Estimating antibiotic exposure in retrospective primary care data: what should we measure and how?

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Background

Antibiotic exposure has been commonly measured as the number of prescriptions over a period of time. However, the focus on prescribing frequency ignores substance strength or pack size.

Defined daily doses (DDD) account for those differences. Using DDDs with appropriate models might provide a better measure of antibiotic exposure than just the frequency of prescribing.

> *"The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults."*
>
> *World Health Organisation definition*

Methods

Systemic antibiotic prescribing (ATC J01) records from English primary care were extracted from the Clinical Practice Research Datalink (CPRD) database for 2013-2015.

Comorbidities mentioned in antibiotic guidelines were identified based on diagnostic Read codes.

Hierarchical negative binomial regression with and without zero inflation were used to estimate associations between comorbidity and yearly antibiotic prescribing.

	Negative binomial model		**Zero-inflated negative binomial model**			
			Logistic part		Neg. binom. part	
	RR	95%-CI	OR	95%-CI	RR	95%-CI
Asthma	1.94	1.85-2.03	1.76	1.72-1.81	1.18	1.15-1.21
Chronic kidney disease	1.35	1.26-1.46	1.30	1.25-1.36	1.04	1.01-1.08
Chronic obstructive pulmonary disease	4.19	3.77-4.65	3.49	3.27-3.71	1.75	1.68-1.82
Diabetes	1.55	1.45-1.65	1.39	1.34-1.44	1.10	1.06-1.13
Heart failure	1.56	1.34-1.82	1.54	1.41-1.68	1.09	1.03-1.16
Peripheral arterial disease	1.30	1.12-1.52	1.26	1.15-1.37	1.03	0.96-1.10
Stroke	1.51	1.37-1.67	1.41	1.33-1.49	1.11	1.06-1.16
Interpretation	Increase in prescr. due to comorbidity		Increased likelihood of receiving at least one antibiotic		Increased amount of antibiotics if one was prescribed	

Table: Rate ratio (RR) estimates for number of DDDs/year in a conventional negative binomial model (NB) compared to joint RR and odds ratio (OR) estimated from a zero-inflated negative binomial (ZI)

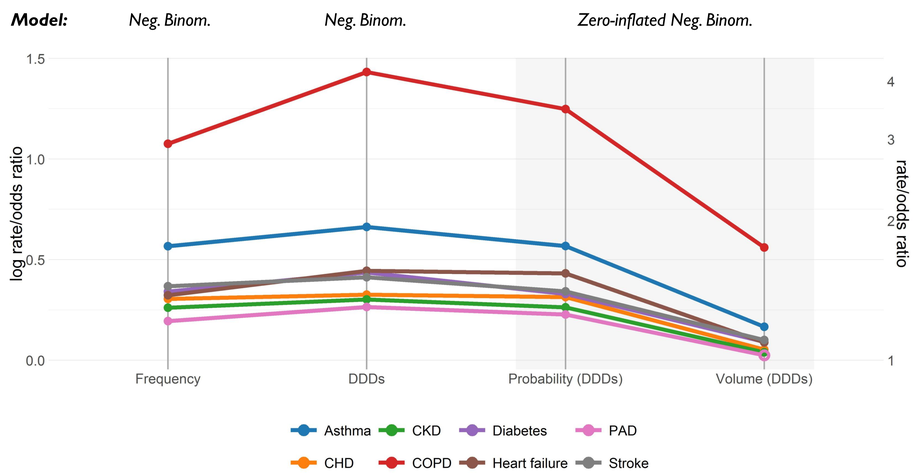

Figure: Comparison of the effect sizes using rate of prescribing (RR with NB), rate of DDDs (RR with NB), and joint estimation of probability of prescribing and rate of DDDs (OR and RR with ZI)

Results

All considered comorbidities increased the rate of antibiotic prescribing.

Using DDDs instead of number of prescriptions increased the estimated rate ratios considerably in asthma patients (1.94; 1.85-2.03) and COPD patients (4.19; 3.77-4.65).

Zero inflation models suggested that most comorbidities increased the rates of prescribing via a higher likelihood that a patient receives at least one antibiotic in any given year. Only COPD (1.75; 1.68-1.82) also notably affected the number of DDDs that a patient received within a year.

Conclusion

Using DDDs allowed us to show that increased prescribing in comorbid patients can be explained by a larger percentage of the population that receive moderate numbers of antibiotics.

Respiratory comorbidities additionally increased the volume of prescribing, suggesting a more common use of intensive or long-term treatment in this group.

Conflicts of interest

AH, NF and LS received funding for this project from the UK Economic and Social Research Council; LS received research grants from the UK National Institute for Health Research, and PR is employed as a research assistant in said grant. No author reports potential conflicts of interest.