Impact of Nitrosamine Contamination Recalls on Angiotensin-Receptor-Blocker (ARB) Utilization in the US, UK, Canada, and Denmark

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Background

In July 2018, several regulatory agencies became aware and notified the public of a potential carcinogenic impurity, N-nitrosodimethylamine (NMDA) in valsartan-containing products.

Additional notices were issued for affected lots of irbesartan and losartan in October and November 2018, respectively.

Listings of uncontaminated lots for these angiotensin-receptor blockers (ARBs) were published along side the recall notices, allowing for patients to continue their treatment.

Objective

To examine ARB utilization and switching patterns in the US, UK, Canada and Denmark before and after July 2018, when the first ARB (valsartan) was recalled.

Methods

Design: Retrospective cohort study

Setting: FDA's Sentinel System, Canadian Network for Observational Drug Effects (CNODES) data, Danish National Prescription Registry and Clinical Practice Research Datalink (CPRD).

Participants: Patients aged 18 years and older between January 2014 and December 2020.

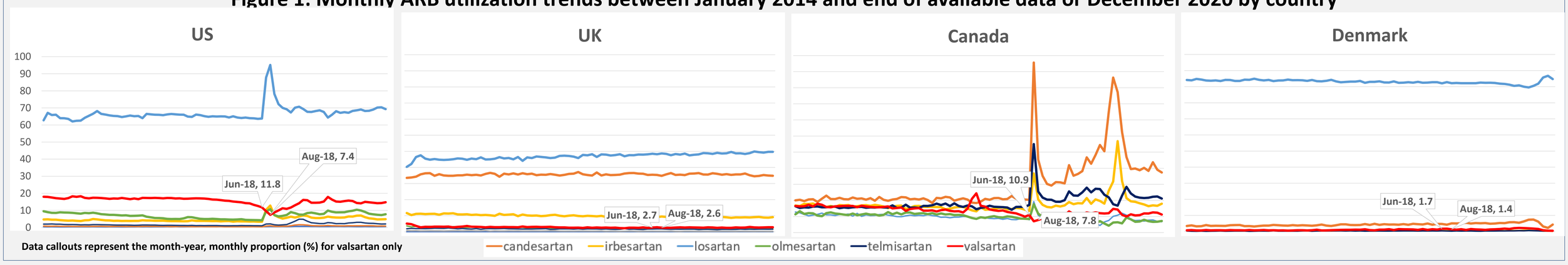
Exposure: azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan and valsartan.

Statistical Analysis: Graphical Trends of monthly percentage of individual ARB utilization; Quarterly proportion of ARB episodes ending in a switch to another ARB.

Analyses were conducted using Cohort Identification and Descriptive Analysis (CIDA) module version 10.1.1 distributed to all participating sites.

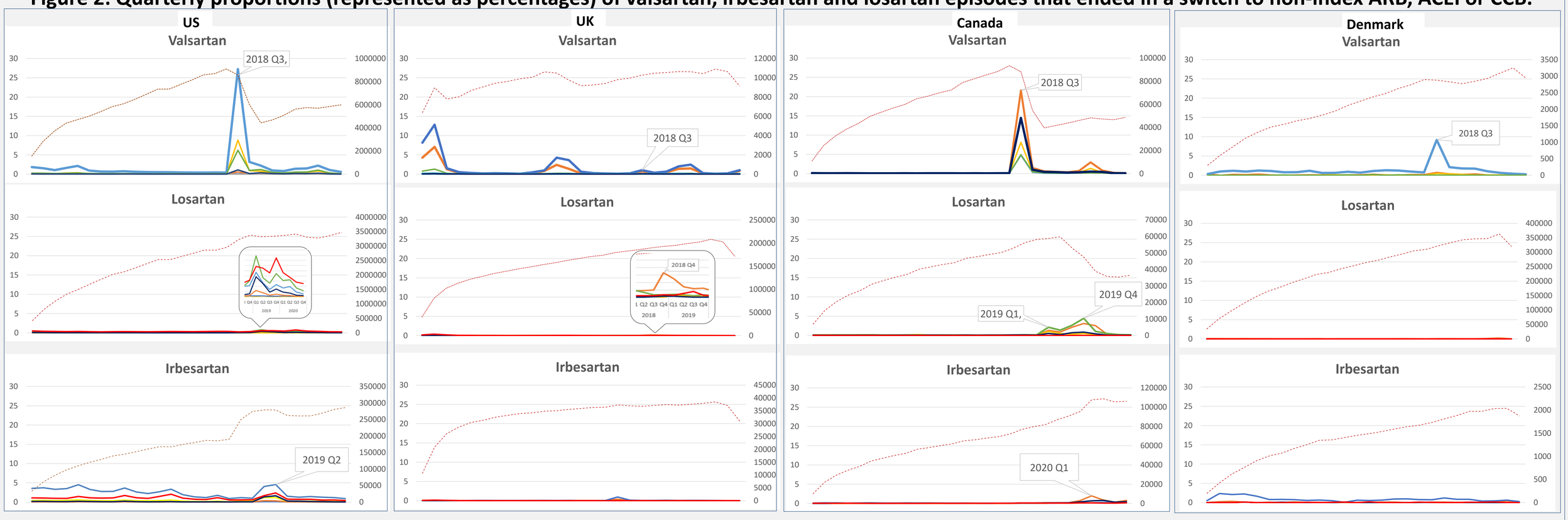
Results

Figure 1: Monthly ARB utilization trends between January 2014 and end of available data or December 2020 by country



Data callouts represent the month-year, monthly proportion (%) for valsartan only

Figure 2: Quarterly proportions (represented as percentages) of valsartan, irbesartan and losartan episodes that ended in a switch to non-index ARB, ACEI or CCB.



Dotted lines on each graph represent the monthly number of exposure episodes for each ARB

Discussion

US and Canada experienced a substantial decline in the monthly percentages of valsartan exposure episodes in July 2018.

Valsartan Switching Patterns: US and Canada had highest proportion of valsartan episodes that ended in a switch in Q3-2018 (valsartan recall: July 2018). Similarly, high rate of switching for valsartan episodes in Q3-2018 occurred in Denmark and UK, though not as high as observed in US or Canada.

Losartan Switching Patterns: Canada had immediate increase in losartan episodes that ended in a switch beginning Q1 2019 (Canada recall: March 2019). Similar high proportion of switching occurred in US, Q1-2019 (US recall: November 2018) and UK, Q4 2018, though not as high as observed in Canada.

Irbesartan Switching Patterns: US and Canada had an immediate increase in irbesartan episodes that ended in a switch in Q2 2019 (US recall: October 2018 and January 2019) and Q1 2020 (Canada recall: March and April 2019), respectively.

Conclusion

Despite availability of uncontaminated valsartan products at the time of the recall, data from three out of four countries revealed a substantial decline in valsartan dispensings due to increased switching to other ARB products.

Subsequent notices for losartan and irbesartan were also associated with increased switching around the time of the recall, however, their utilization trends remained unchanged.

Acknowledgements

Many thanks are due to the Data Partners who provided data used in the analysis. This project was supported by Task Order 75F40119F19002 under Master Agreement 75F40119D10037 from the US Food and Drug Administration (FDA).

Disclaimer

The authors have no conflicts of interest to disclose. The views expressed in this poster represent those of the presenters and do not necessarily represent the official views of the U.S. FDA or Health Canada or the UK Medicines and Healthcare products Regulatory Agency.