How to Calculate The Partial Area When AUC Overlaps Two Parallel Lines

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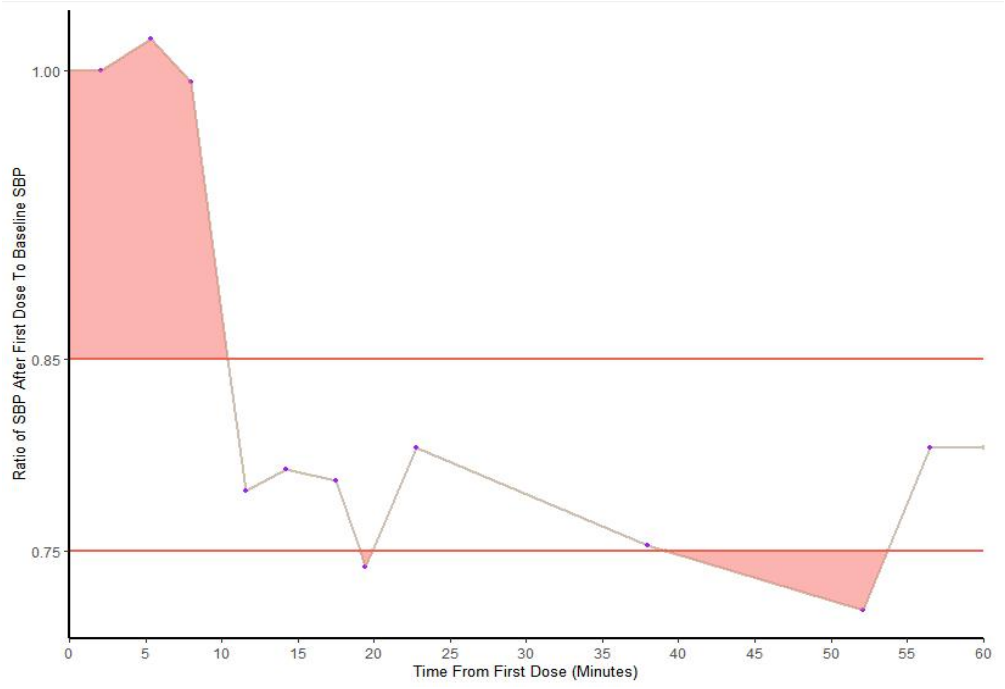
ABSTRACT

Generally, the trapezoidal rule is often used to calculate some important AUC related parameters. However, there are more complicated situations in actual studies. For example, when the AUC overlaps two parallel lines, we would like to calculate the area of the non-overlapping part of the AUC and parallel interval, where the parallel interval is the area between the two parallel lines. In the following paper, we will discuss in detail how to calculate the case mentioned in the above example.

INTRODUCTION

This paper will illustrate the partial AUC area algorithm when AUC overlaps two parallel lines in specific example. Let's start from the following figure 1, which shows the fluctuation of systolic pressure for a subject during one hour after the first dose. As shown in the figure1, the x-axis represents the measurement time of systolic blood pressure after the first dose, While the y-axis represents the ratio of observed systolic blood pressure to baseline systolic blood pressure after the first dose. Obviously, we can see that there are two parallel lines whose Y-values are 0.75 and 0.85 respectively in the figure1, which has been defined in protocol. Moreover, the purple points in the figure1 are the ratio of observed blood pressure to baseline value.

Figure 1:

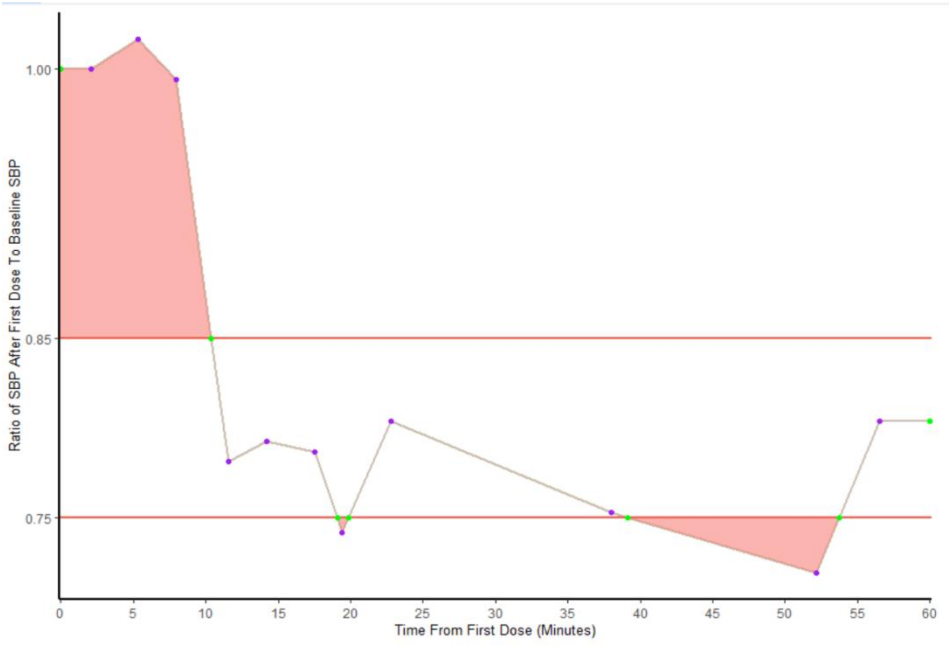


UNIFYING THE LENGTH OF TIME PERIOD

It's important to emphasize that the Integrity of time period for each subject when we compute the pink areas in figure 1. As we all know, the efficacy result of the different groups are comparable only if the same time scale is used for each subject.

It can be clearly seen that the systolic blood pressure ratio from 0th minute to 60th minute after the first dose are required to the calculation of pink areas in the Figure 1. However, it is difficult for all subjects to measure accurately the systolic blood pressure at a certain time point, such as 0th minute or 60th minute after the first dose. Hence, it is necessary for some subjects to compute the systolic blood pressure of 0th minute or 60th minute after the first dose by linear interpolation rule before calculating the pink areas.

Figure 2:



Taking above systolic blood pressure of same subject as an example, We used different color to distinguish the observed systolic blood pressure ratio and derived systolic blood pressure ratio . Furthermore, the purple point represents the observed systolic blood pressure ratio, while the green point indicates the derived systolic blood pressure ratio. In addition, each of the green points in the figure2 could be calculated by linear interpolation rule based on adjacent observed blood pressure ratio and measured blood pressure time.

As we can see, the Figure3 below shows the data set used to draw above Figure 2 by R software.

Figure 3:

Subject Number	Blood pressure measurement time	First dose time	Time to first dosing	systolic blood pressure ratio relative to baseline	Baseline time of systolic blood pressure	Baseline ratio of systolic	First blood pressure observation time after 1 hour from the first dose	First blood pressure observation ratio after 1 hour from the first dose
001	2023-07-13T21:37:58	13Jul2023 21:37:58	0	1	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T21:40:01	13Jul2023 21:37:58	2.05	1	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T21:43:17	13Jul2023 21:37:58	5.3166667	1.016853933	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T21:45:57	13Jul2023 21:37:58	7.9833333	0.994382022	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T21:49:31	13Jul2023 21:37:58	11.55	0.780898876	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T21:52:11	13Jul2023 21:37:58	14.216667	0.792134831	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T21:55:30	13Jul2023 21:37:58	17.533333	0.786516854	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T21:57:23	13Jul2023 21:37:58	19.416667	0.741573034	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T22:00:45	13Jul2023 21:37:58	22.783333	0.803370787	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T22:15:56	13Jul2023 21:37:58	37.966667	0.752808989	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T22:30:05	13Jul2023 21:37:58	52.116667	0.719101124	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T22:34:31	13Jul2023 21:37:58	56.55	0.803370787	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989
001	2023-07-13T22:37:58	13Jul2023 21:37:58	60	0.788354585	2023-07-13T21:37:21	1	2023-07-13T22:46:08	0.752808989

To be more specific, the data in column 4 “Time to first dosing” is displayed on the X-axis of Figure 2 and the data in column 5 “systolic blood pressure ratio relative to baseline” is displayed on the Y-axis of Figure 2.

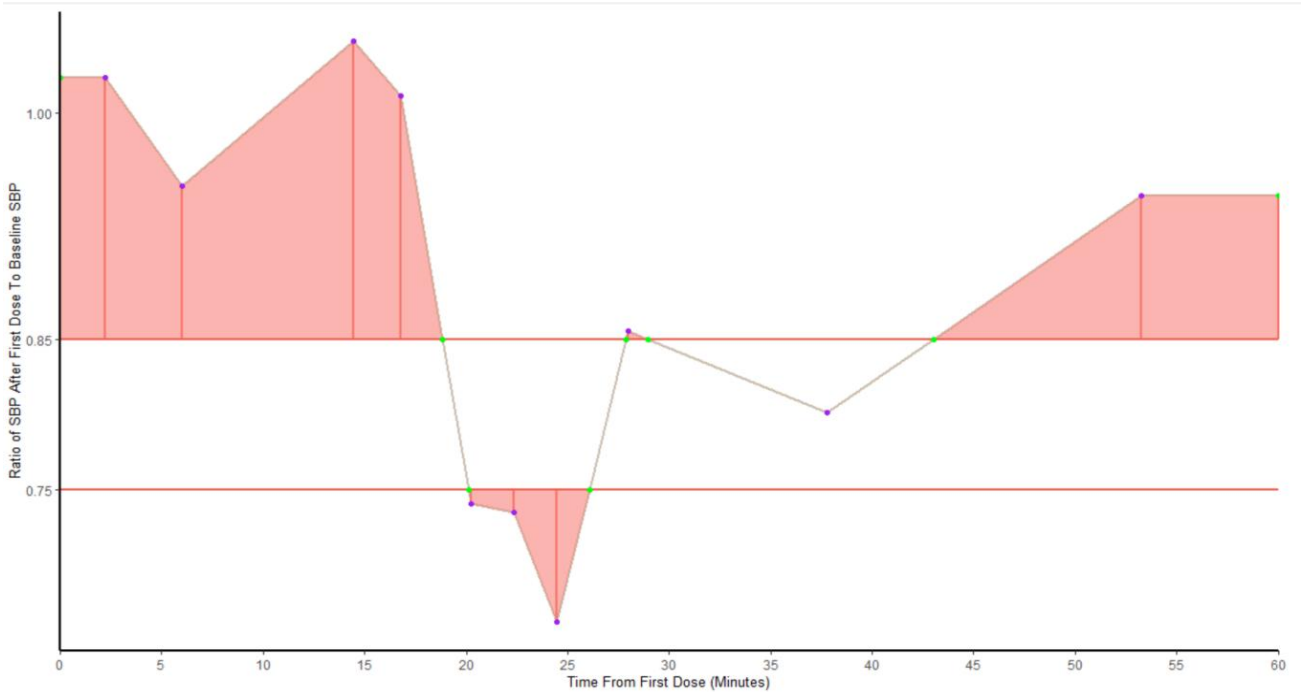
Besides, the two records highlighted in red are derived by linear interpolation, rather than collected directly. In addition, the columns ”Baseline time of systolic blood pressure ” and “Baseline ratio of systolic blood pressure ” are used to derive the first record highlighted in red, While the columns ”First blood pressure observation time after 1 hour from the first dose ” and “First blood pressure observation ratio after 1 hour from the first dose ” are used to derive the last record highlighted in red. The specific application of linear interpolation is displayed in a later example.

CALCULATION OF THE PARTIAL AUC AREA

It is well known that the trapezoidal rule divides the total area under the curve into multiple sub interval areas consisting of two adjacent observation time and adjacent observation values. Therefore, the pink areas outside the two parallel lines was separated into multiple interval areas composed of adjacent observations. For more specific information, see the systolic blood pressure data of another subject in the following Figure 4.

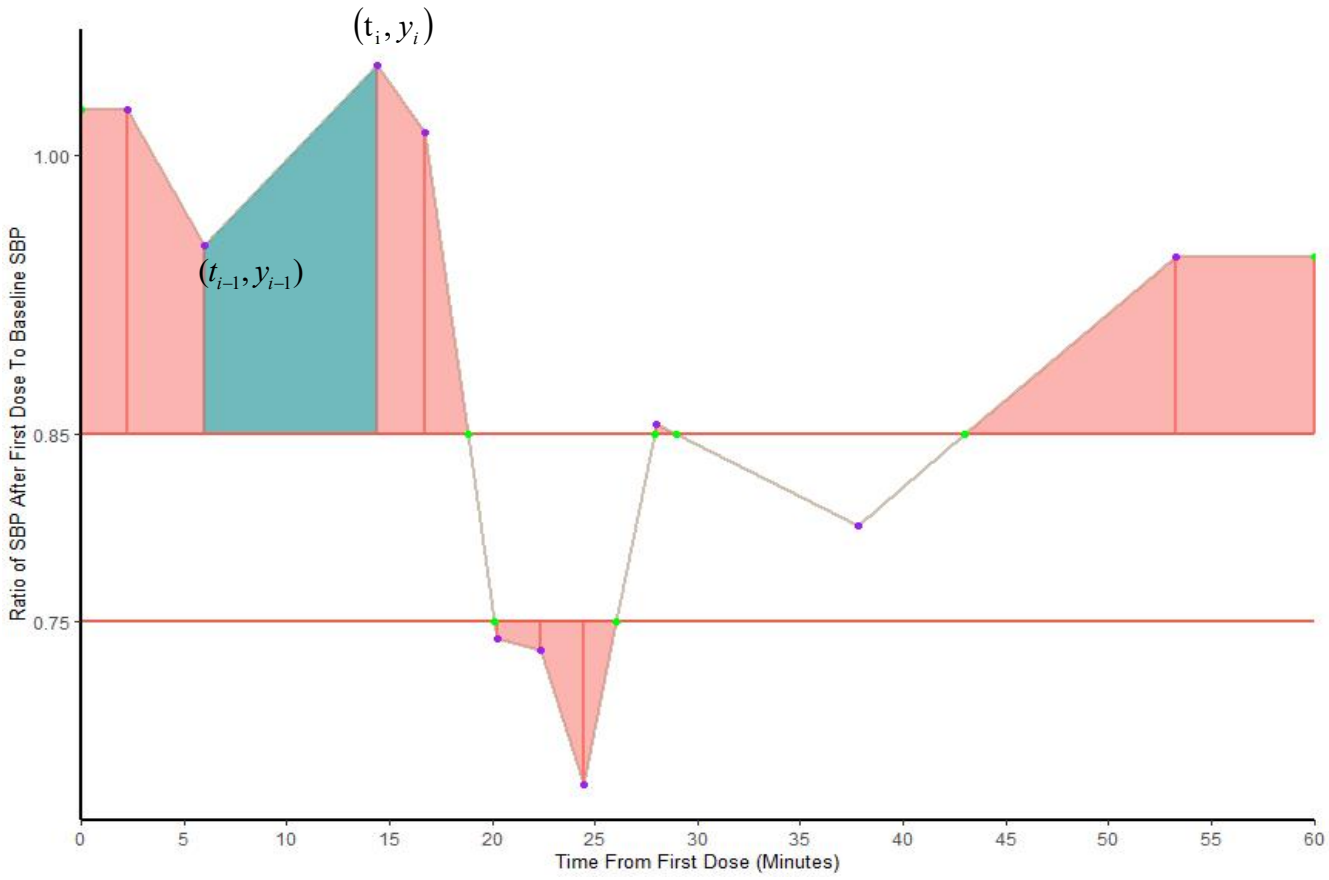
Let's focus on the pink areas above the parallel line whose y value equal to 0.85 in the figure 4. According to the distribution characteristics of the figure 4 , the adjacent observed systolic blood pressure can be divided into three cases.

Figure 4:



(1) In the first case, the ratio of two adjacent blood pressure observations all are more than 0.85. it is obvious that the two observation points with coordinates are shown in the figure 5 below, where t_{i-1} and t_i represent the two adjacent blood pressure observation time on the X axis respectively, while y_{i-1} and y_i represent the ratio of two adjacent systolic pressure on the Y axis respectively.

Figure 5 :



The sub interval area displayed as green area in the Figure 5, which is made up of two adjacent coordinate points (t_{i-1}, y_{i-1}) , (t_i, y_i) and the parallel line whose y value equal to 0.85 can be calculated by the following formula.

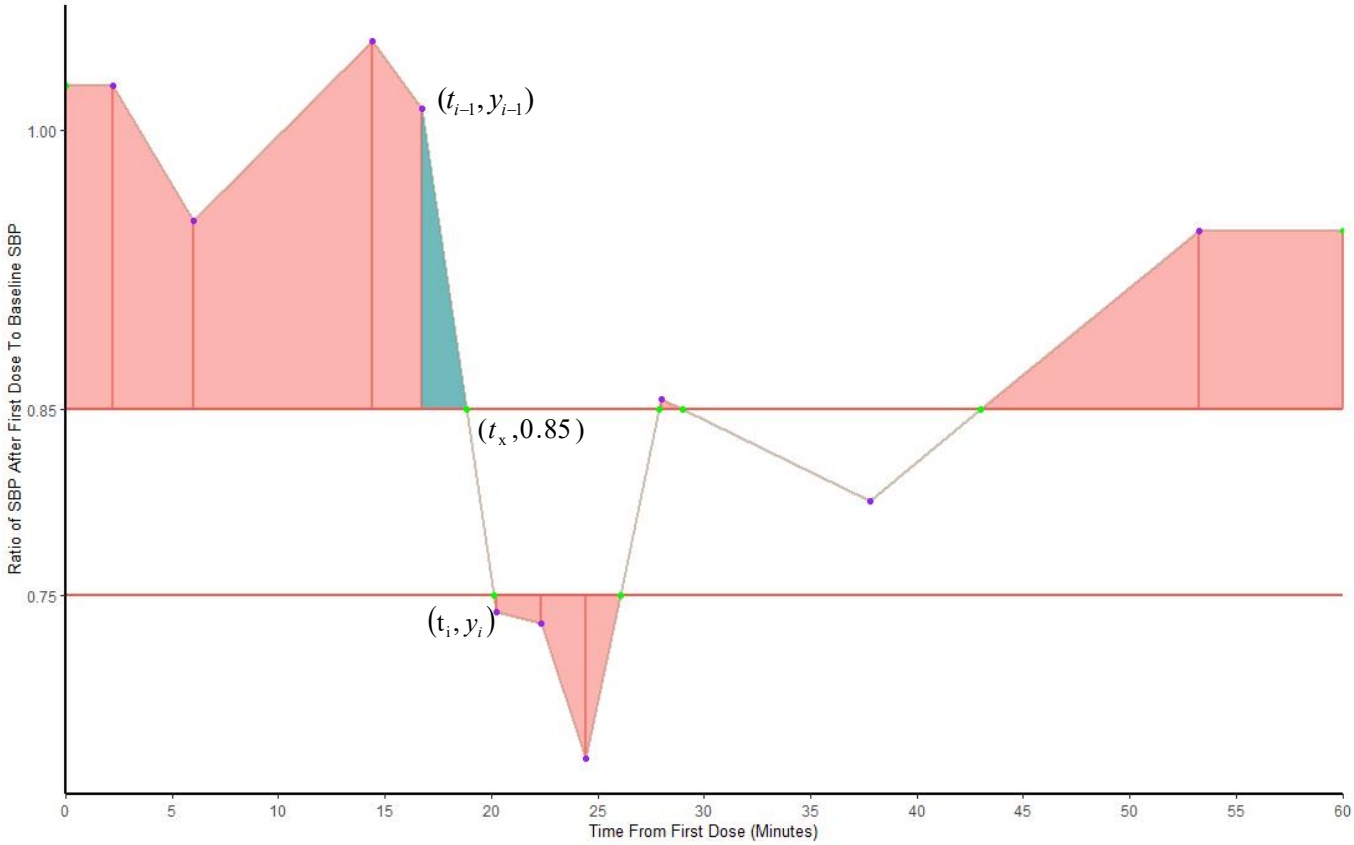
$$AUC_{t_i - t_{i-1}} = (t_i - t_{i-1}) \times \frac{(y_{i-1} - 0.85) + (y_i - 0.85)}{2}$$

In fact, the sub interval area can be calculated base on this formula if adjacent blood pressure observation ratio meet the condition when y_{i-1} >0.85 and y_i >0.85.

(2) In the second case,one of the observed systolic blood pressure ratio is more than 0.85, while the next observed systolic blood pressure ratio is less than 0.85, like (t_{i-1}, y_{i-1}) and (t_i, y_i) in the following figure 6.

Moreover, the point $(t_x, 0.85)$ is necessary to compute the green sub interval area as we can see explicit from the figure 6. However, the t_x is not a observed blood pressure time and that is unknown for us. Hence, We need to compute the t_x by linear interpolation based on (t_{i-1}, y_{i-1}) and (t_i, y_i) before calculating the green sub interval area.

Figure 6 :



The formula of green sub-interval area in figure 6: $AUC_{t_x - t_{i-1}} = (t_x - t_{i-1}) \times \frac{(y_{i-1} - 0.85)}{2}$

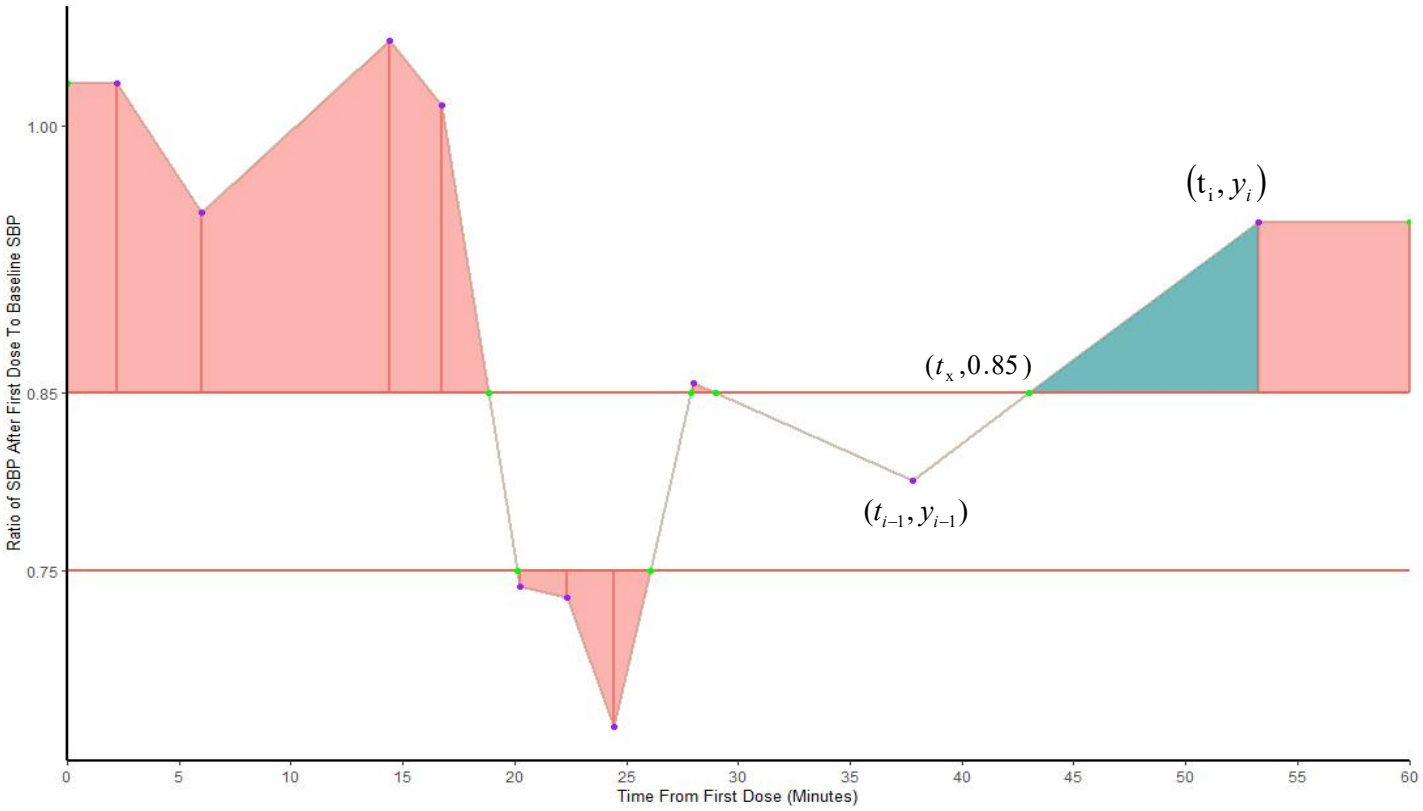
Getting the $t_x - t_{i-1}$ by linear interpolation : $\frac{y_i - y_{i-1}}{t_i - t_{i-1}} = \frac{0.85 - y_{i-1}}{t_x - t_{i-1}}$

Taking the $t_x - t_{i-1}$ into the $AUC_{t_x - t_{i-1}}$ area formula to obtain the below transformed formula, which applies to the situation when $y_{i-1} > 0.85$ and $y_i < 0.85$.

$$AUC_{t_x - t_{i-1}} = \frac{(y_{i-1} - 0.82)^2}{2} \times abs(\frac{t_i - t_{i-1}}{y_i - y_{i-1}})$$

(3) The third case has little difference compared with the second case. As we can see from the below figure 7, one of the observed systolic blood pressure ratio is less than 0.85, while the next observed systolic blood pressure ratio is more than 0.85.

Figure 7:



The formula of green sub interval area in figure 7 : $AUC_{t_i - t_x} = (t_i - t_x) \times \frac{(y_i - 0.85)}{2}$

$t_i - t_x$ is obtained by linear interpolation : $\frac{y_i - y_{i-1}}{t_i - t_{i-1}} = \frac{y_i - 0.85}{t_i - t_x}$

Replacing the $t_i - t_x$ into the area formula $AUC_{t_i - t_x}$ to get the transformed formula ,which is suitable to the case when y_{i-1} <0.85 and y_i >0.85 .

$$AUC_{t_i - t_x} = \frac{(y_i - 0.85)^2}{2} \times \frac{t_i - t_{i-1}}{y_i - y_{i-1}}$$

The three cases listed above can be used to calculate all sub interval areas which systolic blood pressure ratio above the parallel line of 0.85. Furthermore, The total curve area above the parallel line whose y equal to 0.85 is obtained by adding the areas of multiple sub intervals.

what's similar is that the logic also applies to calculating the total area below the parallel line of 0.75. To be more specific, observed systolic blood pressure ratio can also be divided into three categories:

(1) When $y_{i-1} < 0.75$ and $y_i < 0.75$, the sub interval area formula :

$$AUC_{t_i - t_{i-1}} = (t_i - t_{i-1}) \times \frac{(0.75 - y_{i-1}) + (0.75 - y_i)}{2}$$

(2) When $y_{i-1} < 0.75$ and $y_i > 0.75$, the sub interval area formula :

$$AUC_{t_x - t_{i-1}} = \frac{(0.75 - y_{i-1})^2}{2} \times \frac{t_i - t_{i-1}}{y_i - y_{i-1}}$$

(3) When $y_{i-1} > 0.75$ and $y_i < 0.75$, the sub interval area formula :

$$AUC_{t_i - t_x} = \frac{(y_i - 0.75)^2}{2} \times abs(\frac{t_i - t_{i-1}}{y_i - y_{i-1}})$$

CONCLUSION

In summary,the total area outside the parallel interval , including the total area above or below the parallel line interval, could be obtained through the above methods when AUC overlaps two Parallel Lines. Of course, it is necessary to ensure that the time period of each subject is the same to improve the comparability of results between different groups before calculating the area.

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CONTACT INFORMATION

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