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Use of baclofen for the treatment of alcohol use disorders between 2014 and 2021 in France

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Abstract

Introduction

The use of baclofen for the treatment of alcohol use disorders (AUD) in France has increased significantly between 2007 and 2013, initially through off-label prescription (1,2). In April 2014, temporary authorization for use (TAU) was granted, followed by marketing authorization (MA) in October 2018. It was also reported that high doses of baclofen had the potential for serious adverse effects (3). As a result, the maximum dose was limited to 80mg/day in July 2017. We aimed to assess the impact of the medical authorization (MA) of baclofen for alcohol use disorder (AUD) on the number of newly treated patients in France between 2014 and 2021, and the impact of dose restrictions on baclofen dosage.

Methods

A retrospective cohort study of patients newly treated with baclofen for AUD was conducted using data from the French National Health Data System. Characteristics of patients and treatments were described. Interrupted time-series analyses (ARIMA models) were performed to evaluate the effect of MA and dose limitation on baclofen treatment initiations and daily doses.

Results

Between 2014 and 2021, 478,109 patients were newly treated with baclofen for AUD. A significant decline of initiations of baclofen was observed between 2014 (N=98,552) and 2015 (N=67,555), and a gradual decrease after 2016 (N=48,471 in 2021). The MA of baclofen for AUD did not have a statistically significant impact on the number of baclofen initiations for AUD. Before dose limitation, respectively 78.0% and 0.8% of daily doses were lower than 80mg and higher than 300mg, against 88.3% and 0.5% after July 2017.

Conclusion

Since the peak in 2014, baclofen use has been steadily decreasing and MA has not resulted in an increase in baclofen initiations for AUD. The part of patients with a dose greater than 300mg is low and has decreased over the period 2014-2021.

Introduction

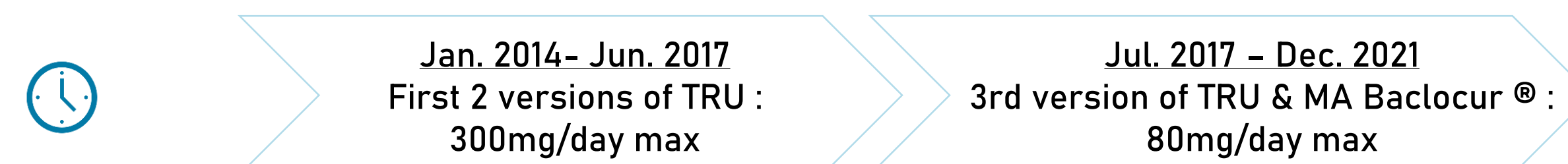
- Since 1989: Indication for baclofen in the treatment of muscle spasticity
- 2007 - 2013: Increase in the use of baclofen for the treatment of alcohol use disorders (AUD) in France, without marketing authorization (1,2)
- April 2014: Temporary recommendation for use (TRU) (1st version) in the AUD indication
- July 2017: Daily dose limited to 80mg/day (3rd version of TRU) following the publication of a study showing an increased risk of hospitalization and mortality with the use of high-dose baclofen, compared to approved drugs in AUD treatment (3)
- October 2018: Marketing authorization (MA) for Baclocur® in the AUD indication
- December 2020: Availability of Baclocur® in pharmacies

Objectives

- ⚙ Evaluate the effects of the marketing authorization for Baclocur® in October 2018 and its availability in pharmacies in December 2020 on the number of baclofen initiations treatment for AUD.
- ⚙ Evaluate the effect of the TRU 3rd version in July 2017 on compliance with daily dose recommendations for Baclofen in the AUD indication.

Materials and methods

- ⚙ Nationwide retrospective cohort study using data from the French National Health Data System (SNDS)
- 👤 Inclusion of all Baclofen initiators for AUD over the period January 2014 - December 2021
- 📄 **Initiators of Baclofen for AUD:** Patients who have received their first reimbursement for Baclofen between January 1, 2014 and December 31, 2021, without reimbursement for this drug for at least the preceding 3 years.
- 📄 **Baclofen indication for AUD:** Absence of consumption of the following treatments during the 3 years preceding the first reimbursement and during the study follow-up (hospitalization or long-term disease for neurological disorder, wheelchair or related device reimbursement, dantrolene reimbursement).



Daily dose : Daily dose between two dispensations was determined by dividing the quantity of Baclofen (in mg) dispensed at the first dispensation by the days between two dispensation dates. Average daily dose for the treatment course was calculated by averaging daily doses between all dispensations, excluding the first dispensation due to common dose adjustments in the initial month. This was only calculated for courses with at least three dispensations.

- 📈 **ARIMA models:** Evaluation of the effect of new recommendations on the number of Baclofen initiations and the proportion of users with average daily dose < 80mg.

Results

Sociodemographic characteristics of new baclofen users for AUD over the 2014-2021 period:

N = 478 109 patients

- 👤 **Age (mean ± sd):** 51.7 year (± 15.7)
- ♂ **Male sex:** N = 260 939, 54.6%
- 💰 **Patients with low income¹:** N = 64 353, 18.2%
- 📄 **History of psychotropic treatment* :** N = 237 711, 49.7%
- 📄 **History of AUD treatment* :** N = 72 316, 15.1%

¹ beneficiaries of complementary solidarity health as a proxy for low income. Calculated among individuals under 60, data available for 73.9% of the population (N = 353 381).

*Treatment history: at least one dispensation between 12 months and 2 months prior to initiation of baclofen. Psychotropic treatment: antipsychotic, anxiolytic, hypnotic, antidepressant or antiepileptic with a psychiatric indication. AUD treatment: nalmefene, acamprosate, naltrexone, disulfiram.

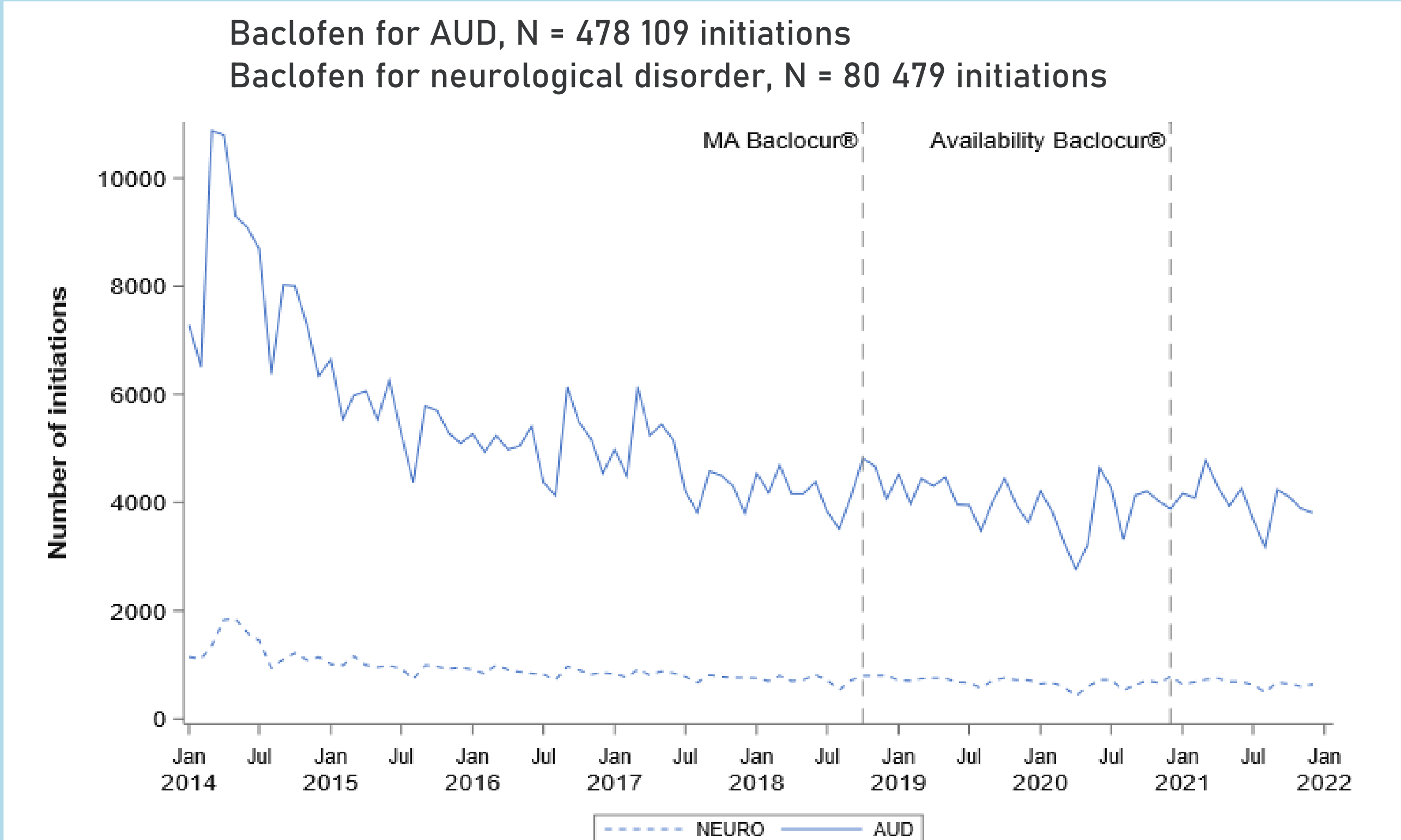


Fig. 1 Number of initiations of Baclofen treatment for AUD, by month over the period 2014-2021

Marketing authorization for Baclocur® and its effective availability :

No statistically significant effect on the number of Baclofen initiations for AUD (step 2018 : p = 0.42 ; ramp 2018 : p = 0.80 ; step 2020 : p = 0.41 ; ramp 2020 : p = 0.53)

Daily doses of baclofen courses for AUD over the period 2014-2021 (N=190 480)

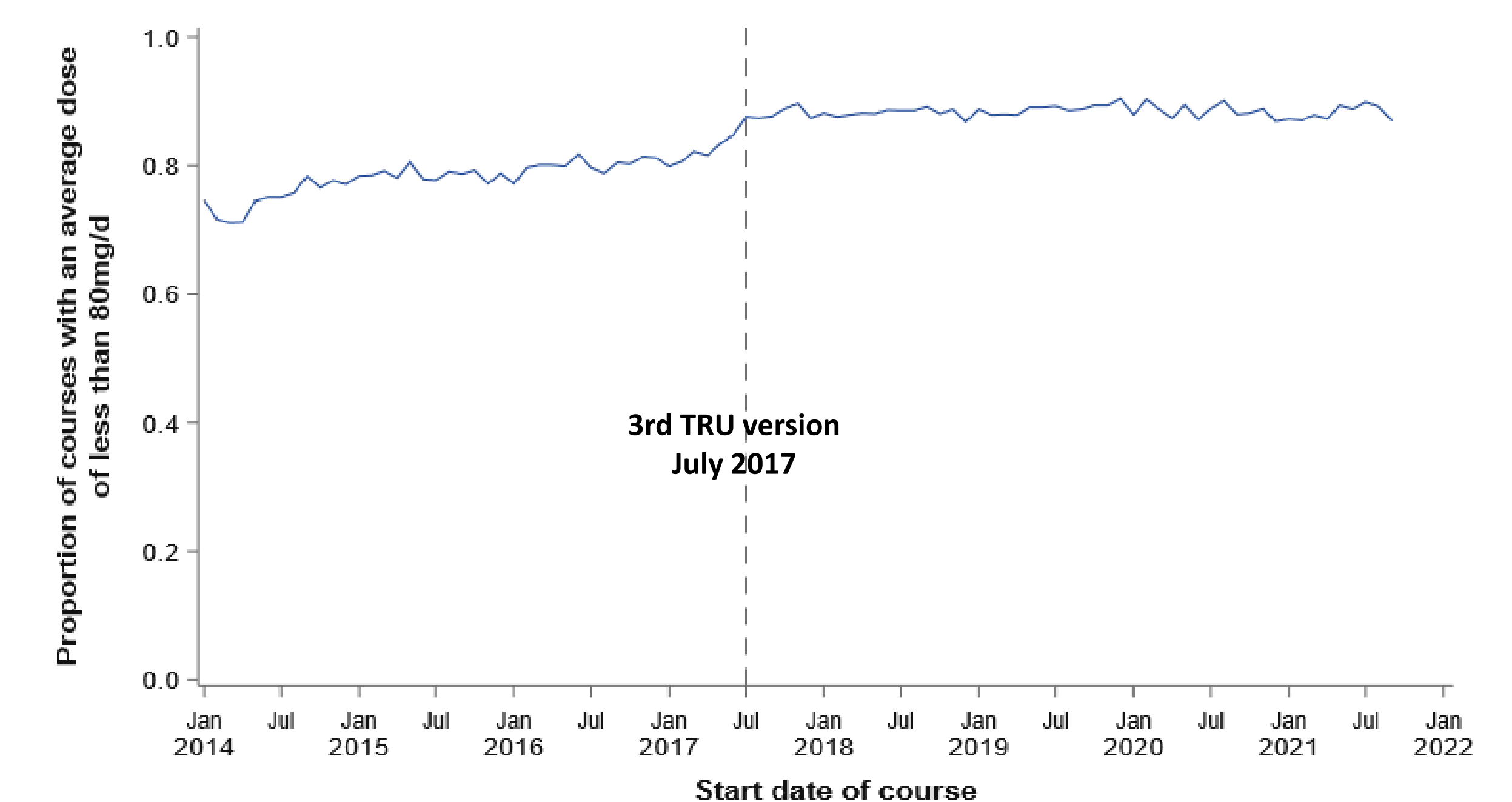
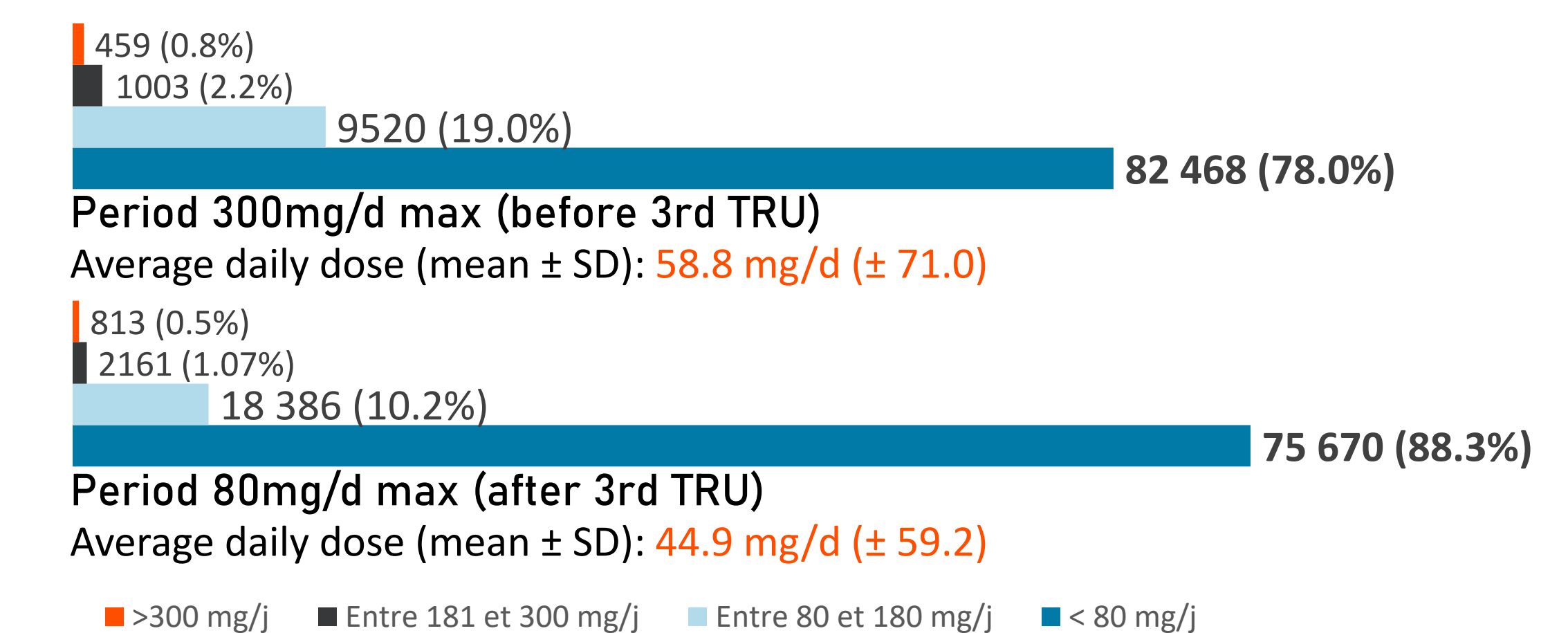


Fig. 2 Proportion of courses with an average dose of less than 80mg/d, per month over the 2014-2021 period

3rd TRU of July 2017:

Immediate significant effect on the proportion of baclofen courses with average daily doses <80mg/day: increase of 4.3% (step: p< 0.001).

In the years following the 3rd version of the TRU, the proportion of courses with average daily doses <80mg/day stabilized compared with the period before July 2017 (ramp: p=0.006).

Conclusion

- ⚙ Baclofen treatment initiations for AUD, after a very high peak in 2014, have decreased considerably between 2014 and 2018, and then stabilized until 2021.
- ⚙ No significant effect of MA and availability in pharmacies of Baclocur® on the number of initiations of baclofen treatment for AUD.
- ⚙ Significant effect of the 3rd version of the TRU on compliance with daily dose recommendation.
- ⚙ The overall trend shows a decrease in daily doses over the period 2014-2021, with a very small proportion of patients with a dose higher than 180 mg per day.

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