Approach to structural break analysis

A structural break represents a point in the time series in which there is a change in the relationship between acetaminophen overdose rates and time. The goal of structural break analyses is to therefore identify a) whether such a structural break exists in the time series and b) how many breaks exist in the time series and which point(s) or date(s) are statistically most likely to represent a break in the time series. The timing of these structural breaks can then be compared to the dates of policy interventions (i.e., labelling change) in question. We applied the following steps to determine if structural breaks existed in each time series and identify the date(s) at which points these occur:

Step 1: An empirical fluctuation process test known as the OLS-CUSUM test was used ascertain the presence of a structural break. Fluctuation tests test for departures from constancy in the time series and can be used as a 'screen' for whether structural breaks exist. This is done through an examination of the residuals to test the null hypothesis that all parameters are stable or constant over time (i.e., no structural break over time). This hypothesis is rejected based on the test statistic being larger than a critical value or plots of the cumulative sum of residuals exceeding critical test boundaries. If the null hypothesis is rejected, a structural break exists. However, determining the exact number and timing of the breaks requires further testing (i.e., Step 2).

Step 2: The number and location of breakpoint(s) is determined by minimizing the residual sum of squares using the Bai-Perron approach.

OLS-based CUSUM test



Step 1: The time series data fall outside the OLS-CUSUM empirical fluctuation process test boundaries, indicating evidence for a structural change. The null hypothesis of parameter stability is rejected at the 5% level because the CUSUM test statistic value of 1.46 exceeds the 5% critical level of 1.36. The number of structural breaks and their timing is determined in step 2 using the Bai and Perron approach.

Step 2: Subsequent evaluation using the Bai-Perron test identified a significant structural break in December 2008 (p < 0.001), prior to the implementation of labelling interventions.

Appendix 4, as submitted by the authors. Appendix to: Antoniou T, Guan Q, Martins D, et al. Impact of acetaminophen product labelling changes in Canada on hospital admissions for accidental acetaminophen overdose: a population-based study. *CMAJ* 2022. doi: 10.1503/cmaj.210842. Copyright © 2022 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca.

Supplemental Figure 2: Cumulative sum of standardized ordinary least square residuals for intensive care unit admissions for accidental acetaminophen overdose in Canada, April 2004 to March 2020



OLS-based CUSUM test

The time series data do not fall outside the OLS-CUSUM empirical fluctuation process test boundaries, indicating no structural change. The null hypothesis of parameter stability is not rejected at the 5% level because the CUSUM test statistic value of 1.02 is less than the 5% critical level of 1.36. Because there is no structural break in the time series and therefore no structural break locations to identify, we did not proceed to Step 2 and perform a Bai-Perron test.

Appendix 4, as submitted by the authors. Appendix to: Antoniou T, Guan Q, Martins D, et al. Impact of acetaminophen product labelling changes in Canada on hospital admissions for accidental acetaminophen overdose: a population-based study. *CMAJ* 2022. doi: 10.1503/cmaj.210842. Copyright © 2022 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca.

Supplemental Figure 3: Cumulative sum of standardized ordinary least square residuals for hospital admissions for accidental acetaminophen overdose involving opioids in Canada, April 2004 to March 2020



OLS-based CUSUM test

Step 1: The time series data fall outside the OLS-CUSUM empirical fluctuation process test boundaries, indicating evidence for a structural change. The null hypothesis of parameter stability is rejected at the 5% level because the CUSUM test statistic value of 1.40 exceeds the 5% critical level of 1.36. The number of structural breaks and their timing is determined in step 2 using the Bai and Perron approach.

Step 2: Subsequent evaluation using the Bai-Perron test identified significant structural breaks in the fourth quarter of 2008 (p < 0.001) and the first quarter of 2016 (p < 0.001).

Appendix 4, as submitted by the authors. Appendix to: Antoniou T, Guan Q, Martins D, et al. Impact of acetaminophen product labelling changes in Canada on hospital admissions for accidental acetaminophen overdose: a population-based study. *CMAJ* 2022. doi: 10.1503/cmaj.210842. Copyright © 2022 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca.