Comparing the impact of clean windows across cohorts and databases

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Background

In cohort studies we often rely on selection strategies to eliminate bias within a population of interest. New user designs often utilize a clean window in observational data to remove prevalent cases(1). These clean periods of observed person-time allow for the removal of prior exposures (conditions, drugs or procedures) within a cohort(2). The selection of this time can vary based on design of the study, prior knowledge, or random assignment by researchers. The trade offs between longer and shorter time periods vary, while shorter time periods allow for additional patients or events to enter the cohort, this decision may reduce the precision in the identification of new events. In this study we examine the trade-offs between various time-windows for a clean window to identify new events within a phenotype across a variety of databases.

Methods

The initial phenotypes used in this analysis are ten event-based cardiac condition cohorts. The phenotypes include acute myocardial infarction, myocarditis/pericarditis, deep vein thrombosis, pulmonary embolism, disseminated intravascular coagulation, non-hemorrhagic stroke, hemorrhagic stroke, cerebral venous thrombosis, peripheral thrombosis, and thrombosis with thrombocytopenia. For each of these phenotypes the following clean windows were applied: 0, 28, 180, and 365 days. The cohorts were developed in ATLAS and evaluated using the CohortDiagnostics (CD) package. Figure 2 illustrated how clean windows were applied in ATLAS. Custom code was written to compare the number of events per person identified across the database. The number of events was capped at 10 events per phenotype/washout period cohort. The databases used in this study included Optum© De-Identified Clinformatics® Data Mart Database – Date of Death-(DOD) (Optum DOD) dataset, IBM MarketScan® Databases [Commercial Claims (CCAE), Medicaid (MDCD) and Medicare (MDCR)] and Optum® de-identified Electronic Health Record Dataset (Panther).

Results

The results presented only include 5 of 10 phenotypes for a single database (CCAE) for brevity. The total number of persons with at least 365 days clean window in each phenotype are show in Table 1. The percentage of persons with a single event in each phenotype for each cohort shows the sharpest increase from 0 to 28 days between ~15% to 30% depending on the phenotype. The change between using a washout of 180 days to 365 days displays the smallest change ~1%-8%. The distribution of events (Figure 2) for each cohort show a similar pattern across phenotypes; they show the steepest decline from 1 event to 2 events irrespective of time period, and the distribution coverages faster to 0 as clean window time is increased. DVT events showed the smallest change of events over time compared to hemorrhagic stroke.

Conclusions

Clean windows in cohort studies play an important role in eliminating prevalent cases for accurate identification of new events. This analysis highlights the need to consider this diagnostic when building a cohort. The results from these cardiac conditions show wide variability among them and highlight the need for careful consideration in a study design. Further areas of exploration include exploration of additional time windows and other phenotypes over a broader set of databases. Plausibility of events occurring in observational data and identification of new events or continuation of care from a prior event should be carefully evaluated for conditions that could have reoccurrence.

Table 1. Percentage of persons with a single event by washout period cohort and phenotype (CCAE)

Phenotype	(N)	Washout time (days)			
		0	28	180	365
Hemorrhagic Stroke	117,431	59.36%	90.77%	97.44%	98.60%
Non-hemorrhagic stroke	365,925	66.17%	86.09%	93.04%	95.30%
Deep vein thrombosis	757,852	44.15%	61.04%	83.22%	89.99%
Pulmonary embolism	419,227	37.43%	56.28%	82.81%	90.55%
Acute myocardial infarction	511,199	70.43%	87.74%	94.12%	95.57%

Figure 1. Clean window implementation in ATLAS example for DVT (28 days)

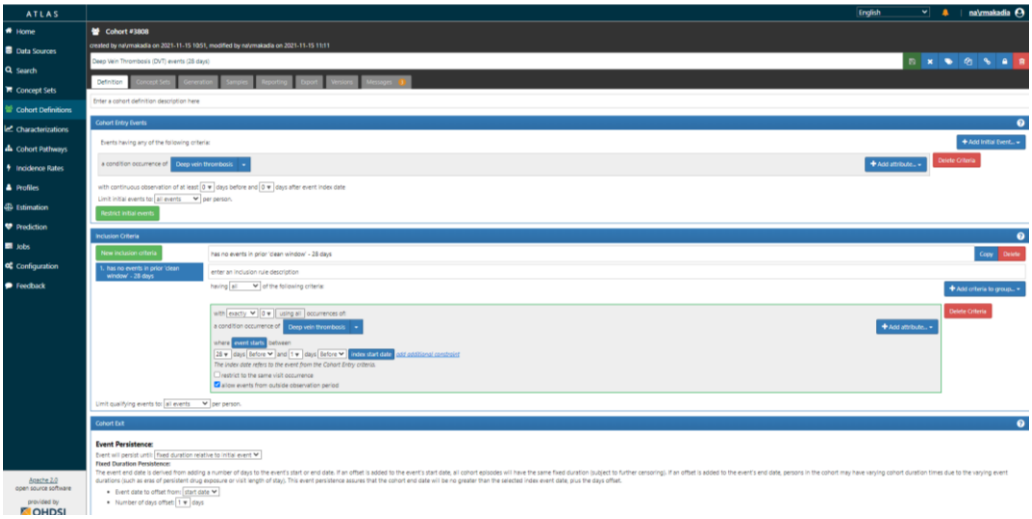
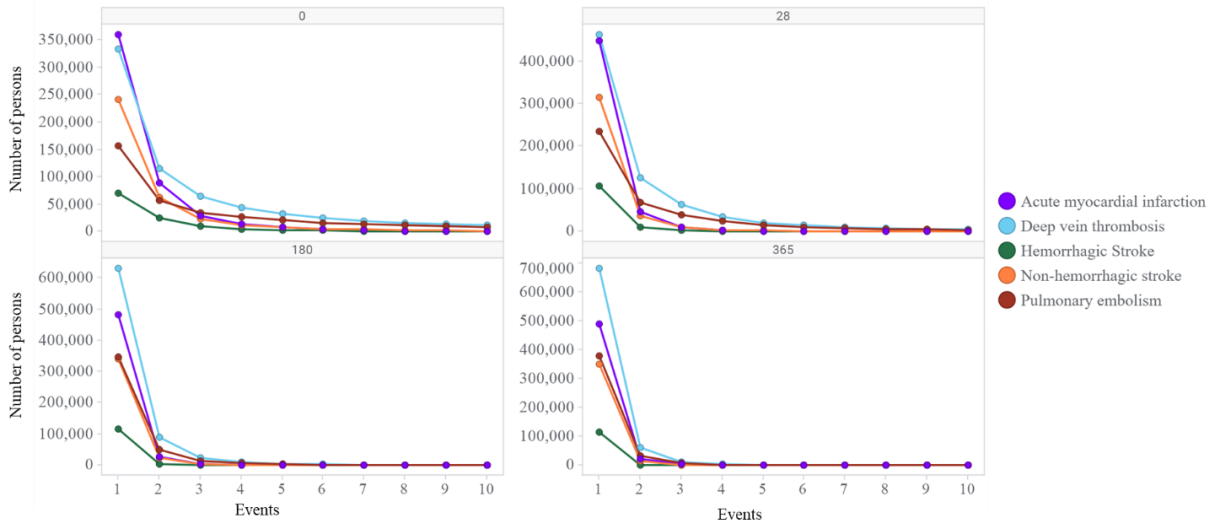


Figure 2. Distribution of total persons (y-axis) by number of events (x axis) for each washout period cohort (trellis) and phenotype (color) (CCAE)



References

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2. Johnson ES, Bartman BA, Briesacher BA, Fleming NS, Gerhard T, Kornegay CJ, et al. The incident user design in comparative effectiveness research. Pharmacoepidemiology and drug safety. 2013;22(1):1-6.