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Abstract

Little is known on the impact that nocturia (the need to wake up at night to urinate) has on a nation's economy. While there are many individual factors associated with inadequate sleep (e.g. bad sleep hygiene, chronic sleep disorders such as insomnia or sleep apnea), frequently having to wake up at night to urinate fragments sleep, with negative consequences on an individual's health and well-being as well as daytime functioning. Using a large-scale UK workforce data, we estimate the prevalence of nocturia in the working population and quantify the lost worker productivity caused by nocturia, measured by absenteeism and presenteeism. This enters our multi-country general equilibrium model, which we calibrate to the UK economy, to estimate the annual macroeconomic cost of nocturia. We find the annual cost of clinically significant nocturia (waking up at least twice to urinate) is around £5.4 billion, or equivalently £1996 per worker with nocturia. This cost estimate is larger than previous estimates on the productivity effects of nocturia using cost-of-illness (COI) methods, suggesting the importance of taking into account general equilibrium effects when assessing the economic burden of health conditions.

Key words: nocturia, sleep, general equilibrium model, economic cost, urology JEL: **C1, C68, E2, I10, J10**

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Conflict of interest statement

Provided for each author as separate forms in the attachments.

1 Introduction

Alongside physical activity and healthy nutrition, it is increasingly recognized that sleep is an equally important pillar of health. The evidence suggests that sleep is not only an important factor for individual physical and mental health but also for perceived quality of life and performance at work (Grandner, 2018). It also has been shown that inadequate sleep is associated with negative consequences for national economies (Hafner et al., 2017; Hillman et al., 2018). While there are many individual factors associated with inadequate sleep (e.g. bad sleep hygiene, chronic sleep disorders such as insomnia or sleep apnea), frequently having to wake up at night to urinate fragments sleep. Sleep fragmentation has adverse implications for the most restorative sleep stages and therefore is associated with negative consequences for an individual's health, well-being and daytime functioning (Stepanski, 2002; Bonnet and Arand, 2003; Bliwise et al., 2015a).

The waking to pass urine at least once during the main sleep period is generally referred to as *nocturia* (Hashim et al., 2019) and is regarded as one of the most bothersome lower urinary tract symptoms (Agarwal et al., 2014; Chapple et al., 2006; Kupelian et al., 2012). However, individuals reporting less than two nocturnal voids are generally not regarded as having clinically significant nocturia (Bosch and Weiss, 2010; Tikkinen et al., 2010a). There are different etiologies of nocturia which are associated with different factors, including excessive fluid intake before bedtime, but among the most common are a large urine volume produced during the night (nocturnal polyuria) or a reduced bladder capacity.

Nocturia is commonly perceived as a problem of elderly men, however nocturia is also relatively common among all population groups (Wein et al., 2002). At any given point in time, on average, up to 50 per cent of the adult population report having to get up at night to urinate at least once, whereas up to 20 per cent experience the need to get up at least twice (Bosch and Weiss, 2010). Independent of the number of nocturnal voids, the prevalence of nocturia is increasing with age (Cornu et al., 2012). However, even among individuals aged 20 to 30, about 30 percent of women and 20 percent of men experience regularly the need to get up at night to urinate at least once. While in younger years, nocturia tends to be more prevalent among women, in older age the prevalence is higher in men (Bliwise et al., 2019).

Nocturia is associated with negative health consequences, such as increased risk of cardiovascular disease, depression and – in older individuals – a higher risk of injury through falls (Asplund, 2005; Chartier-Kastler and Chapple, 2006; Weidlich et al., 2017). Due to the associated underlying chronic health conditions and the higher fall risk for the elderly, nocturia is also associated with higher relative mortality risk, but the causal pathway between nocturia and mortality remains unclear (Pesonen et al., 2020).

The challenge with nocturia is that often it is not acknowledged as a condition. Doctors and health practitioners overlook nocturia as a potential health problem associated with sleep loss, and individuals that suffer from it often do not report it until it becomes unbearable, substantially affecting individual quality of life. Younger people with nocturia often do not feel comfortable talking about it, and many late-middle age people just see nocturia as part of getting older (Marinkovic et al., 2004).

Given competing health priorities and finite financial resources, it is important to provide a perspective on the cost of nocturia, which has three components: (i) intangible costs on the quality of life (e.g. lower life satisfaction, behavioral modification, feeling loss of control); (ii) direct costs of treatment; (iii) indirect costs through loss of productivity in the labor market. While (i) and (ii) have received considerable attention in the existing literature (e.g., Zeng et al., 2019; Weidlich et al., 2017; Andersson et al., 2016b; Tikkinen et al., 2010b), an understudied issue is the link between nocturia and productivity loss in the working population. As the key complaint of nocturia is disrupted sleep, the consequences of nocturia are felt at daytime, especially for the population that is active in the labor market.

The sleep disruption associated with nocturia has been linked to daytime fatigue, decreased concentration, cognitive impairment, lower performance at work and higher levels of absenteeism and presenteeism (Asplund, 2005; Bliwise et al., 2019; Miller et al., 2016). Yet, beside a few studies that use a cost-of-illness (COI)¹ approach to estimate the direct healthcare burden of nocturia, predominantly associated with nocturia in the elderly population (Dmochowski et al., 2019), to our knowledge, there is very little empirical work on the economic impact on a nation's economy beyond the effect on healthcare expenditure (see Jhaveri et al., 2019; Weidlich et al., 2017; Holm-Larsen, 2014).

In addition, existing COI studies only consider partial equilibrium effects and do not account for the potential spillovers on other agents or markets that occur when parts of the population suffer from ill-health or lower productivity (e.g., labor-capital substitution, effect of one sector on others, and trade effects). In contrast, a general equilibrium model includes the ripple effects across the economy.²

To consider these points, we estimate the macroeconomic cost of nocturia associated with lost productivity on the UK economy through the application of an economy-wide computable general equilibrium (CGE) macroeconomic model. We add to the existing literature in three ways: First, this is the first study that seeks to quantify the cost of nocturia associated with lost productivity using a CGE method. Second, unlike previous studies, we are able to link the frequency of nocturnal voids and labor productivity in the working population using large-scale workforce data from UK employers and their employees. We provide a unique perspective into this health condition by combining a comprehensive econometric analysis that calibrates key parameters of the augmented human capital component of the CGE model. Finally, our study contributes beyond COI methods. By taking a more holistic general equilibrium approach, we account for the wider macroeconomic effects on the economy and we compare the findings to existing partial equilibrium analyses.

In this study, we provide new estimates for the macroeconomic cost of nocturia associated with productivity loss for two different nocturia thresholds: (i) one or more nocturnal voids; and (ii) two or more nocturnal voids, where the latter represents a more clinically relevant threshold for nocturia. We estimate that nocturia considered as one or more nocturnal voids costs the UK economy about £16.6 billion annually, or about £1110 per worker with nocturia. Using the clinically significant definition for nocturia, we estimate a cost to the UK economy of £5.4 billion annually or about £1996 per person in the workforce experiencing two or more nocturnal voids.

2 Methods

In this section, we begin with a description of the economy-wide multi-country computable general equilibrium model. Next, we expand on the link between nocturia and the effective-labor supply. We

 $^{^{1}}$ COI summarizes the direct and indirect cost associated with ill-health, taking into account, for instance, the sum of all direct personal medical costs, as well as the indirect cost (e.g. income loss due to absenteeism or premature death).

 $^{^{2}}$ See examples of studies that support this view: Hafner et al. (2020c); CCA (2019); Yerushalmi et al. (2019); Bloom et al. (2018); Taylor et al. (2014); Keogh-Brown et al. (2010); Smith et al. (2005).

conclude with the econometric analysis that calibrates how nocturia affects labor productivity.

2.1 A general description of the multi-country CGE model

Economy-wide computable general equilibrium (CGE) models have become more common due to some advantage over traditional approaches, such as COI methods (e.g., Bloom et al., 2018). They have already been used in the application to HIV/AIDS (Thurlow et al., 2009), Malaria (Yerushalmi et al., 2019), antimicrobial resistance (AMR) (CCA, 2019; Taylor et al., 2014; Smith et al., 2005), pandemic influenza and non-communicable disease (Keogh-Brown et al., 2010; Smith et al., 2011) and various health policy assessments (Yerushalmi and Ziv, 2020; Hsu et al., 2015; Rutten and Reed, 2009; Borger et al., 2008). But to our knowledge, applied health focused CGE methods have never been used to quantify the macroeconomics cost of nocturia.

Our core multi-country, multi-sector, CGE model closely resembles Hafner et al. (2020b), Yerushalmi et al. (2019) and Lanz and Rutherford (2016). (We refer readers to them for more technical details.) We choose to report more closely on our approach to link between nocturia and the effective-labor supply and on the econometric analysis that calibrates labor productivity loss from nocturia. Thus, given limited space, we provide only a general description of the model below.

Our multi-country model simultaneously solves multiple equations of production supply and household demand, within a country, and between countries through trade linkages. In each country, a household maximizes a multi-level, extended linear expenditure system utility function with a fixed proportion between private savings (Howe, 1975). Each government receives income from collecting taxes, tariffs, and *net* funds from the household and other countries. Governments provide public goods and services by purchasing commodities. To simplify our results and analysis, but without overly affecting them, we focus on four main sectors that supply final and intermediate goods (i.e., agriculture, industry, services and health care).

Finally, to quantify the cost of nocturia³, we compare a baseline nocturia scenario (i.e., the current situation) with two counterfactual scenarios in which less individuals are affected by nocturnal voiding. The two scenarios differ by the number of nocturnal voids: one or more voids treated, and two or more voids treated. The latter scenario is considered a clinical relevant threshold for diagnostics and treatment.

The model is programmed in the computer program GAMS⁴, using the MPSGE solver by Rutherford (1999), and calibrated to the GTAP 10, multi-country database (Aguiar et al., 2019). GTAP 10 includes social accounting matrices (SAMs) of 141 countries, which are a double entry accounting system for incomes and expenditures. To focus our attention on the United Kingdom (UK), we aggregate the database into two countries: UK and the rest of the world (RoW). These countries are interlinked by trade flows of goods and services. Finally, GTAP 10 reference year is USD 2014, which we convert to GBP 2019 by chaining the USD implicit price deflator⁵ and using the yearly average 2019 USD/GBP spot exchange rate⁶.

Below we provide more specific detail on how nocturia affects the effective labor supply in our model.

³Or, in other words, the benefits of treating nocturia

⁴www.gams.com

⁵https://fred.stlouisfed.org/series/GDPDEF

⁶https://www.bankofengland.co.uk/boeapps/database/default.asp

2.2 The link between nocturia and the effective-labor supply

A perfectly competitive economic sector $j \in J$ produces goods using a multi-level, differentiable, constant return to scale (CRS) production function $Y_j = f(K_j, N_{jq}, L_j)$. Each sector demands the following inputs: capital K_j , intermediate inputs N_{jq} that are produced by sector $q \in J$, and effective-labour L_j , which is supplied by the household so that $L^s = \sum_j L_j$, i.e., the labor market clears. Effective-labor supply L^s is determined by two elements: the physical supply of labour (e.g. number of employed workers) \overline{L} , augmented by their productivity level E that depends on an individual's health status. Thus, the effective labor supply is adjusted for efficiency units by $L^s = \overline{L} \cdot E$.

An increase in effective-labor supply is manifested through the removal of prolonged periods of sickness or levels of presenteeism that temporarily reduce the country's effective workforce. In order to take account of the counterfactual changes to sickness absence and presenteeism associated with nocturia, labor productivity E is obtained by adding the relative increase in productivity e to the total baseline productivity level: $E = \overline{E} + e$, where $\overline{E} = 1$ is the baseline productivity labor supply with nocturia, and $e \ge 0$ is the *additional* productivity once nocturia is removed in the counterfactual scenarios.

The parameter e is obtained by summing all the additional productivity across the working population by

$$e = \sum_{v=0}^{V} \theta_v \alpha_v \tag{1}$$

with θ_v defined as the prevalence of nocturia among the working population, with v number of voids per night. α_v is the marginal productivity effect of each additional nocturnal void. As most existing research on nocturia focuses on data for individuals over 60 years old, θ_v and especially α_v , are generally unknown parameters. As discussed in the next section, we calibrate both parameters using information on nocturia prevalence and the productivity effects associated with the condition using a unique health and well-being survey of UK workers. As there is uncertainty related to the parameter inputs, we further test our model assumptions by applying a Monte-Carlo simulation to randomly generate a range for θ_v and α_v . Due to a lack of a prior, the parameters are generated from a uniform probability distribution function (PDF) that jointly enters the model.⁷ For each counterfactual scenario, we execute the model 5000 times with randomly generated parameter combinations.

2.3 Econometric analysis linking nocturia with productivity

2.3.1 Data

We use rich UK working population data based on *Vitality UK's Britain's Healthiest Workplace (BHW)* survey, which has been collected annually since 2014 among UK companies and their workers.⁸ The BHW survey is collected annually among UK organizations with 20 or more employees and provided by organizations to their workforce. Its main purpose is to support employees in better understanding their health and well-being via a personalized individual report whilst providing a comprehensive aggregated report to organizations to support their well-being strategies and improvement for productivity. Employees were surveyed with over 100 questions related to socio-demographic factors (e.g. age,

⁷A uniform PDF gives equal probability to all randomly selected values along their chosen range.

⁸See BHW (2019) for further details.

gender, ethnicity, education, income, marital status, informal carer responsibilities), lifestyle behavior (e.g. nutrition, smoking habits, alcohol consumption, physical activity, sleep behavior), health factors (e.g. mental and physical health indicators, body mass index, chronic and musculoskeletal conditions), subjective well-being and workplace productivity. All survey participants provided electronic written consent for anonymized usage of their records for research purposes as required. The ethics committee at the data collecting organization RAND Europe has reviewed and approved the data collection and research plan. More detailed information about the data collection process of the BHW survey can be found in Hafner et al. (2020a); Stepanek et al. (2019); Hafner et al. (2020c).

We use the BHW survey waves for the year 2017 and 2018 as they provided unique questions relating directly to nocturia, when survey participants were asked about the frequency of nocturnal voids. Our analysis uses a retrospective observational cross-sectional study design using the survey waves 2017 and 2018, where data is pooled across the two years. We only include workers aged 20 to 65 and exclude those on zero-hours flexible work contracts. We also exclude female workers that report to be pregnant at the time of the survey response. The final sample based on the pooled cross-sectional BHW data includes 52,887 observations.

2.3.2 Empirical approach

We empirically estimate the association between the severity of nocturia, measured through the number of nocturnal voids v, and productivity w. The associations are examined based on different model specifications by ordinary least squares (OLS). The fully specified model takes the form:

$$w_{ict} = \alpha_v v_{ict} + \beta X_{ict} + \delta_c + \gamma_t + \mu_{ict}$$
⁽²⁾

where w_{ict} is the observed productivity, measured as work impairment due to absenteeism and presenteeism,⁹ of individual *i* employed in company *c* at time *t*; v_{ict} represents the number of nocturnal voids and our key parameter of interest is α_v , which we use to calibrate the efficiency parameter *e* in (1) that represents the marginal increase (decrease) in work impairment (productivity) for the number of reported voids.

The dependent variable w_{ict} is productivity impairment, represented by the sum of the percentage of working time missed (absenteeism) and percentage of work time adversely affected by productivity impairment while at work (presenteeism). This data was assessed with the Work Productivity and Activity Impairment-General Health (WPAI-GH) questionnaire. WPAI is a validated instrument to measure workplace productivity loss Prasad et al. (2004); Reilly et al. (1993), and frequently applied to assess health-related productivity loss measured through absenteeism and presenteeism (Brunner et al., 2019). The instrument consists of different questions with a recall time frame of seven days. The questions asked the respondent about the total hours worked, the number of hours missed from work; and the degree to which the respondent feels that a health problem has affected productivity while at work and their ability to do daily activities other than work. Following the coding and scoring rules of the instrument, WPAI outcomes were expressed as impairment percentages, due to absenteeism and presenteeism, where higher percentages indicate greater impairment and lower productivity.

The main explanatory variable of interest is the number of reported nocturnal voids v_{ict} by each individual ("How often do you usually get up during the night to go to the bathroom?"). The continuous

⁹With higher levels of work impairment reflecting lower productivity.

variable is based on applied standard scales from voiding diaries applied in nocturia patient-reported outcomes research.

Furthermore in (2), X_{ict} represents a large set of potential confounding variables that are available in the BHW survey. Based on previous evidence, these are expected to be associated with work productivity as well as nocturnal voiding (Yoshimura, 2012; Tikkinen et al., 2009). First, a number of socio-demographic covariates are considered, including age, gender, ethnicity, education, income, irregular working hours (e.g. night shifts), marital status, informal care responsibilities for a child and engagement in voluntary or charity activities.

Second, a number of health and lifestyle covariates including body mass index, smoking status (current smoker), physical inactivity (performing less than 150 mins per week), excessive salt intake (adding regularly more than a pinch of salt to a meal), excessive alcohol consumption (drinking more than 14 alcohol units of 10 ml/8mg per unit), the number co-morbid clinically diagnosed health conditions (cancer, asthma, heart disease, kidney disease, diabetes, hypertension), as well as the number of musculoskeletal condition the individual suffers (e.g. back pain). Mental health was assessed through the Kessler Psychological Distress Scale which measures different emotional states based on a sixitem scale (Kessler et al., 2002). In line with previous research, a dichotomous variable was generated taking the value one if the overall Kessler score across all items is above 13, which is generally applied as the threshold of medium to severe psychological distress and anxiety (Kessler et al., 2003).

Finally, one challenge when estimating the effects of nocturia is the bidirectional relationship between sleep and nocturia (Ancoli-Israel et al., 2011). Previous research suggests that nocturnal voiding is predicting poor sleep quality (Araujo et al., 2014). However, individuals suffering from sleep-onset insomnia may also just get out of bed at night and to the bathroom, without nocturnal voiding being the main reason for their rise out of bed and subsequent sleep fragmentation. Disrupted sleep could also be caused by other factors such as sleep apnea, which contributes to sleep fragmentation, and has been associated with nocturia episodes and increased urine production (Miyazato et al., 2017). Our data does not include a direct question about chronic sleep problems like insomnia or sleep apnea.

However, the data includes a question based on the Pittsburgh Sleep Quality Index (Buysse et al., 1989) on a 5-point scale whether the individual generally has problems falling asleep ('During the last seven days, did you have problems falling asleep; 0 not at all – 4 very much'). We use this variable as a proxy for sleep-onset insomnia and also control for whether an individual on average sleeps less than 6 hours or more than 9 hours, taking into account short and long sleep duration. Furthermore, our large set of control variables include already factors which are strongly correlated with sleep apnea, such as age, gender and obesity (Prasad et al., 2018) and hence at least indirectly we control for sleep apnea as a potential confounder as well. Descriptive statistics of the key variables included in the analysis are provided in the Appendix A.

Each econometric model specification includes company fixed-effects δ_c which take into account any potential confounders at the company-level such as the workplace environment. We also include time fixed-effects γ_t controlling for the week, month and year when the online survey response by the individual was submitted. μ_{ict} denotes an idiosyncratic error term.

As the dependent variable w_{ict} is a non-negative count variable containing a larger mass of zeros, using OLS could lead to biased estimates. As a robustness check we therefore transform the dependent variable into a count variable measuring the weekly hours of work lost due to absenteeism and presenteeism and use a negative binomial regression (NBR) model. If the marginal effects of OLS and NBR

| Voids | Total (%) | Women (%) | Men (%) |
|--------------|-----------|-----------|---------|
| 0 | 50.1 | 47.7 | 52.5 |
| 1 | 40.8 | 42.1 | 39.5 |
| 2 | 6.8 | 7.6 | 6.0 |
| 3+ | 2.3 | 2.7 | 2.0 |
| Observations | 52,887 | 26,552 | 26,628 |

Table 1: Prevalence of nocturia by number of nocturnal voids (parameter θ_v)

Notes: Table entries based on a BHW pooled cross-sectional (CS) sample for the years 2017 and 2018. Chi-square test suggests a statistically significant different distribution between male and female (p<0.01). The maximum number of nocturnal voids reported in the data sample is 5 nocturnal voids. Due to the relative small number of individuals reporting 4 or 5 nocturnal voids we have grouped them into one category of 3 or more voids.

are similar in magnitude, the parameter estimates are robust against the choice of estimation method. For all analyses statistical significance was assessed at a significance level of 5% with standard errors (se) clustered at the company level. All statistical analyses were conducted in STATA 16.¹⁰

3 Findings

First, we present the results for the econometric analysis that link nocturnal voids v with work impairment w, arising from absenteeism and presenteeism. Second, we provide the key calibrated parameters derived from the econometric analysis and their corresponding lower and upper values. Finally, we summarize the results of the CGE simulation analysis.

3.1 Prevalence of nocturia and the association with productivity

Table 1 reports the prevalence of nocturia by the number of nocturnal voids symptom severity and by gender for the sample population. This calibrates parameter θ_v in (1).

About 50 percent of workers report zero nocturnal voids. 40.8 percent report on average one nocturnal void and about 6.8 percent of the sample population experiencing two nocturnal voids. 2.3 percent of the sample population reports on average three or more nocturnal voids. In our data sample of workers aged 20 to 65, women tend to experience on average more nocturnal voids than men. These estimates are roughly inline with other countries and studies (Jhaveri et al., 2019; Cornu et al., 2012; Tikkinen et al., 2009).

Next, Table 2 reports the main regression results for estimating the association between the number of nocturnal voids and the work impairment percentage loss (parameter α_v in 1). Each column reports the results for different model specifications, starting with model OLS-1 and building up to model OLS-3, adding more covariates.

The results show that, adjusted for company and time fixed effects, as well as socio-demographic characteristics, one nocturnal void is associated with a 2.4 percentage points (95% CI 2.0-2.8) increase in work impairment; two nocturnal voids are associated with a 5.7 percentage points (95% CI 4.8-6.6) increase in work impairment; and three or more nocturnal voids are associated with a 7.9 percentage points (95% CI 6.4-9.5) increase in work impairment (OLS-1). To put this into perspective, if the weekly working hours per full-time worker in the UK is about 40 hours, then compared to a worker without nocturia, a worker with two nocturnal voids loses on average about 2.3 hours of their total

¹⁰https://www.stata.com/.

| () | | | |
|-------------------------------|----------------|-----------|-----------|
| | (1) | (2) | (3) |
| Parameter α_v (% loss) | OLS-1 | OLS-2 | OLS-3 |
| 1 void | 2.390 | 1.641 | 1.354 |
| se | (0.206)** | (0.189)** | (0.188)** |
| 95% CI: Low | 1.985 | 1.269 | 0.985 |
| 95% CI: High | 2.796 | 2.013 | 1.724 |
| 2 voids | 5.720 | 3.426 | 2.641 |
| se | $(0.442)^{**}$ | (0.394)** | (0.396)** |
| 95% CI: Low | 4.849 | 2.650 | 1.862 |
| 95% CI: High | 6.59 | 4.201 | 3.42 |
| 3 + voids | 7.954 | 4.583 | 3.572 |
| se | (0.789)** | (0.007)** | (0.689)** |
| 95% CI: Low | 6.401 | 3.191 | 2.215 |
| 95% CI: High | 9.507 | 5.975 | 4.929 |
| Covariates | | | |
| Company FE | Yes | Yes | Yes |
| Time FE | Yes | Yes | Yes |
| Socio-demographics | Yes | Yes | Yes |
| Lifestyle & Health | No | Yes | Yes |
| Sleep | No | No | Yes |
| Observations | 52,887 | 52,887 | 52,887 |
| | | | |

Table 2: Associations between nocturnal voids and work impairment due to absenteeism and presenteeism (Parameter α_v , % loss)

Notes:** p<0.01, * p<0.05. Standard errors (se) clustered at the company-level. 95% confidence intervals (CI) provided. Dependent variable is percentage of work impairment due to absenteeism and presenteeism (e.g. % of working time lost). Data sample based on BHW pooled cross-sectional (CS) sample of the years 2017 and 2018. All models in columns 1 to 3 are adjusted for company- and time (FE) fixed effects (week, month and year of given survey response). Model OLS-1 is adjusted for age, gender, ethnicity, education, income, marital status, caring responsibilities (child), irregular working hours, the prevalence of financial concerns or whether the individual performs voluntary or charity work alongside normal working hours. Model OLS-2 is additionally adjusted for smoking status, excessive salt intake, body mass index, alcohol consumption, physical activity levels, mental health (Kessler score), chronic health conditions (cancer, heart disease, kidney disease, hypertension, diabetes). Model OLS-3 is also adjusted for problems falling asleep, as well as short and long sleep duration.

| Parameter | Description | | Lower value | Mid value | Upper value | Source |
|-----------|--|---|--------------------------------|--------------------------------|--------------------------------|--------------------------------------|
| $	heta_v$ | Prevalence rate among the sampled working population (% of total) | 0 voids: 1 voids: 2 voids: 3+ voids: | -25% | 50.1% 40.8% 6.8% 2.3% | +25% | Own calculation, BHW survey |
| $lpha_v$ | Work impairment (% loss) due to absenteeism and presenteeism among the sampled working population | 0 voids: 1 voids: 2 voids: 3+ voids: | $0 \\ 0.985 \\ 1.862 \\ 2.215$ | $0\\1.354\\2.641\\3.572$ | $0 \\ 1.724 \\ 3.420 \\ 4.929$ | Own calculation: Table 2, Column (3) |

Table 3: CGE calibration parameters and Monte-Carlo simulation sample range

Note: the table summarizes the calibrated inputs θ_v and α_v used in the CGE model, with the corresponding upper and lower values for the Monte-Carlo simulations.

working time per week due to absenteeism and presenteeism¹¹, and workers with three or more voids lose about 3.2 hours.

Adding lifestyle factors and chronic health conditions (OLS-2), reduces the point estimates for one nocturnal void to 1.6 percentage points (95% CI 1.3-2.0); the point estimate for two nocturnal voids to 3.4 percentage points (95% CI 2.7-4.2) and the point estimate for three or more nocturnal voids to 4.6 percentage points (95% CI 3.2-6.0). Finally, adjusting additionally for a sleep-onset insomnia proxy variable and short and long sleep duration, the point estimates reduce further in magnitude (OLS-3). The point estimate for one nocturnal void is 1.4 percentage points (95% CI 0.9-1.7); the point estimate for two nocturnal voids is 2.6 percentage points (95% CI 1.9-3.4); and the point estimate for three or more nocturnal voids is 3.6 percentage points (95% CI 2.2-4.9). The reduction in magnitude between point estimates presented in column 2 and 3 highlights the importance of taking into account potential sleep disorders as confounding factors when estimating the associations between nocturnal voiding and productivity loss.

As previously explained, the purpose of the econometric analysis is to calibrate key parameters in the CGE model - see equation (1). We use the parameter estimates provided in column 3 of table 2 as they are adjusting for the largest number of covariates and have the lowest magnitude compared to the estimates provided in column 1 and 2. This leads to the lowest productivity loss associated with nocturia of the three model specifications and hence the most conservative. Table 3 presents the mid-value inputs used for θ_v and α_v , as well as their lower and upper bound values applied in the Monte-Carlo simulations based on the 95% confidence interval of the estimated parameters.¹²

Robustness Checks

In order to be confident in our approach, we also check whether the results depend on the choice of estimation method. We transformed the dependent variable into a count variable corresponding to the weekly hours lost due to absenteeism and presenteeism using NBR models. The results are shown in Table 4. Column 1 and 2 replicate our baseline estimates using the transformed dependent variable (OLS-2T and OLS-3T). For instance, column 2 reports that a worker with three or more nocturnal voids loses on average about 1.4 hours a week more than a worker without nocturia. Columns 3 to 6 report the NBR results based on the same covariate specifications, whereas NBR-1 and NBR-2 report

¹¹2.3=5.720/100 x 40 hours/week

¹²This means that for α_v , the change of the bound values relative to the mid-value ranges from 27 to 38 percent, rising with each additional void, and adds substantial variability.

| | (1) | (2) | (3) | (4) | (5) | (6) |
|--------------------|----------------|-----------|----------------|----------------|----------------|-----------|
| | OLS-2T | OLS-3T | NBR-1 | NBR-2 | NBR-3 | NBR-4 |
| 1 void | 0.656 | 0.542 | 0.914 | 0.787 | 0.697 | 0.578 |
| se | (0.076)** | (0.075)** | (0.104)** | (0.107)** | (0.077)** | (0.077)** |
| 2 voids | 1.370 | 1.056 | 1.723 | 1.402 | 1.314 | 1.030 |
| se | $(0.158)^{**}$ | (0.158)** | (0.174)** | (0.181)** | $(0.128)^{**}$ | (0.130)** |
| 3 + voids | 1.833 | 1.429 | 1.995 | 1.518 | 1.522 | 1.041 |
| se | $(0.283)^{**}$ | (0.276)** | $(0.255)^{**}$ | $(0.247)^{**}$ | (0.192)** | (0.181)** |
| Covariates | | | | | | |
| Company FE | Yes | Yes | Yes | Yes | Yes | Yes |
| Time FE | Yes | Yes | Yes | Yes | Yes | Yes |
| Socio-demographics | Yes | Yes | Yes | Yes | Yes | Yes |
| Lifestyle & Health | Yes | Yes | Yes | Yes | Yes | Yes |
| Sleep | No | Yes | No | Yes | No | Yes |
| Observations | 52,887 | 52,887 | 52,887 | 52,887 | 52,887 | 52,887 |

Table 4: Robustness checks - Associations between nocturnal voids and working hours lost due to absenteeism and presenteeism

Notes:** p<0.01, * p<0.05. Standard errors (se) clustered at the company-level. Dependent variable is the number of working hours lost per week due to absenteeism and presenteeism (assuming a work week of 40 hours). Data sample based on BHW pooled cross-sectional (CS) sample of the years 2017 and 2018. All models in columns 1 to 6 are adjusted for company- and time (FE) fixed effects (week, month and year of given survey response). Model OLS-2T and OLS-3T represent same models as reported in Table 2 columns 2 and 3 but with the transformed dependent variable. Columns 3 and 4 present the results of using a NBR model instead of OLS and showing the average marginal effects for each number of nocturnal voids. Columns 5 and 6 report the NBR model effects but at the mean characteristics of all covariates.

the estimates for average marginal effects of NBR and NBR-3 and NBR-4 present the estimates for NBR at mean characteristics of the covariates. The comparison shows that the models lead to similar marginal effects and hence suggesting that the results are not driven by the choice of the model.

3.2 Macroeconomic cost of nocturia

This section reports on the estimated macroeconomic cost of nocturia to the UK. We assess this for two nocturia thresholds: (i) nocturia defined as one or more nocturnal voids; and (ii) nocturia defined as two or more nocturnal voids, which is generally considered as a clinically relevant void threshold that warrants more in-depth diagnostics and treatment. As summarized in Table 5, based on the distribution of nocturnal voids across our UK workforce survey, we estimate that around 14.9 million (mln) adults in the UK workforce experience on average at least one nocturnal void, and about 2.7 mln adults in the UK workforce experience two or more nocturnal voids.¹³ Combining this information with the corresponding working impairment estimates associated with each nocturnal void, this amounts to a weighted average productivity loss of 1.6 percent (95% CI 1.2-2.1) when nocturia is defined as one or more nocturnal voids, and 2.9 percent (95% CI 2.0-3.8) when considering the clinically relevant nocturia threshold of two or more nocturnal voids.

Table 5 and Figure 1 further report our estimates of the cost of nocturia. To distinguish between the macroeconomic impact of nocturia for each of the two thresholds, we simulate two separate scenarios: (i) removing all voids (1+), and (ii) removing two or more voids (2+) while maintaining single nocturnal voids. Our findings suggest that one or more nocturnal voids costs the UK economy about £16.6 billion

 $^{^{13}}$ This is based on using the frequency of nocturnal voids based on table 1 in combination with 2019 UN Population Data for the UK and the average 2019 employment rate of 76 percent provided by the UK Office of National Statistics.

| | Scenario | | | |
|---|-----------|---------------|-------------------|-------------|
| | 1+ | Voids | 2+` | Voids |
| | Estimate | CI | Estimate | CI |
| Nocturia in figures | | | | |
| Total number in workforce with nocturia | 14.9 mln | | 2.7 mln | |
| Average productivity loss in workforce | 1.6% | (1.2-2.1) | 2.9% | (2.0-3.8) |
| with nocturia | | | | |
| Average working hours lost per week in | 0.7 hr | (0.5-0.8) | $1.2~\mathrm{hr}$ | (0.8-1.5) |
| workforce with nocturia | | | | |
| Measures of economic loss | | | | |
| Cost of nocturia (£ bln, 2019 real terms) | £16.6 bln | (16.51-16.65) | £5.4 bln | (5.38-5.44) |
| As percent of GDP | 0.43% | | 0.14% | |
| Cost per worker with nocturia | £1105 | (1101-1110) | £1969 | (1959-1978) |

Table 5: Results of the economy-wide CGE model

Note: The table provides various measures of the economic loss arising from nocturia in the UK. The corresponding 95% confidence intervals (CI) are reported in parentheses.

(bln) annually in terms of real total expenditure¹⁴, which is around 0.43 percent of the UK GDP. Clinically significant nocturia with two or more nocturnal voids costs the UK economy about £5.4 bln in real total expenditure, which is around 0.14 percent of UK GDP.

Figure 1 plots the sample distributions for each nocturia threshold and highlights the average cost of nocturia with a dashed line. Two interesting points to note: first, the distribution around 2+ voids is narrower compared with 1+ voids because the single nocturnal void follows the baseline scenario (i.e., it is fixed to the current situation). Therefore, as expected, the Monte-Carlo simulation loses one element of variability. Second, the difference in estimated costs between the two nocturia thresholds is about £11.2 bln. This cost could be partially reduced by lowering the prevalence of one nocturnal void. For example, by making simple behavioral lifestyle changes such as improving individual sleep hygiene, minimizing fluid intake past a certain time in the evening or making changes to nutritional intake (e.g. avoiding food that increases bladder activity or reducing salt intake).

Finally, an alternative measure is the cost per person in the workforce with nocturia. We compute this value to allow comparison with other nocturia related studies and also with other medical conditions. We estimate that nocturia considered as one or more nocturnal voids costs about £1105 per worker with nocturia. Using the clinically significant definition for nocturia, we estimate a cost of £1969 per worker with two or more nocturnal voids. In other words, if a treatment for nocturia is less than £1969 (e.g. including physician meetings, medicine and associated treatments), the net-benefit for the economy would be positive.

¹⁴Total expenditure is the sum of private consumption, public consumption and investment.

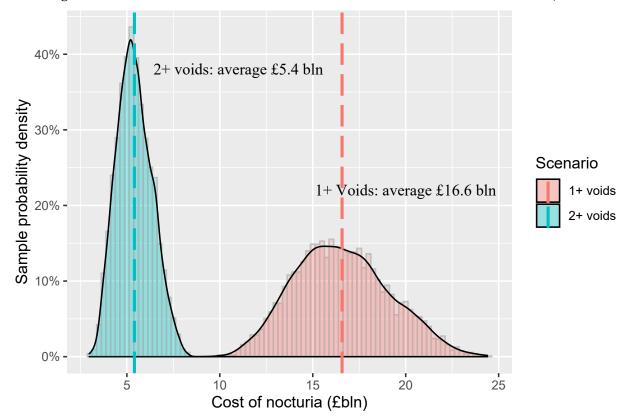


Figure 1: Lost economic value due to nocturia (PDF of the Monte Carlo simulation, £bln)

Notes: The figure reports two scenarios: treating all nocturnal voids (1+) and clinical nocturia (2+). We estimate that the lost monetary value due to clinical nocturia (i.e., 2+ voids) is around £5.4 bln in real expenditure (i.e., the sum of private consumption, public consumption, and investment). The 95% confidence interval falls between £5.38 and 5.43 bln. Each scenario is executed 5000 times and plotted on the same graph.

4 Discussion

Nocturia is a condition that is still relatively poorly understood and most research focuses on clinical studies with the elderly. However, given its sleep disturbing effects and relative high prevalence, especially among the workforce, it can have substantial negative economic consequences for national economies. Studies on the productivity loss and the associated economic costs of nocturia are very limited and we aim to address this important gap in the literature. The key contributions of this study are twofold: First, we provide new estimates on the associations between nocturnal voiding and productivity loss, measured as percentage work impairment due to absenteeism and presenteeism. Second, based on these new productivity loss estimates, we calculate the macroeconomic cost of nocturia to the UK economy using a general equilibrium approach which, unlike existing partial equilibrium analyses, also takes into account second-order effects such as spill-over or multiplier effects on other economic agents like firms or the government.

Using unique and rich survey data, conducted in 2017 and 2018 among among UK employers and their employees, we find that about 50 percent of the working population in our sample report on average at least one nocturnal void and about 9 percent of the sample population report on average two or more nocturnal voids, which is generally considered a clinically important nocturia threshold. We further estimated the association between the number of experienced nocturnal voids and productivity loss. In our UK worker sample population, we found that, even after adjusting for a large set of relevant covariates, workers experiencing nocturnal voids report on average higher percentages of work impairment than workers without nocturnal voids and the magnitude of the productivity loss is increasing with the number of nocturnal voids. For example, our findings suggest that the average productivity loss for those workers reporting one or more nocturnal voids is 1.6 percent and for workers reporting two or more nocturnal voids the estimated productivity loss is estimated to be about 2.9 percent of their total working time.

Previous studies that have examined the association between nocturia and work impairment using the WPAI instrument reported between 5 to 39 percent higher relative total work impairment for individuals with two or more nocturnal voids (Kobelt et al., 2003; Miller et al., 2016; Weidlich et al., 2017), but these studies were limited to very small sample sizes or the inability to adjust the analysis for relevant confounding factors. Also when we convert the percentage loss in productivity into lost working hours per week, we find that on average individuals with more than two nocturnal voids lose on average about 1.2 hours of working time per week. This is also considerably lower than the 3.9 hours of working time lost estimated by (Jhaveri et al., 2019). The ability to use rich UK worker survey data with information on the prevalence of nocturnal voids enables us to adjust for a larger number of relevant covariates that simultaneously may affect nocturnal voiding and productivity. Therefore our estimates represent more robust productivity loss estimates associated with nocturnal voiding than most previous studies.

Moreover, previous studies assessing the economic burden of nocturia use the COI partial equilibrium approach to calculate the direct healthcare cost associated with nocturia (Dmochowski et al., 2019; Holm-Larsen, 2014; Weidlich et al., 2017) and do not specifically focus on the productivity losses associated with nocturia in the workforce. To the best of our knowledge, only four studies estimate the indirect cost of nocturia associated with lower work productivity using the COI approach (Weidlich et al., 2017; Jhaveri et al., 2019; Holm-Larsen et al., 2013; Dmochowski et al., 2019). These studies use the average working time lost associated with nocturia and multiply it with the average salary of the worker to derive the cost of lost productivity.

However, these partial equilibrium calculations are not capable of taking into account second-order effects on other agents/markets in the economy. In our analysis we have addressed this shortcoming and estimate that clinically significant nocturia is associated with an indirect annual cost of £5.4 bln to the UK economy, corresponding to around £1969 per worker with nocturia. We can compare our results with others.

For example, using the COI approach, Weidlich et al. (2017) estimate the indirect cost of nocturia associated with productivity loss in the UK at around £4.3 bln, or £500 per person with nocturia. They assume a productivity loss of about 5 percent per person which is higher than ours (2.9 percent).¹⁵ Despite the higher productivity loss assumption, they find a lower indirect cost per person with nocturia. However, it is important to highlight that Weidlich et al. (2017) do not take into account the cost of presenteeism associated with nocturia, which tend to be higher than the cost associated with absenteeism (e.g., supported by Brunner et al., 2019; Hafner et al., 2020a). Our findings are therefore only partially comparable.

Jhaveri et al. (2019) is another comparable study, which uses the US National Health and Examination Survey (NHANES). They estimate the indirect cost per person with clinically significant nocturia due to productivity loss at around £1933, which is close to our estimate of £1996.¹⁶ However, Jhaveri et al. (2019) base their analysis on an average productivity loss which is considerably higher than ours (e.g. 3.9 hours per week compared to our finding of 1.2 hours per week). This suggests that the general equilibrium spillovers and multiplier effects are important, and that the partial equilibrium COI approach might seriously underestimate the actual indirect cost associated with a health condition. That is, the findings of our study suggest that in order to get a more accurate picture of the economic burden associated with a health condition, future studies should consider taking a general equilibrium approach instead of the traditional partial equilibrium approach which is prevalent in the existing literature.

Finally, as outlined above, this study has several strengths. Yet, it also has limitations. Firstly, it is important to stress that all data used to estimate the prevalence of nocturia and the link between nocturia and productivity is self-reported. This creates potential for the under-reporting of the real prevalence of certain lifestyle habits – such as smoking or alcohol consumption – or for overstating others, as physical activity for instance. Specifically, as we define the nocturia population based on the self-reported frequency of nocturnal bathroom visits, the main variable in the analysis may be subject to inaccuracies since it has not been clinically diagnosed by a health professional.

Secondly, when interpreting the empirical results on the association between nocturia and productivity, caution should be applied with regards to causality. While the applied regression models capture a large set of potential confounding factors, there are still potential unobserved individual and time-varying factors that the analysis has not taken into account.

Thirdly, this study only focuses on the effect of nocturia on the efficiency parameter of the labor supply but not the physical amount of labor. There is some evidence that nocturia is associated with a higher relative mortality risk and hence could reduce the overall labor supply in an economy. However,

 $^{^{15}}$ Weidlich et al. (2017) assumes a productivity loss of 0.4 months a year, which is about 12 days a year. Assuming 225 working days per year, this corresponds to about 5 percent of working time lost due to nocturia.

 $^{^{16}}$ The original indirect cost estimate provided in (Jhaveri et al., 2019) is about \$2468 per person. We use the average \pounds \$ exchange rate 1.2766 for 2019 provided by the Bank of England.

the existing evidence on the link between nocturia and mortality is inconclusive and needs further research to clarify the corresponding causal pathways. If there is indeed a link between nocturia and excess mortality, our estimated economic effects are an underestimation of the true burden.

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A Appendix: Econometric modeling of Nocturia and labor productivity

| | trol variables from the BHW U | 1 | | - | |
|-----------------------|----------------------------------|--------|--------|-----|-----|
| Variable | Description | Mean | SD | Min | Max |
| Work impairment | | | | | |
| Work impairment total | % work time lost due to | 12.4 | 20.2 | 0 | 100 |
| | absenteeism and presenteeism | | | | |
| Work impairment | % work time lost due to | 0.9 | 5.5 | 0 | 100 |
| absenteeism | absenteeism | | | | |
| Work impairment | % work time lost due to | 11.5 | 18.6 | 0 | 100 |
| presenteeism | presenteeism | | | | |
| Socio-demographics | | | | | |
| Female | Gender: female (1 yes - 0 no); | 0.502 | 0.500 | 0 | 1 |
| Age | Age (continuous) | 39 | 11 | 20 | 65 |
| White | Ethnicity: White (1 yes - 0 no) | 0.912 | 0.283 | 0 | 1 |
| Asian | Ethnicity: Asian (1 yes - 0 no) | 0.014 | 0.116 | 0 | 1 |
| Black | Ethnicity: Black (1 yes - 0 no) | 0.042 | 0.201 | 0 | 1 |
| No tertiary education | Education: less than | 0.399 | 0.490 | 0 | 1 |
| | university degree (1 yes - 0 no) | | | | |
| Income (£, 1000s) | Annual income 1000£ | 43.815 | 27.801 | 15 | 150 |
| | (continuous) | | | | |
| Divorced | Marital status: divorced (1 yes | 0.036 | 0.187 | 0 | 1 |
| | - 0 no) | | | | |
| Widowed | Marital status: widowed (1 yes | 0.004 | 0.061 | 0 | 1 |
| | - 0 no) | | | | |
| Child | Caring responsibility: child | 0.271 | 0.445 | 0 | 1 |
| | younger than 18 (1 yes - 0 no) | | | | |
| Irregular hours | Irregular working hours (e.g. | 0.138 | 0.345 | 0 | 1 |
| | night shifts (1 yes - 0 no) | | | | |
| Financial concerns | Having financial concerns (1 | 0.081 | 0.273 | 0 | 1 |
| | yes- 0 no) | | | | |
| Engaged | Engaged in voluntary | 0.258 | 0.438 | 0 | 1 |
| - | activities or charity work | | | | |
| | outside work (1 yes - 0 no) | | | | |

| Table 6: Control variables from the BHW UK work | force survey |
|---|--------------|
|---|--------------|

Note: The table provides descriptive statistics of the pooled BHW survey waves 2017 and 2018 based on 52,887 observations. Provided are the mean, standard deviation (SD) and the minimum and maximum values for each variable.

| Variable | Description | Mean | SD | Min | Max |
|-----------------------|--|-------|----------------|-----|-----|
| Lifestyle & Health | | | | | |
| Smoker | Currently smoking (1 yes - 0 | 0.097 | 0.296 | 0 | 1 |
| | no) | | | | |
| Excessive alcohol | Consumption > 14 units (8mg) | 0.296 | 0.457 | 0 | 1 |
| | per week (1 yes - 0 no) | | | | |
| Physically inactive | Less than 150 minutes of | 0.339 | 0.473 | 0 | 1 |
| | activity per week (1 yes - 0 no) | | | | |
| Excessive salt intake | Salt addition to every meal | 0.043 | 0.203 | 0 | 1 |
| | regularly more than a pinch of | | | | |
| | salt (1 yes - 0 no) | | | | |
| Obese | Body mass index >30 (1 yes - 0 | 0.184 | 0.388 | 0 | 1 |
| | no) | | | | |
| Overweight | Body mass index >25 to 30 (1 | 0.343 | 0.475 | 0 | 1 |
| | yes - 0 no) | | | | |
| Underweight | Body mass index < 18.5; (1 yes | 0.015 | 0.120 | 0 | 1 |
| | - 0 no) | | | | |
| At risk of mental | Kessler Psychological Distress | 0.064 | 0.244 | 0 | 1 |
| health problems | scale > 13 (1 yes - 0 no) | | | | |
| MSK | Number of musculoskeletal | 2.095 | 1.870 | 0 | 9 |
| | conditions (continuous) | | | | _ |
| Asthma | Clinically diagnosed with | 0.082 | 0.274 | 0 | 1 |
| | Asthma within the last 12 | | | | |
| | months; (1 yes - 0 no) | | | | |
| Heart | Clinically diagnosed with | 0.012 | 0.110 | 0 | 1 |
| | Cardiovascular disease within | | | | |
| | the last 12 months; (1 yes - 0 | | | | |
| 77:1 | no) | 0.000 | 0.000 | 0 | 1 |
| Kidney | Clinically diagnosed with | 0.006 | 0.080 | 0 | 1 |
| | Kidney disease within the last | | | | |
| Comon | 12 months; (1 yes - 0 no) | 0.005 | 0.000 | 0 | 1 |
| Cancer | Clinically diagnosed with Cancer within the last 12 | 0.005 | 0.069 | 0 | 1 |
| | | | | | |
| Diabetes | months; (1 yes - 0 no) Clinically diagnosed with | 0.017 | 0.129 | 0 | 1 |
| Diabetes | Diabetes within the last 12 | 0.017 | 0.129 | 0 | 1 |
| | | | | | |
| Hypertension | months; (1 yes - 0 no) Clinically diagnosed with | 0.051 | 0.219 | 0 | 1 |
| 11yper tension | Hypertension within the last | 0.031 | 0.213 | 0 | 1 |
| | 12 months; (1 yes - 0 no) | | | | |
| | 12 monuns, (1 yes - 0 m) | | | | |
| Sleen | | | | | |
| Sleep Insomnia | Difficulties falling aslean: (0 | 0.018 | 1 1/0 | 0 | 1 |
| Sleep Insomnia | Difficulties falling asleep: (0 | 0.918 | 1.149 | 0 | 4 |
| | Difficulties falling asleep: (0 never - 4 often) Hours of sleep < 6 (1 yes - 0 no) | 0.918 | 1.149 0.249 | 0 | 4 |

Table 7: Control variables from the BHW UK workforce survey (continued from previous table)

Note: The table provides descriptive statistics of the pooled BHW survey waves 2017 and 2018 based on 52,887 observations. Provided are the mean, standard deviation (SD) and the minimum and maximum values for each variable.