Hypertension Treatment Intensification Among Stroke Survivors With Uncontrolled Blood Pressure

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Background and Purpose—We examined blood pressure 1 year after stroke discharge and its association with treatment intensification.

Methods—We examined the systolic blood pressure (SBP) stratified by discharge SBP (≤140, 141–160, or >160 mm Hg) among a national cohort of Veterans discharged after acute ischemic stroke. Hypertension treatment opportunities were defined as outpatient SBP >160 mm Hg or repeated SBPs >140 mm Hg. Treatment intensification was defined as the proportion of treatment opportunities with antihypertensive changes (range, 0%–100%, where 100% indicates that each elevated SBP always resulted in medication change).

Results—Among 3153 patients with ischemic stroke, 38% had ≥1 elevated outpatient SBP eligible for treatment intensification in the 1 year after stroke. Thirty percent of patients had a discharge SBP ≤140 mm Hg, and an average 1.93 treatment opportunities and treatment intensification occurred in 58% of eligible visits. Forty-seven percent of patients discharged with an SBP 141 to160 mm Hg had an average of 2.1 opportunities for intensification and treatment intensification occurred in 60% of visits. Sixty-three percent of the patients discharged with an SBP >160 mm Hg had an average of 2.4 intensification opportunities, and treatment intensification occurred in 65% of visits.

Conclusions—Patients with discharge SBP >160 mm Hg had numerous opportunities to improve hypertension control. Secondary stroke prevention efforts should focus on initiation and review of antihypertensives before acute stroke discharge; management of antihypertensives and titration; and patient medication adherence counseling.

Key Words: health services research ■ hypertension ■ medication adherence ■ secondary prevention

Having a stroke increases risk for recurrent stroke.1,2 Systolic blood pressure (SBP) remains the most modifiable risk factor for stroke and antihypertensive medications are efficacious in reducing SBP.3 Patients who experience a recent stroke may be more motivated to adhere to their medications and attain better risk factor control. Conversely, a recent study of patients with a stroke demonstrated that 25% had discontinued ≥1 secondary prevention medication within 3 months of hospital discharge.4

Given that hypertension is the risk factor with the greatest population attributable risk for stroke and is present in the majority of patients,5 we were interested in examining the patterns of hypertension management in the 1-year poststroke period. Uncontrolled SBP after a stroke may be related to a variety of factors including nonadherence, inappropriate medication selection, clinical inertia, or resistant hypertension refractory to treatment. The aim of this study was to determine whether some of these factors are associated with uncontrolled SBP. We determined the quality of hypertension care after a stroke by describing (1) the patient’s SBP trajectory after stroke; (2) antihypertensive treatment intensification (proportion of treatment intensification opportunities [denominator] associated with medication intensifications [numerator]); and (3) the association between patient adherence and treatment intensification. This first step was important to understanding factors that affect uncontrolled hypertension in the poststroke period and in designing interventions to improve risk factors among patients with ischemic stroke.

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Methods

Study Design and Data Sources
The Office of Performance Measurement Stroke Special Study was a retrospective cohort of Veterans admitted during fiscal year 2007 with a primary diagnosis of ischemic stroke, identified using a modified high-specificity algorithm of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes (n=5721 possible stroke events). A systematic sample of 5000 records that included all patients with ischemic stroke at hospitals with <55 stroke hospitalizations and an 80% random sample of patients at hospitals with >55 stroke hospitalizations were selected for abstraction. Because of this sampling, the number of patients per hospital ranged from 1 to 198 (mean=38 and SD, 28). Among the 307 data elements abstracted, 90% demonstrated good or very good inter-rater reliability (κ statistic ≥0.70). Abstracted data were linked to Veterans Health Administration (VHA) outpatient treatment and pharmacy files. Data on antihypertensive prescriptions dispensed included medication name, date filled, days supplied, quantity, and dosage. Vital signs data included all outpatient SBP measurements. Dates of death were obtained from VHA vital status files. For Medicare eligible Veterans, we obtained supplemental race data from the Centers for Medicaid and Medicare Services. The study received institutional review board approval.

Study Population
Veterans were excluded if the hospitalization was for rehabilitation, elective carotid endarterectomy, or another condition in which they experienced an in-hospital ischemic stroke. We excluded patients who died during their index hospitalization, had hospice or long-term care, or did not have postdischarge SBP values. We included SBP from the following clinics: internal medicine; primary care/medicine; women’s health; mental health primary care; geriatrics; hypertension; cardiology; anticoagulation; diabetes mellitus/endocrine; infectious disease; renal/nephrology; pulmonary/chest; or neurology. These clinics were chosen because these clinicians often manage BP by prescribing antihypertensive medications.

Outcome: Clinically Appropriate Treatment Intensification
Clinically appropriate treatment intensification was defined as the proportion of medication intensifications (numerator) to medication intensification opportunities (denominator) of elevated SBP in the year after stroke. This proportion could range from 0% to 100%, where 100% represented a patient wherein every elevated SBP opportunity resulted in medication intensification.

Antihypertensive Medication Intensification (Numerator)
Medication intensification occurred if a new antihypertensive was added, a dose was increased, or a medication switch occurred within 30 days of an opportunity. The date of the new prescription or dose change was the intensification date. For validation, we randomly reviewed 38 charts and correctly identified 12 of 12 patients who intensified therapy (positive predictive value 100%; 95% confidence intervals, 75.8–100). We also predicted 21 of 26 patients as not having intensified therapy (negative predictive value, 80.8; 95% confidence interval, 62.1–91.5). We missed 5 of 26 patients (20%) in which the provider told the patient to change the dose and did not alter the prescription.

Opportunities of Elevated BP (Denominator)
A visit was a potential intensification opportunity if it satisfied 1 of 3 criteria: (1) SBP >160 mm Hg, (2) the second of 2 consecutive visits where the SBP was >140 mm Hg, or (3) the SBP in which >50% of the preceding visits were >140 mm Hg. If multiple BP measures were recorded on the same day, then the lowest BP was used. We excluded SBPs considered data entry errors or improbable outpatient values, including diastolic BP >SBP, SBP <60 mm Hg, diastolic BP <30 mm Hg, or SBP minus diastolic BP <10 mm Hg.

To allow medication changes to take effect and assure that the SBP was not falsely elevated, we excluded opportunities within 30 days after medication changes. Because providers may request a repeat measurement on another day to confirm the elevated SBP, we excluded SBP measures between 141 and 160 mm Hg. If there were multiple BP measures recorded on the same day, then the lowest BP was used. We excluded SBPs considered data entry errors or improbable outpatient values, including diastolic BP >SBP, SBP <60 mm Hg, diastolic BP <30 mm Hg, or SBP minus diastolic BP <10 mm Hg.

Medication Adherence
Medications in the adherence assessment included the following classes: angiotensin-converting enzyme inhibitor or receptor blocker; β-blocker; diuretics (except furosemide); calcium channel blocker; and centrally acting antihypertensive or α-adrenergic antihypertensives. Furosemide was excluded given the potential for as needed use.

Medication adherence was computed using the medication possession ratio (MPR) defined by Steiner et al12 as a continuous, cumulative measure of days of therapy within a defined time horizon, ranging from 0 to 1. MPR is calculated as the number of days of therapy divided by the number of days at risk. A perfect adherence is represented by an MPR value of 1. The adherence measurement was based on the total number of days at risk and includes intervals of at least 7 days between visits.

Figure 1. Flowchart of participants.
multiple-interval measure of medication availability.13 An average of all drugs’ MPRs within a therapeutic class was computed to produce one averaged MPR accounting for medication stockpiling; average MPR was then dichotomized with noncompliance defined as <0.8.14 We calculated for each patient an MPR as the ratio of the number of days with antihypertensive available divided by the medication eligible days.12,13,16 The MPR ranges from 0 to 1, and higher values indicate greater adherence. For patients with 0 or 1 antihypertensive medication fill, their MPR was considered missing.

Statistical Analyses
Covariates were chosen based on clinical significance and included sex, race (white, black, and other), number of antihypertensives prescribed at the index stroke, National Institutes of Health Stroke Scale,17 and Charlson Comorbidity Score.18 We accounted for clustering of patients within medical centers because of the correlation of outcomes (level of hypertension control among patients from the same facility).

We used a mixed-effects regression model to examine the average SBP trajectory of all patients from stroke discharge during the 1 year after stroke stratified by their last SBP at discharge (≤140 mm Hg; 141 to ≤160 mm Hg; and >160 mm Hg). Then we analyzed treatment intensification among patients who had ≥1 elevated SBP (treatment opportunity) during the 1 year after stroke. For these analyses, we excluded patients with controlled SBP during the follow-up period (no treatment opportunities). We used linear regression to examine the association between adherence (MPR) and treatment intensification. Statistical analyses were done using SAS for Windows 9.2. (SAS Institute, Cary, NC).

Results
Of the 3965 patients with ischemic stroke, we excluded cases (n=812 [20.4%]) for in-hospital mortality (n=152), hospice care (n=44), or no SBP values (n=616; Figure 1). Sixty-two percent (n=1956) of the 3153 patients in the sample had no opportunities for treatment intensification because SBP was <140 mm Hg in the year after stroke. The remaining patients (n=1197) had ≥1 elevated SBP or a treatment intensification opportunity. Patients in both groups were aged 65 years and the majority were men (Table 1). Patients without treatment intensification opportunities did not differ in age, National Institutes of Health Stroke Scale, Charlson Score, or smoking status compared with those who had ≥1 intensification opportunities. A higher proportion of black patients (27.2%) had ≥1 intensification opportunity during follow-up versus those with no opportunities (20.6%).

BP Trajectory in the Year After Stroke
Among the 3153 patients who were discharged from an ischemic stroke hospitalization, 1973 (62.6%) had a discharge SBP <140 mm Hg, 819 patients (26.0%) with SBP between 141 and 160 mm Hg, and 361 patients (11.4%) with SBP >160 mm Hg (Table 2). The average SBP and diastolic BP increased among each of these 3 groups, with no difference in the average number of clinic visits (mean, 4.7; SD 3.8; P=0.18). When adjusted for covariates, the discharge SBP strongly influenced SBP trajectory during the following year (Figure 2).

Treatment Intensification Among Those With Elevated SBP
There were 1197 patients with ≥1 elevated SBP who had on average 6 clinic visits during follow-up. Thirty percent of patients discharged with a SBP ≤140 mm Hg had an average 1.93 opportunities for medication intensification. Forty-seven percent of patients with discharge SBP between 141 and 160 mm Hg had an average of 2.1 opportunities for intensification and 63% of patients with a discharge SBP >160 mm Hg had an average of 2.4 intensification opportunities. Because the number of medication intensifications also increased; the proportion of clinically appropriate treatment intensifications was similar between the 3 categories, ranging from 58% to 65% (P=0.15). In other words, in about one third of visits with elevated SBP, there was no evidence that medications were intensified (Table 3).

Relationship Between Adherence and Treatment Intensification
Among patients with ≥1 intensification opportunity, 48% were adherent (MPR >0.8) to their antihypertensive medications in the prestroke period and 46% were adherent in the
poststroke period. Alternatively, among those with an elevated SBP, >50% had an MPR <0.8 (indicating low adherence). There was no statistical difference in average MPR or in the proportion considered adherent across the 3 groups based on discharge SBP (Table 3). No relationship between medication adherence and treatment intensification ratio was detected ($P=0.71$; Figure 3). Patients with an MPR of 1 (excellent adherence) had a treatment intensification ratio of 0% (indicating no medication changes). Similarly, patients with an MPR of <0.3 (poor medication adherence) had treatment intensification ratios of 100% (every elevated SBP resulted in a medication change).

**Discussion**

We report 3 main findings. First, among patients hospitalized for ischemic stroke, SBP trajectory after stroke was highly influenced by discharge SBP. Second, regardless of discharge SBP, the ratio of medication intensification to opportunities is 58% to 65%. An alternate interpretation is that we did not see evidence of medication titration in 35% to 42% of visits among poststroke patients with elevated SBP values. Third, there was no relationship between poststroke medication adherence and treatment intensification evidenced by the ≈50% of patients with an elevated SBP in the poststroke period with an adherence level of <80%. This finding suggests that many patients would benefit from adherence counseling and that often providers do not account for or assess adherence when deciding to intensify treatment.

Our results prompt 3 modifiable targets for improvement in stroke care. Deficiencies in delivery of secondary prevention are common after cerebrovascular events.19–21 Hospital initiation of secondary prevention strategies is the standard of care for acute cardiac conditions and can improve risk factor control.22 As a result, the 2014 American Heart Association/American Stroke Association Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack emphasized initiation or resumption of hypertension treatment after the acute stroke period (24–48 hours) in neurologically stable patients with documented blood pressures of ≥140/90 mm Hg.5 Increased efforts to improve hypertension management before discharge (including reinitiation or modification of antihypertensives) could be highly beneficial to patients, given the robust relationship between discharge SBP and SBP trajectory after stroke in this study.

Second, efforts to assure that patients are on the correct medications and to titrate those medications should be implemented...

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**Table 2. One-Year Follow-Up Mean Blood Pressure, Clinic Visits, and Number of Medications Among Patients With Ischemic Stroke Stratified by Discharge Blood Pressure**

<table>
<thead>
<tr>
<th>Clinical Measures in the Year After Stroke</th>
<th>Blood Pressure at Hospital Discharge Full Cohort (n=3153)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;140 mm Hg</td>
</tr>
<tr>
<td></td>
<td>n=1973 (62.6%)</td>
</tr>
<tr>
<td></td>
<td>141–160 mm Hg</td>
</tr>
<tr>
<td></td>
<td>n=819 (26%)</td>
</tr>
<tr>
<td></td>
<td>&gt;160 mm Hg</td>
</tr>
<tr>
<td></td>
<td>n=361 (11.4%)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg, mean (SD)</td>
<td>126.1 (11.9)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg, mean (SD)</td>
<td>72.9 (9.9)</td>
</tr>
<tr>
<td>No. of outpatient clinic visits,* mean (SD)</td>
<td>4.6 (4.1)</td>
</tr>
<tr>
<td>Antihypertensive drugs at discharge, median (IQR)</td>
<td>2 (1–3)</td>
</tr>
<tr>
<td>Patients with ≥1 elevated blood pressure opportunity after discharge, n (%)</td>
<td>590/1973 (30%)</td>
</tr>
</tbody>
</table>

IQR indicates interquartile range.

*Eligible clinic visits include general internal medicine; primary care/medicine; women’s health; mental health primary care; geriatrics; hypertension; cardiology; anticoagulation; diabetes mellitus, endocrine, or metabolism; infectious disease; renal/nephrology; pulmonary or chest; or neurology.

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**Figure 2.** Systolic blood pressure trajectory in the year after stroke. Quadratic model adjusted for sex, race, Charlson Score, number of antihypertensive drugs at discharge, and interactions for discharge blood pressure by time.
to avoid untreated/undertreated hypertension. At particular risk are those with resistant hypertension or black patients who are both more likely to be uncontrolled in the poststroke period and may not have their medications changed or titrated.8,23 The lack of treatment intensification which we report is similar to those reported by Heisler et al.11 These investigators studied 38,327 Veterans with hypertension; treatment intensification occurred at 30% of 68,610 elevated BP visits. Although we observed higher proportion of intensifications (58%–65%), these investigators also found no relationship between intensification and medication adherence. Another study by Rose et al.24 evaluated 819 patients with hypertension for 2 years. They reported that adherent patients received more treatment intensification (≈1 intensification every 11 visits) compared with nonadherent patients. However, patients with the worst adherence generally took approximately half their medication and any intensification resulted in blood pressure reductions. Nevertheless, clinicians should assess a patient’s medication taking behavior and their self-efficacy for using medication at each treatment intensification decision.

Finally, programs to improve antihypertensive medication adherence should be implemented. Many patients are discharged with instructions that include resume home regimen. This home regimen is never revisited or modified despite the new risk factor of ischemic stroke. Additional counseling on adherence and evaluation of new barriers that may exist because of limitations resulting from the stroke should be addressed. All of the above issues are preliminary steps in understanding and optimizing risk factor management among patients with stroke.

There are limitations to our study. First, the population was mostly male Veterans admitted with ischemic stroke. Hypertension management in the poststroke period may not reflect the management of the general population. However, we do not believe that providers in the private sector are systematically more or less aggressive in hypertension management than VHA providers.25–27 Our sample included persons with milder strokes and those discharged home; therefore, our results may be more generalizable to this population. It is also possible many patients received their antihypertensive care outside VHA, or that our treatment intensification algorithm missed patients with reasons for not intensifying therapy such as orthostatic hypotension. Similarly, we did not extensively review charts to determine whether after discussion, patients and providers chose not to titrate medications (because of

### Table 3. One-Year Follow-Up for Patients With ≥1 Elevated Blood Pressure Opportunity by Discharge Blood Pressure (n=1197)

<table>
<thead>
<tr>
<th>Characteristics in the Year After Stroke</th>
<th>&lt;140 mm Hg (n=590)</th>
<th>141–160 mm Hg (n=381)</th>
<th>&gt;160 mm Hg (n=226)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, mm Hg, mean (SD)</td>
<td>137.5 (8.9)</td>
<td>143.5 (9.7)</td>
<td>151.0 (12.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg, mean (SD)</td>
<td>78.4 (9.8)</td>
<td>77.7 (8.6)</td>
<td>78.4 (10.6)</td>
<td>0.519</td>
</tr>
<tr>
<td>Number of antihypertensives, median (IQR)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>3 (2–4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of eligible clinic visits, * mean (SD)</td>
<td>5.8 (5.4)</td>
<td>5.8 (4.6)</td>
<td>5.8 (3.8)</td>
<td>0.987</td>
</tr>
<tr>
<td>Antihypertensive intensifications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1 (0–2)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.13 (1.11)</td>
<td>1.23 (1.11)</td>
<td>1.46 (1.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intensification opportunities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1 (1–2)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.93 (1.54)</td>
<td>2.12 (1.45)</td>
<td>2.39 (1.64)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proportion of intensifications to opportunities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% confidence interval)</td>
<td>58% (55–62)</td>
<td>60% (55–64)</td>
<td>65% (59–70)</td>
<td>0.150</td>
</tr>
<tr>
<td>Proportion with calculable prestroke medication possession ratio (%)</td>
<td>492/590 (83.4)</td>
<td>325/381 (85.3)</td>
<td>187/226 (82.7)</td>
<td>0.641</td>
</tr>
<tr>
<td>Medication possession ratio, mean (SD)</td>
<td>0.74 (0.23)</td>
<td>0.73 (0.23)</td>
<td>0.75 (0.21)</td>
<td>0.725</td>
</tr>
<tr>
<td>Medication possession ratio &gt;0.8 (%)</td>
<td>47.8</td>
<td>47.1</td>
<td>49.7</td>
<td>0.905</td>
</tr>
<tr>
<td>Proportion with calculable poststroke medication possession ratio (%)</td>
<td>573/590 (97.1)</td>
<td>364/381 (95.5)</td>
<td>219/226 (96.9)</td>
<td>0.399</td>
</tr>
<tr>
<td>Medication possession ratio, mean (SD)</td>
<td>0.74 (0.20)</td>
<td>0.76 (0.18)</td>
<td>0.76 (0.19)</td>
<td>0.190</td>
</tr>
<tr>
<td>Medication possession ratio &gt;0.8 (%)</td>
<td>46.4</td>
<td>45.6</td>
<td>46.6</td>
<td>0.963</td>
</tr>
<tr>
<td>Prestroke/poststroke comparison†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.937</td>
<td>0.047</td>
<td>0.944</td>
<td></td>
</tr>
</tbody>
</table>

*Eligible clinic visits include general internal medicine; primary care/medicine; women’s health; mental health primary care; geriatrics; hypertension; cardiology; anticoagulation; diabetes mellitus, endocrine, or metabolism; infectious disease; renal/nephrology; pulmonary, or chest; or neurology.
†Comparison of pre- vs poststroke medication possession ratio P value reported.
Summary and Conclusions

SBP improves in the year after stroke; however, 12% of patients were discharged with SBP >160 mm Hg and many remained high in the year after stroke. This population had no statistically significant difference in treatment intensification compared with patients who were discharged with lower SBP. This finding suggests that the place to affect the most change in the poststroke BP trajectory is before discharge. Interventions to systematically improve modifiable risk factors should span inpatient and outpatient spectrum to deliver optimal patient care.

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Disclosures

We are responsible for its content. Statements in the report should not be construed as endorsement by the Department of Veterans Affairs.

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Supplemental Table I: Example scenarios and rules applied in the analysis of each scenario

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Visit 1</th>
<th>Intensification occurred?</th>
<th>Visit 2</th>
<th>Intensification occurred?</th>
<th>Analysis</th>
</tr>
</thead>
</table>
| 1        | July 1  | No                        | July 7  | Yes                       | First visit satisfied by intensification within 7 days  
|          | 160/100 |                           | 160/100 |                           | Second visit excused  
|          |         |                           |         |                           | Numerator =1, denominator =1 |
| 2*       | July 1  | No                        | July 7  | No                        | First visit excused by second visit within 7 days  
|          | 160/100 |                           | 160/100 |                           | Second visit not satisfied by intensification  
|          |         |                           |         |                           | Numerator =0, denominator =1 |
| 3        | July 1  | Yes                       | July 5  | Yes                       | First visit satisfied by intensification within 7 days  
|          | 160/100 |                           | 160/100 |                           | Second visit satisfied by intensification within 7 days in the past  
|          |         |                           |         |                           | Numerator =1, denominator =1 |
| 4        | July 1  | Yes                       | July 5  | Yes                       | First visit satisfied by intensification within 7 days  
|          | 160/100 |                           | 160/100 |                           | Second visit satisfied by another intensification  
|          |         |                           |         |                           | Numerator =2, denominator =2 |
| 5        | July 1  | No                        | July 7  | No                        | First visit > 160 so not excused by second visit within 7 days  
|          | 160/100 |                           | 130/80  |                           | Second visit not eligible for intensification  
|          |         |                           |         |                           | Numerator =0, denominator =1 |
| 6        | July 1  | No                        | July 7  | No                        | First visit between 141 and 160 visit excused by second visit within 7 days  
|          | 145/80  |                           | 130/80  |                           | Second visit not eligible for intensification  
|          |         |                           |         |                           | Numerator =0, denominator =0 |
| 7        | July 1  | No                        | July 5  | Yes                       | First visit satisfied by intensification within 7 days  
|          | 160/100 |                           | 130/80  |                           | Second visit not eligible for intensification  
|          |         |                           |         |                           | Numerator =1, denominator =1 |

* 7-day look-ahead rule only applied once for consecutive overlapping situations.