consistent with CC analysis, but had tighter CI. Results were robust to varying approaches to MI implementation. We conclude that MI is a valid methodological approach for handling missing data in this complex setting.

441. **Association between Antidepressant Drugs and Cancer in the UK-Based General Practice Research Database: A Cohort Study**


**Background:** There has been a concern based on both human and experimental studies that antidepressants might cause or promote some types of cancer. Several epidemiological studies have examined the potential association of antidepressants with cancer, yet the association has not been confirmed.

**Objectives:** To examine the association between antidepressant drugs including Selective Serotonin Reuptake Inhibitors (SSRIs), Tricyclic Antidepressants (TCAs), and other antidepressants and the risk of cancer.

**Methods:** A cohort of new users of antidepressants aged 18+ were identified using the U.K General Practitioner Research Database (GPRD) during the period 1990 to 2010. The primary outcome will be incident cases cancer

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