

**ORIGINAL REPORT**

WILEY

Using the waiting time distribution with random index dates to estimate prescription durations in the presence of seasonal stockpiling

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Abstract

Purpose: A pervasive problem in registry-based pharmacoepidemiological studies is what exposure duration to assign to individual prescriptions. The parametric waiting time distribution (WTD) has been proposed as a method to estimate such durations. However, when prescription durations vary due to seasonal stockpiling, WTD estimates will vary with choice of index date. To counter this, we propose using random index dates.

Methods: Within a calendar period of a given length, δ , we randomly sample individual index dates. We include the last prescription redemption prior to the index date in the analysis. Only redemptions within distance δ of the index date are included. In a simulation study with varying types and degrees of stockpiling at the end of the year, we investigated bias and precision of the reverse WTD with fixed and random index dates, respectively. In addition, we applied the new method to estimate durations of Norwegian warfarin prescriptions in 2014.

Results: In simulation settings with stockpiling, the reverse WTD with random index dates had low relative biases (−0.65% to 6.64%) and high coverage probabilities (92.0% to 95.3%), although when stockpiling was pronounced, coverage probabilities decreased (2.7% to 85.8%). Using a fixed index date was inferior. The estimated duration of warfarin prescriptions in Norway using random index dates was 131 (130; 132) days.

Conclusions: In the presence of seasonal stockpiling, the WTD with random index dates provides estimates of prescription durations, which are more stable, less biased and with better coverage when compared to using a fixed index date.

KEYWORDS

maximum likelihood, parametric modelling, pharmacoepidemiology, prescription duration, seasonal variation, waiting time distribution

1 | INTRODUCTION

Assigning prescription durations from routinely collected data on prescription redemptions is fundamental to several types of studies in pharmacoepidemiology. Unfortunately, many data sources do not hold information on the days' supply or the prescribed daily dose. Instead, the prescription duration has to be inferred, for example, from patterns of prescription renewal. The parametric waiting time distribution (WTD) is a method, which allows estimation of durations without use of decision rules.¹⁻³ The WTD is based on renewal process theory and yields similar results regarding durations using both the ordinary and reverse WTD. A key requirement for this method is that the index date is chosen independently of the individual redemption processes. This assumption is violated when prescription durations have markedly different distributions over the year, for example, due to stockpiling at the end of the year. Such stockpiling has been observed in Norway, where the patient pays for medical services during the year up to a certain limit, after which medications become free of charge for the remainder of the year.⁴ By using January 1st as index date, we would expect this stockpiling to result in shorter estimated durations when using the reverse WTD instead of the ordinary WTD. In fact, if we were to use different fixed index dates over the year, we would obtain varying estimates of treatment durations in such a scenario.

To ensure that the index date is chosen independently of the individual processes of prescription redemptions, we propose to pick uniformly distributed individual index dates over a pre-specified sampling period, for example, a calendar year. We then use the ordinary or reverse WTD to analyze either the time to the first subsequent or the time since last preceding prescription relative to their individual random index date for all individuals. With the random sampling of individual index dates we utilize information over the entire sampling period, and thus obtain a marginal estimate of the duration for the entire period. We further expect estimates of prescription redemptions based on the ordinary and reverse WTD to be more similar with random sampling of index dates. Although we in this paper compare the ordinary WTD to the reverse WTD, our main focus is on the reverse WTD as it is the more flexible version since it allows covariates.¹

We first describe the new random sampling procedure with respect to the sampling window and the need for data in an adjacent window. We then investigate the performance of the method in simulation studies, where we induce stockpiling at the end of the year due to either larger or more frequent redemptions. Finally, we apply the method to Norwegian data on prescription redemptions of warfarin, to assess whether stockpiling occurs at the end of the year, and we investigate whether the new method can reliably estimate prescription durations.

2 | METHODS

The ordinary and reverse WTDs have been introduced in previous papers together with examples of how to apply these parametric

Key Points

- Many pharmacoepidemiological databases do not record information on prescription duration
- The reverse Waiting Time Distribution (WTD) considers the last prescription of each patient before an index time point
- The reverse WTD with a fixed index date is misspecified if there is seasonal variation in redemption rates, for example, if stockpiling at the end of the year
- The reverse WTD with random index dates provides estimates with low relative bias and near-nominal coverage if the mixture of inter-arrival densities (IADs) does not consist of distinctly different single IADs
- Estimates can be found in Stata using the publicly available-wtdttt-package

models to real world data.^{2,3} The two WTDs resemble each other and both rely on an observation window, often a single calendar year. Both are two-component mixture distributions, each consisting of a prevalent component and either an incident or a stopping component (Appendix, Figure A1). For the ordinary and reverse WTD, the forward recurrence density (FRD) or backward recurrence density (BRD), respectively, models the prevalent component of the distribution. Both recurrence densities are related to the inter-arrival density (IAD) with distribution function F and mean M through the formula

$$g(r; \theta) = \frac{1 - F(r; \theta)}{M}.$$

Here r is either time to next redemption after the index time (ordinary WTD) or time from last redemption to the index time (reverse WTD).

Instead of a fixed index date, we now suggest to sample a random index date, t_{0i} , for each individual, i , within a sampling window of length δ . Based on the sampled index date, we define an individual observation window, that is, $(t_{0i}; t_{0i} + \delta)$ for the ordinary WTD and $(t_{0i} - \delta; t_{0i})$ for the reverse WTD. For convenience, we let the sampling window of the random index dates equal the length of the individual observation windows, which we suggest fixing at 1 year in applications. As in the fixed index date version, we proceed by considering the time from each person's individual index date until the first prescription redemption (ordinary WTD) or time from last prescription until their individual index dates (reverse WTD) within each person's individual observation window. Then, after aligning all index dates by individually shifting the time scales, we use the same estimation procedure for prescription durations as has been described in previous papers for the parametric WTD. Following this approach, we express prescription durations as the

time within which 80% of the current users have redeemed a new prescription, $\tau_{80\%}$, that is, the 80% percentile of the IAD. Since the location of the individual observation windows varies with the sampled index dates, we need the full data window to be wide enough to contain all individual observation windows, that is, length 2δ .

3 | SIMULATION STUDIES

We evaluated the performance of the proposed methods in four scenarios with varying degrees of misspecification, as briefly described below—for details see the Appendix. All scenarios assume that patients have a treatment episode consisting of a sequence of prescription durations. The prevalence of treated patients is assumed constant over time due to a constant incidence rate and a stable distribution of the length of treatment episodes. The durations of treatment episodes vary independently of the distribution of prescription durations within the treatment episode as described below. For convenience in the simulations stockpiling can occur in the same way for both prevalent and incident users initiating treatment in the stockpiling period.

3.1 | Scenario 0: No stockpiling and constant probability of each prescription redemption within a treatment episode being the last

We assume no stockpiling at the end of the year and hence the same distribution of prescription durations within all patients' treatment episodes throughout the year. We further assume that each prescription redemption has a constant probability of being the last in a treatment episode.

3.2 | Scenario 1: No stockpiling and Log-Normally distributed durations of treatment episodes

As Scenario 0, only now we assume that treatment episodes have Log-Normally distributed durations, which induces misspecification.

3.3 | Scenario 2: Stockpiling due to larger redemptions at the end of the year and Log-Normally distributed durations of treatment episodes

As Scenario 1, only now we introduce stockpiling at the end of the year such that all prescriptions redeemed in the last 2 months of a year are larger, and hence have longer durations to next prescription, than prescriptions redeemed in the first 10 months. The degree of stockpiling is related to how distinctly different the two IADs are.

3.4 | Scenario 3: Stockpiling due to more frequent redemptions at the end of the year and Log-Normally distributed durations of treatment episodes

As Scenario 2 but now stockpiling occurs due to more frequent redemptions at the end of the year. Stockpiling can occur in the last 2 or 3 months of the year and only for patients with at least two prescription redemptions within this period. In this stockpiling period, patients who stockpile have shorter average durations to next prescription except for their last prescription of the year, which has longer average duration than any other prescriptions of the year.

Let IAD_1 and IAD_2 denote the Log-Normal IADs for prescriptions redeemed in periods without and with stockpiling, respectively. For Scenario 3 we further have IAD_3 , which denotes the Log-Normal IAD for the last prescription of the year redeemed after stockpiling.

Simulated datasets are analyzed using the ordinary and reverse WTD with both random index dates and the start of the stockpiling period and the end of the year as fixed index dates. The prevalent component of the WTD corresponds to a single Log-Normal IAD. We estimate the relative bias, root mean square error and coverage probability of nominal 95% confidence intervals of the estimates of $\tau_{80\%}$ for each setting.

4 | APPLICATION

In the empirical analysis we used Norwegian data on prescription redemptions of warfarin in the period from 2013 to 2015.⁵ We applied the new method with random index dates between January 1st and December 31st 2014, as well as the versions of WTD with November 1st 2014 and January 1st 2015 as fixed index dates.

All statistical analyses were conducted in Stata 15.1.⁶ A dedicated software package (wtdttt) implementing the method is provided at the IDEAS repository (<http://ideas.repec.org>) and may be installed in Stata using a search for the package name, that is, `-search wtdttt, all-`.

5 | RESULTS

5.1 | Simulation studies

Results based on analyses of simulated data (annual period prevalence of $n = 5,000$) made with the reverse WTD are shown in Table 1. Similar results were found for $n = 1,000$ and $n = 15,000$ and are hence not presented here (Appendix, Table A1-A2). Note, however, that when there is misspecification in the model, the coverage probability decreases substantially as sample size increases, as would be expected. Further, the ordinary WTD with random index dates yielded results very similar to the reverse WTD with random index dates (Appendix, Table A3-A5).

For Scenario 0, the simulated data were analyzed with a correctly specified model in all WTD versions, which was a single Log-Normal

TABLE 1 Simulations results for four different types of scenarios analyzed with the reverse waiting time distribution (WTD) with a Log-Normal backward recurrence density (BRD)

Scenario	IADs concerning stockpiling						True IAD 80% percentile (days)	Random index date			End of year as index date			Beginning of stockpiling period as index date		
	M1	M2	M3	VF3	MoS	VF3		RB (%)	RMSE (days)	CP (%)	RB (%)	RMSE (days)	CP (%)	RB (%)	RMSE (days)	CP (%)
	VF1	VF2	M3	VF3	MoS	VF3		RB (%)	RMSE (days)	CP (%)	RB (%)	RMSE (days)	CP (%)	RB (%)	RMSE (days)	CP (%)
0	1.5	1.5	-	-	-	-	54.3	-0.02	0.5	94.8	-0.02	0.5	95.2	-0.00	0.6	93.8
0	2	1.5	-	-	-	-	72.5	-0.04	0.7	94.8	-0.03	0.8	94.4	-0.02	0.8	94.2
0	3	1.5	-	-	-	-	108.7	-0.07	1.3	94.6	-0.02	1.3	94.9	-0.01	1.3	94.6
1	1.5	1.5	-	-	-	-	54.3	-0.21	0.5	94.5	-0.22	0.6	94.0	-0.23	0.6	93.7
1	2	1.5	-	-	-	-	72.5	-0.32	0.8	93.5	-0.25	0.8	95.0	-0.27	0.8	94.2
1	3	1.5	-	-	-	-	108.7	-0.40	1.3	93.6	-0.38	1.3	92.6	-0.47	1.4	91.4
2	1	2	1.5	2	-	2	44.1	-0.28	0.6	93.9	36.96	16.3	0.0	-7.54	3.4	0.0
2	1	1.5	1.5	1.5	-	2	39.1	0.97	0.6	85.8	46.03	18.0	0.0	-7.59	3.0	0.0
2	1	1.5	1.5	2	-	2	38.6	2.76	1.2	39.8	55.56	21.5	0.0	-6.38	2.5	0.0
2	1.5	2	2	-	-	2	64.9	-0.65	1.0	92.0	5.64	3.8	0.2	-5.95	3.9	0.4
2	1.5	1.5	2	1.5	-	2	57.6	0.09	0.6	95.0	7.53	4.4	0.0	-5.84	3.4	0.0
2	1.5	1.5	2	2	-	2	57.4	1.44	1.1	77.7	8.23	4.8	0.0	-5.58	3.3	0.0
2	1.5	2	3	2	-	2	71.0	0.32	1.2	95.3	-3.09	2.6	30.4	-13.97	10.0	0.0
2	1.5	1.5	3	1.5	-	2	61.7	6.01	3.8	3.4	-0.55	0.6	32.5	-12.17	7.5	0.0
2	1.5	1.5	3	2	-	2	60.8	6.64	4.2	2.7	1.16	0.9	3.1	-10.76	6.6	0.0
3	1.5	1.5	1	1.5	2	1.5	55.0	-0.21	0.6	94.5	-36.23	19.9	0.0	-1.39	0.9	69.2
3	1.5	1.5	1	1.5	2	1.5	55.3	-0.50	0.7	92.8	-34.84	19.3	0.0	-1.95	1.2	48.9
3	1.5	2	1.5	2	1.5	2	106.3	-0.42	1.4	93.0	0.19	1.3	94.4	2.67	3.0	27.2
3	1.5	2	1.5	2	1.5	3	108.2	-0.87	1.7	89.1	-32.29	35.0	0.0	-2.74	3.2	28.7

No stockpiling (Scenario 0 and 1) and stockpiling at the end of the year due to either larger redemptions (Scenario 2) or more frequent redemptions (Scenario 3). Stockpiling can occur in the last 2 or 3 months of the year. For all four scenarios on average 25% are stopping treatment within a one-year period. For Scenario 0 there is a constant probability of ending treatment and for Scenario 1, 2 and 3 the duration of the treatment episodes are Log-Normally distributed with a mean of 3 years and a SD of 2 years. Prescriptions redeemed in periods without and with stockpiling follows IAD₁ and IAD₂, respectively. For Scenario 3 the last prescription after stockpiling follows IAD₃. All IADs are Log-Normal and are specified by their median and variation factor. A variation factor of 1.5 means that the 97.5% percentile of the density is 1.5 times the median. The simulated data for the different scenarios are all analyzed using three different versions of the reverse WTD: with random index dates, January 1st as fixed index date and November or October 1st as fixed index date. For each scenario 2500 datasets were simulated with an annual period prevalence of 5000.

M is the median in months.

VF is the variation factor.

MoS is the number of months of stockpiling.

RB is the relative bias and is computed as the average relative difference between the estimated 80th percentile and the true 80th percentile.

RMSE is the root mean square error of the estimates around the true value of the 80th percentile.

CP is the coverage probability defined by the percentage of nominal 95% confidence intervals, obtained by the normal approximation, containing the true 80th percentile.

IAD. Hence, all three WTD methods had a low relative bias (-0.07% to -0.00%) and near-nominal coverage (93.8% to 95.2%). The root mean square errors (RMSE) were 0.5 to 1.3 days implying that the 80th percentile of the IAD can be estimated within approximately ± 1 day of the true values when the model is correctly specified.

In Scenario 1, all three WTD methods suffer from misspecification due to the mechanism that induces stopping. Consequently, all three methods have slightly higher relative biases (-0.47% to -0.21%) and RMSEs (0.5 to 1.4 days), and somewhat lower coverages (91.4% to 95.0%) as compared to Scenario 0.

For the settings with stockpiling (Scenario 2 and 3), data is generated from two or three separate Log-Normal IADs, whereas the WTD methods all use a recurrence density corresponding to a single Log-Normal IAD. This induces further misspecification using both random and fixed index dates.

Using a random index date for each patient led to low relative biases (-0.87% to 0.32%), low RMSEs (0.6 to 1.7 days) and near-nominal coverage (89.1% to 95.3%) when the IADs are not very different and the mixture of the two or three IADs resemble a single IAD (Appendix, Figure A2-A6). This is the case in Scenario 2 when both distributions have the highest variation factor (2); when the two medians are close to each other (1.5 and 2 months) and they have the same variation factor; and in all settings of Scenario 3. In the settings of Scenario 2 where the two distributions are markedly different, the relative biases (0.97% to 6.64%) and RMSEs (0.6 to 4.2 days) are slightly higher, but still lower than when using a fixed index date. However, nominal coverage is not retained here (2.7% to 85.8%).

When using fixed index dates, performance depends on the choice of index date. For example, using the end of the year as index date gave low relative bias (-0.55%) in the setup of Scenario 2 with the largest difference in medians and lowest variation factors, but when using the start of the stockpiling period as index date a substantial relative bias of -12.17% was obtained. Also note that both of the fixed index dates still led to low coverage probabilities. Hence, in scenarios with seasonal stockpiling the WTD model is clearly misspecified, cf. diagnostic plots (Appendix, Figure A7) and its occasional good performance appears to be coincidental. For Scenario 3 most redemptions occur without stockpiling and hence the mixture of the three IADs resembles IAD₁ and a lower relative bias is seen (absolute values from 1.39% to 2.74%), when using the beginning of the stockpiling period as the index date.

5.2 | Empirical study

The 80th percentiles for prescription durations of warfarin in Norway, 2013-2015, were estimated with the ordinary and reverse WTD with both fixed and random index dates (Table 2). Using January 1st, 2015 as the index date the 80th percentile was estimated at 161.1 (159.7; 162.5) and 100.8 (99.7; 101.9) days for the ordinary and reverse WTD respectively. Since the ordinary and reverse estimates differ substantially, it appears that there is a seasonal variation in the prescription redemptions. This is further supported by using November 1st as index date in an analysis based on the reverse WTD, which yielded an estimate of the 80th percentile of 121.7 (120.6; 122.9) days. The reverse WTD with random index dates gave an estimate of 131.0 (129.8; 132.3) days which is higher than the estimates obtained with the reverse WTD based on either of the fixed index dates. The ordinary WTD with random index dates resulted in an estimate of 133.8 (132.6; 134.9), which is similar to the reverse WTD with random index dates.

6 | DISCUSSION

In settings without stockpiling at the end of the year, using the WTD with random or fixed index dates led to similar estimates with low relative bias and near-nominal coverage. For settings with stockpiling, estimates based on random index dates generally had lower relative bias and higher coverage probabilities than using a fixed index date. In the case with seasonal stockpiling due to larger redemptions, the estimates based on random index dates had low relative bias and near nominal coverage when the two IADs were similar. For seasonal stockpiling due to more frequent redemptions at the end of the year, all estimates based on random index dates had low relative bias and near-nominal coverage.

The primary advantage of randomly sampling individual index dates is the use of information from prescriptions across the entire sampling window. This essentially smooths the possible variations in prescription redemption patterns throughout the year, since periods with shorter prescription durations are combined with periods with longer. The approach is simple, since after aligning the individual index dates, we can use the previously developed parametric WTD to obtain an estimate of the 80th percentile of the prescription duration. Due to the sampling, the estimate is marginal and can be interpreted as the average prescription duration within the sampling period.

TABLE 2 Estimated 80th percentiles for prescription durations of warfarin in 2013-2015

n	WTD	Index date	Estimated 80th percentile in days (95% CI)
69 207	Ordinary	Fixed, Jan 12 015	161.1 (159.7; 162.5)
77 674	Reverse	Fixed, Jan 12 015	100.8 (99.7; 101.9)
79 850	Reverse	Fixed, Nov 12 014	121.7 (120.6; 122.9)
82 867	Reverse	Random	131.0 (129.8; 132.3)
73 896	Ordinary	Random	133.8 (132.6; 134.9)

Note: Both the ordinary and reverse waiting time distribution (WTD) used a Log-Normal forward/backward recurrence density for the prevalent component. The WTD is used with both fixed index dates and with a random index date for each patient sampled uniformly between January 1st, 2014 and December 31st, 2014.

The new method has limitations similar to the previous versions using fixed index dates, that is, it ignores censoring and it is sensitive to misspecification.¹⁻³ The first limitation implies that hospitalizations, emigrations and deaths are not taken into account, which may lead to inflated durations or contribute to the estimated fraction of stopping. The events are however comparatively rare following a randomly chosen prescription and they will therefore likely have a limited impact on estimated durations. The second limitation is that although we randomly sample index dates we still have misspecification in the presence of seasonal stockpiling since we use a single IAD to fit a mixture of IADs. In the simulation settings, with stockpiling due to larger redemptions, we considered a two-component mixture of IADs, which is likely extreme. More realistically, the mixture will consist of gradually changing durations over the year and then we would expect the marginal density to be smoother without distinctly different peaks. This was apparent when we considered three-component mixtures in the settings with stockpiling due to more frequent redemptions. In practice, incident patients probably would not stockpile right after having initiated treatment in a stockpiling period and a stockpiling period of 3 months might be too extreme. Both shorter stockpiling periods and no stockpiling of incident users would result in comparatively fewer stockpiling redemptions and hence the marginal mixture density will be less affected by this smaller stockpiling component. In our simulations this is evident, since the model performs better when stockpiling is only possible in the last 2 months as compared to 3. This trend is continued when the stockpiling period is shortened to 1 month (results not shown, available upon request). We can therefore expect the method based on randomly sampled index dates to perform even better with shorter stockpiling periods, gradually increasing stockpiling or other more fluent types of seasonal variation. We expect such settings to be frequent in practice. Although using random index dates led to lower relative bias, lower RMSE and higher coverage, coverage probabilities were still quite low and relative biases high whenever the IADs were substantially different from each other. Hence, it is important to make diagnostic plots of the empirical distribution to examine how well the parametric WTD fits the empirical distribution.

Often prescription durations are not recorded in pharmaco-epidemiological databases and durations will then have to be estimated. Commonly, prescription and treatment episode durations are estimated based on decision rules that assume consumption of, for example, a defined daily dose or one tablet per day. In a recent development the second generation method PRE2DUP has been proposed for estimating durations of treatment episodes as it is more flexible than fixed decision rules.⁷ Instead of using the same fixed dosage assumption for everyone, PRE2DUP takes individual redemption histories into account, as well as stockpiling. In a validation study, assessment by two independent experts was compared to estimated treatment status based on using the PRE2DUP. In general, the method gave accurate estimates of treatment episode durations for most drugs with long-term usage. The method also works for drugs with seasonal variation and short-term usage, but then more predefined parameters are required. Since PRE2DUP estimates durations of treatment episodes, it only implicitly estimates prescription

durations. A similar decision algorithm was introduced by Williams et al.⁸ As the fixed decision rules, the second generation methods are based on decision algorithms and hence it is difficult to assess their general validity and improve them from general principles. By contrast, the WTD is explicitly model-based, which facilitates development from well-established statistical principles for model refinement. As with previous versions of the WTD, however, there is still uncertainty about the optimal choice of percentile, which is a topic to be explored in future research. In specific studies the choice should likely be made based on considerations regarding the impact of misclassification, see the discussion in Støvring et al. (2016).³

When there is stockpiling at the end of the year, it is relevant to revisit what we mean by the duration of a prescription, since we have different prescription durations over the year. If we were only interested in the duration of prescriptions redeemed in the period without stockpiling, we could obtain estimates with a low relative bias and high coverage probability if we knew the beginning of the period with stockpiling and used this date as our fixed index date for a WTD analysis. For example, if stockpiling solely occurred in November and December, then using November 1st as our fixed index date for the reverse WTD will lead us to only consider durations following prescriptions redeemed before November 1st and hence they will be from the IAD without stockpiling, assuming that no prescription durations exceed 10 months. However, in practice we will likely see gradually changing durations over the year and hence it is not straightforward to explicitly delimit the periods of stockpiling.

With the reverse WTD it is possible to estimate the effect of covariates on parameters in the model. In a scenario with seasonal variation, one could therefore consider using the time of the prescription redemption as a covariate. It is however not clear how this should be done.

In conclusion, we suggest using the ordinary or reverse WTD with a random index date to obtain estimates of the marginal prescription duration over a sampling period of interest, as this generally leads to better estimates in terms of bias and precision. Further work is needed to model seasonality in prescription durations due to stockpiling such that it becomes possible to provide explicit estimates of its magnitude.

ACKNOWLEDGEMENTS

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS STATEMENT

The Regional Committee for Medical and Health Research Ethics of South Eastern Norway has granted ethical approval for use of the Norwegian prescription data in the study (2010/131).

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REFERENCES

1. Støvring H, Pottegård A, Hallas J. Refining estimates of prescription durations by using observed covariates in pharmacoepidemiological databases: an application of the reverse waiting time distribution. *Pharmacoepidemiol Drug Saf.* 2017;26(8):900-908.
2. Støvring H, Pottegård A, Hallas J. Estimating medication stopping fraction and real-time prevalence of drug use in pharmaco-epidemiologic databases. An application of the reverse waiting time distribution. *Pharmacoepidemiol Drug Saf.* 2017;26(8):909-916.
3. Støvring H, Pottegård A, Hallas J. Determining prescription durations based on the parametric waiting time distribution. *Pharmacoepidemiol Drug Saf.* 2016;25(12):1451-1459.
4. Kjerpeseth LJ, Selmer R, Ariansen I, Karlstad Ø, Ellekjær H, Skovlund E. Comparative effectiveness of warfarin, dabigatran, rivaroxaban and apixaban in non-valvular atrial fibrillation: a nationwide pharmaco-epidemiological study. *PLoS One.* 2019;14(8):e0221500.
5. Furu K. Establishment of the nationwide Norwegian prescription database (NorPD)—new opportunities for research in pharmaco-epidemiology in Norway. *Nor Epidemiol.* 2008;18(2):129-136.
6. StataCorp. *Stata Statistical Software: Release 14.* College Station, TX: StataCorp LP; 2015.
7. Taipale H, Tanskanen A, Koponen M, Tolppanen A-M, Tiihonen J, Hartikainen S. Agreement between PRE2DUP register data modeling method and comprehensive drug use interview among older persons. *Clin Epidemiol.* 2016;8:363-371.
8. Williams R, Brown B, Peek N, Buchan I. Making medication data meaningful: illustrated with hypertension. *Stud Health Technol Inform.* 2017; 228:247-251.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Bødkergaard K, Selmer RM, Hallas J, et al. Using the waiting time distribution with random index dates to estimate prescription durations in the presence of seasonal stockpiling. *Pharmacoepidemiol Drug Saf.* 2020;1-7. <https://doi.org/10.1002/pds.5026>