177

Estimating the Clinical and Economic Effects of High- and Low-Sodium Oxybate Agents Among the US Population With Narcolepsy: Microsimulation Cost Analysis

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Introduction

- Excess sodium intake is associated with increased risk of cardiovascular (CV), cardiometabolic (CM), and cardiorenal (CR) disorders[1-4]
- People with narcolepsy have a higher prevalence and risk of development or progression of certain CV/CM/CR conditions and events compared with those without narcolepsy[5,6]
- High-sodium oxybate agents, indicated to treat narcolepsy, contain 1640 mg of sodium per nightly 9 g dosage,[7,8] while low-sodium oxybate agents contain 131 mg per nightly 9 g dosage[9-13]

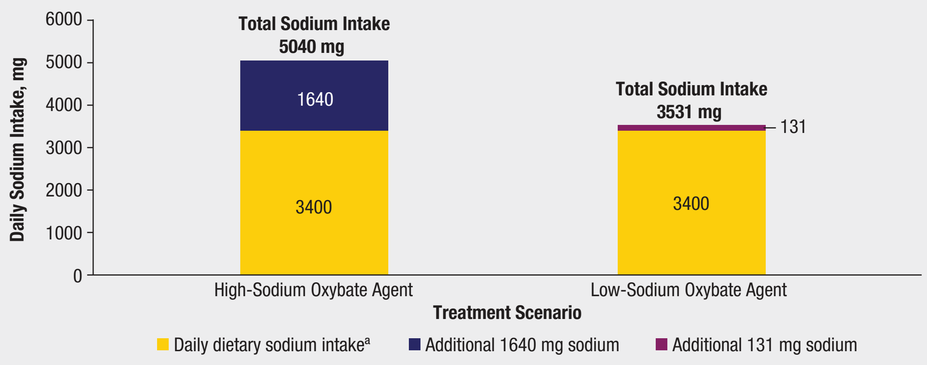
Objective

- This study aimed to estimate the potential clinical and economic impacts associated with the use of high-sodium versus low-sodium oxybate agents in the treatment of narcolepsy

Methods

- A microsimulation model was developed to estimate the 10-year clinical and economic impacts of sodium intake in US adults with narcolepsy
- Two treatment scenarios were modelled (assuming continuous treatment over the 10-year horizon until death, or until the patient reached 100 years of age):
  1) taking a high-sodium oxybate agent at a 9 g nightly dosage—1640 mg of sodium added to average US daily dietary sodium intake (based on age- and sex-stratified National Health and Nutrition Examination Survey [NHANES] data[14]) and
  2) taking a low-sodium oxybate agent at a 9 g nightly dosage (131 mg of sodium added to daily dietary sodium intake)

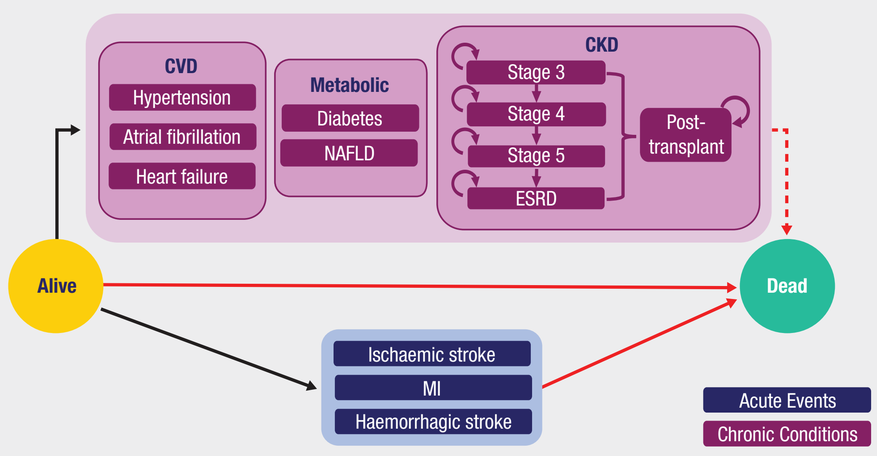
Figure 1. Average Daily Sodium Intake With High- and Low-Sodium Oxybate Agents



[a]Average daily dietary sodium intake for age and sex of simulated individuals in the United States was sourced from age- and sex-stratified published data.[14]

- The number of US adults with narcolepsy was estimated using US Census Bureau population data and US narcolepsy prevalence estimates[15]
- Individuals' characteristics (ie, age and sex) were simulated and used to estimate daily sodium intake[5,14]
- Individuals entered the model with or without chronic condition(s) associated with narcolepsy, based on narcolepsy-specific prevalence estimates[5,6,16-23]

Figure 2. Model Structure



CKD, chronic kidney disease; CVD, cardiovascular disease; ESRD, end-stage renal disease; MI, myocardial infarction; NAFLD, non-alcoholic fatty liver disease.

- Every 3 months, individuals could develop new-onset chronic conditions or acute events, with risks adjusted by the difference in sodium intake from the average estimated daily intake, or could die from an acute event or competing causes

Table 1. Key Model Assumptions

Assumption
Incidence of chronic conditions and acute events are independent of each other
Mortality rates are reflective of the general population adjusted for the additional risk observed in the literature among those with narcolepsy
Any increase in dietary sodium intake is associated with the same increase in urinary sodium excretion
The incidence of chronic conditions persists throughout the model life cycle or until death
Incidence rate sources were assumed to reflect the sodium intake levels of the general US population

Table 2. Key Model Inputs

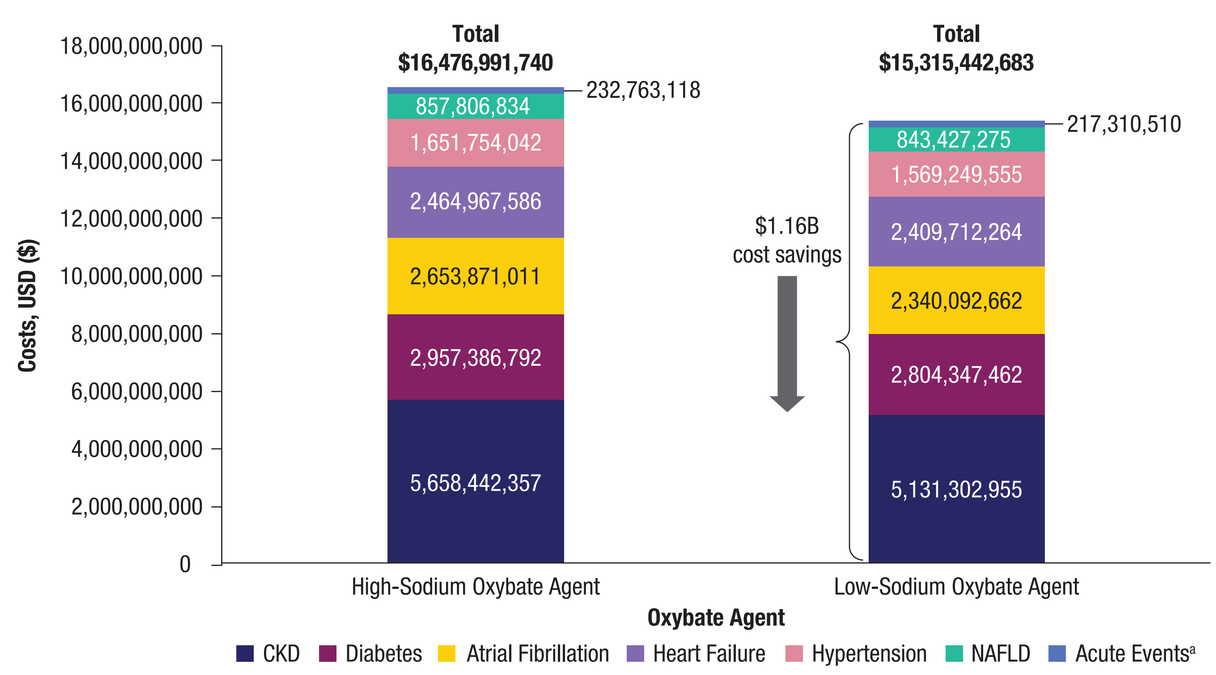
Outcome	Incidence Rate per 1000 PYs	Effect of Per-gram Increase in Sodium Intake (HR/OR)	Cost per Cycle/Event (2025 USD)[a]
Atrial fibrillation	5.0[5]	HR: 1.36[b]	$7639[24]
CKD	4.9[25]	HR: 1.05[26]	Stage 3 = $8203 Stage 4 = $9931 Stage 5 = $10,914[27]
CKD progression[c]	Varies	HR: 1.22[28]	
ESRD[c]	Varies[27]	HR: 1.02[b]	Cycle 1 = $80,429 Cycle 2+ = $45,547[27]
Diabetes	5.9[16]	OR: 1.43	$3213[29]
Heart failure	5.7[5]	HR: 1.06[b]	$8493[30]
Hypertension	67.6[31]	OR: 1.18[b]	$801[32]
NAFLD	3.3[33]	OR: 1.30[b]	$885[34]
Haemorrhagic stroke	0.6[5]	HR: 1.09[b]	$43,180[35]
Ischaemic stroke	3.7[5]	HR: 1.09[b]	$21,593[35]
Myocardial infarction	1.5[5]	HR: 1.05[b]	$29,997[35]

[a]Condition and event costs are presented per cycle and hospitalisation, respectively. The effects of per-gram increase in sodium intake (HR/OR) is applied multiplicatively to the outcomes' rates/odds, respectively, for every gram difference between patients' sodium intake (ie, dietary plus oxybate agent) and the average sodium intake. [b]Results from network meta-analyses data on file. [c]CKD progression and ESRD incidence rates are sourced from a previously published cost-effectiveness model (FINE-CKD), from which incidence rates are derived from transition probabilities between CKD stages 3+.[27]
CKD, chronic kidney disease; ESRD, end-stage renal disease; HR, hazard ratio; NAFLD, non-alcoholic fatty liver disease; OR, odds ratio; PYs, person-years; USD, US dollars.

- Incidence rates of chronic conditions and acute events were identified from narcolepsy-specific published literature, where available, and large nationally representative population-based studies (eg, NHANES)[5,16,25,27,31,33]
- The effects of increasing sodium intake by 1 g on included health outcomes were sourced from network meta-analyses (NMA; data on file) or individual studies
- Costs from administrative claims and the Healthcare Cost and Utilization Project were applied per condition/event per cycle (3 months)
- Model outputs included clinical event counts and total and condition/event-specific direct costs (2025 USD) over 10 years for each treatment scenario
- Total costs for each treatment scenario are additionally presented on a per-person-year (PY) basis
- A sensitivity analysis considered an alternative US incidence rate of hypertension (32.3/1000 PYs)[36]

Results

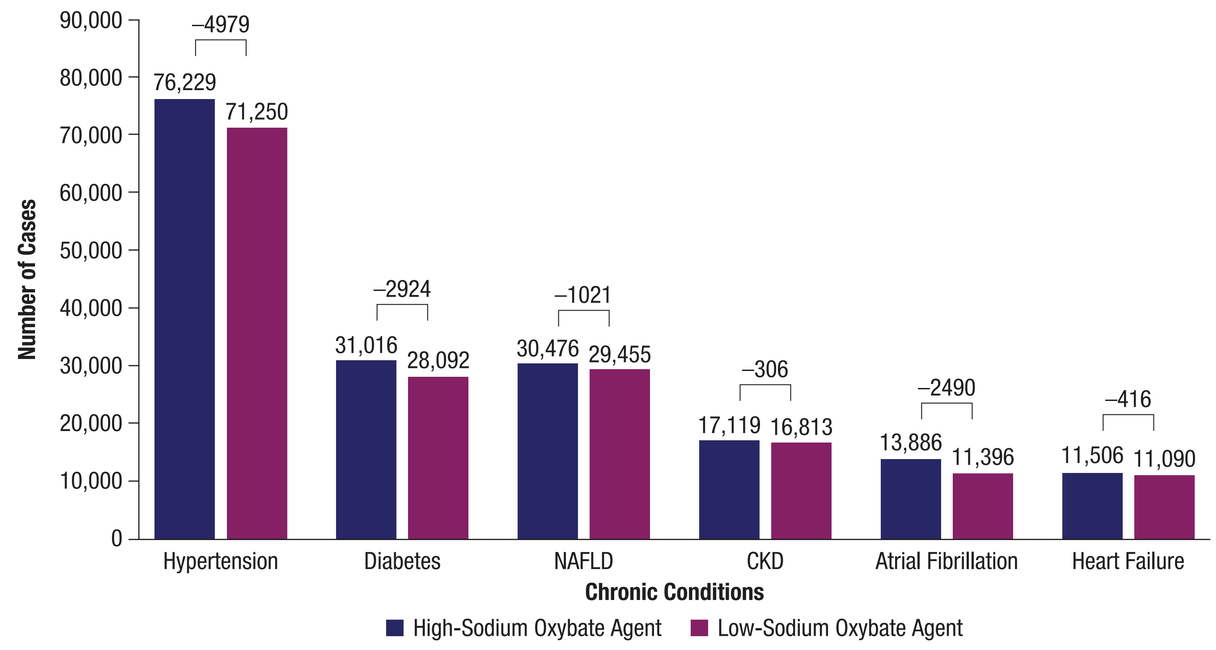
Figure 3. Total Costs Over 10 Years Among 101,135 Adults With Narcolepsy for High- and Low-Sodium Oxybate Agents



[a]Acute events include haemorrhagic stroke, ischaemic stroke, and myocardial infarction.
CKD, chronic kidney disease; NAFLD, non-alcoholic fatty liver disease; USD, US dollars.

- Over the 10-year horizon, total direct healthcare costs among 101,135 individuals with narcolepsy treated with a high-sodium oxybate agent were $16.48B versus $15.32B for individuals treated with a low-sodium oxybate agent, representing $1.16B in cost savings with a low-sodium oxybate agent

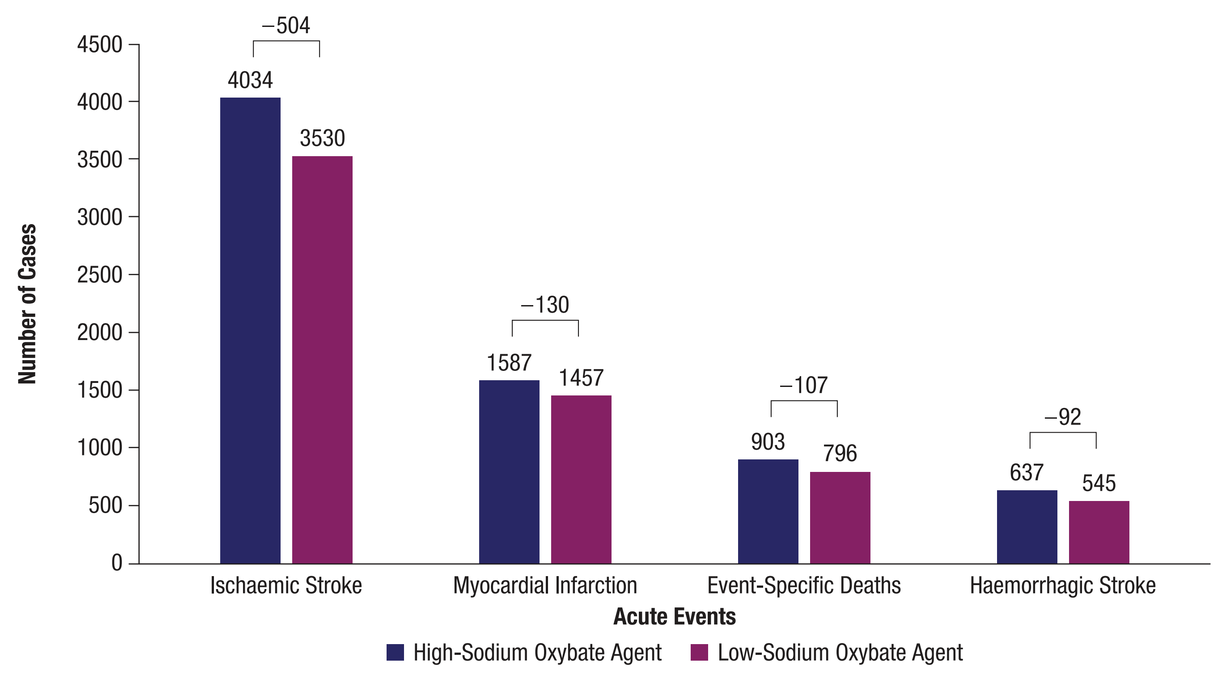
Figure 4. Total Cases of Chronic Conditions Over 10 Years



CKD, chronic kidney disease; NAFLD, non-alcoholic fatty liver disease.

- A low-sodium oxybate agent was associated with a reduction in the number of cases across each chronic condition assessed, including hypertension (n=4979), diabetes (n=2924), and atrial fibrillation (n=2490)
- In the sensitivity analysis reducing the estimated rate of hypertension, the number of avoided cases of hypertension (n=3599) and hypertension-related cost savings over 10 years ($51.0M) remained high

Figure 5. Total Cases of Acute Events Over 10 Years



- Avoidance of acute events was also observed with a low-sodium oxybate agent, including 504 fewer ischaemic strokes, 130 myocardial infarctions, and 92 haemorrhagic strokes; 107 event-specific deaths were also avoided

Conclusions

- This robust microsimulation model, informed by narcolepsy-specific inputs and an expansive NMA, suggests that treatment with a low-sodium versus high-sodium oxybate agent was associated with a notable reduction in negative cardiovascular, cardiometabolic, and cardiorenal outcomes (eg, hypertension, diabetes, and non-alcoholic fatty liver disease) among US adults with narcolepsy, translating to $1.16B in healthcare cost savings over 10 years
- Limitations of this analysis include the potential of ecological fallacy, as meta-analysis of aggregate sodium effects may not reflect individual-level effects, and the exclusion of other conditions and events which may underestimate total economic and clinical consequences
- These findings underscore the importance of treatment strategies that minimise excess sodium exposure to mitigate elevated CV/CM/CR risks and associated costs in this high-risk population

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