Received: 13 June 2018 | Revised: 10 December 2018 | Accepted: 10 December 2018

DOI: 10.1111/ijcp.13306

ORIGINAL PAPER

WILEY THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

Development of a multivariate prediction model for nocturia, based on urinary tract etiologies

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Summary

Purpose: The main objective of our study was to determine which combination of modifiable and non-modifiable parameters that could discriminate patients with nocturia from those without nocturia. This was a post-hoc analysis of 3 prospective, observational studies conducted in Ghent University. Participants completed frequency volume chart (FVC) to compare characteristics between patients with and without nocturia.

Method: This was a post hoc analysis of three prospective, observational studies conducted in Ghent University. Participants completed frequency volume chart (FVC) to compare characteristics between adults with and without nocturia.

Study 1: adults with and without nocturia (n = 148);

Study 2: patients ≥65 years with and without nocturnal LUTS (n = 54);

Study 3: menopausal women before and after hormone replacement therapy (n = 43).

All eligible patients (n = 183) completed a FVC during 24 hours (n = 13), 48 hours (n = 30) or 72 hours (n = 140). The combination of algorithms and number of determinants obtaining the best average area under the receiver operating curve (AUC-ROC) led to the final model. Differences between groups were assessed using the AUC-ROC and Mann- Whitney-Wilcoxon tests. Holm corrections were applied for multiple statistical testing. Also, the stability of the feature selection was evaluated.

Results: The best discrimination was obtained when 13 determinants were included. However, a logistic regression model based on seven determinants selected with random forest had comparable discrimination including an optimal signature stability. It was able to discriminate almost perfectly between nights with and without nocturia.

Conclusion: Relevant information to accomplish the excellent predictability of the model is; functional bladder capacity, 24 hours urine output, nocturnal output, age, BMI. The multivariate model used in this analysis provides new insights into combination therapy as it allows simulating the effect of different available treatment modalities and its combinations.

1 | INTRODUCTION

Nocturia, or waking at night at least once to void, is a common and bothersome lower urinary tract symptom (LUTS) that results from an imbalance between functional bladder storage capacity and urine production.[1] Inadequate functional bladder storage results in small voided volumes and can be caused by different underlying conditions, such as urinary tract infections, idiopathic/neurogenic detrusor over activity, and bladder outlet obstruction because of benign prostate enlargement (BPE). Increased urinary output, which can be overnight only or during a 24-hour period, can also develop for a variety of reasons such as heart failure, diabetes insipidus or mellitus, decreased vasopressin levels, venous insufficiency or obstructive sleep apnoea. In order to initiate appropriate treatment, a frequency volume chart (FVC) is recommended as an indispensable tool to subtype nocturia patients according to the underlying aetiology: reduced functional bladder capacity (FBC), 24 hours polyuria, nocturnal polyuria (NP) or combined aetiology.[2] Treatments to improve FBC include anticholinergics in patients with detrusor over activity and symptoms of overactive bladder (OAB), whereas recently introduced treatment for OAB – beta-3-agonist – stimulates beta-3 receptors, causing smooth muscle relaxation in the bladder and α-blockers or 5α-reductase inhibitors in the case of BPE. Therapeutic measures directed to reduce nocturnal urinary output include evening fluid restriction, leg elevation during daytime, timed diuretics and antidiuretic treatment with desmopressin.[3,4] Despite this knowledge, management of nocturia patients remains to be challenging because unambiguous definitions of NP and reduced FBC are lacking, and there is little evidence with reference to the effect of all possible combinations of treatment modalities in case of a combined aetiology of nocturia.[2,3,5,6]

Therefore, the aim of this study was to determine which combination of parameters derived from FVCs could discriminate patients with nocturia from those without nocturia, in addition to determining the modifiable factors to minimise nocturia. This will allow to study the aetiology of nocturia and to estimate the effect of treatment approaches that address FBC or nocturnal urine production (NUP) on the number of nocturnal voids without the need of uniform definitions for NP or a reduced FBC.

What's known

- It is known that the diagnosis of nocturnal polyuria is difficult. Applying the many definitions suggested to other populations than the original has shown low accuracy. The ICS definition is the most widely evaluated definition and studies found sensitivity and specificity low, of the studies that have tested the prevalence found many of the non-nocturic subject having nocturnal polyuria, which is evidence of moderate accuracy and the possibility of having a fair amount of false positive subjects.

What's new

- Admitting the difficulty in defining nocturnal polyuria the paper has a more practical pragmatic approach. By determining which combination of parameters derived from frequency volume chart that can discriminate patients with nocturia from those without nocturia. This will allow to study the etiology of nocturia and to estimate the effect of treatment approaches that address functional bladder capacity or nocturnal urine production on the number of nocturnal voids without the need of uniform definitions for NP or a reduced FBC.

2 | MATERIALS AND METHODS

2.1 | Study design and protocol

This was a post hoc analysis of three prospective, observational studies conducted in Ghent University Hospital between October 2011 and March 2016. Participants completed a FVC in order to compare FVC characteristics between adults with and without nocturia (study 1; n = 148), patients 65 years or older with and without nocturnal LUTS (study 2; n = 54) and menopausal women before and after hormone replacement therapy (study 3; n = 43; unpublished data). In study 2, missing values were corrected if it concerned one voided volume (VV) during daytime on condition that there were at least four other daytime voids and that it was not the first morning void. In that case, an average of the other daytime voids was calculated for the missing value. The procedure was implemented as a FVC review session by the nurse with an unsolicited question. Incomplete FVCs were excluded in study 1 and 3. Study 1 and 3 did not have the same review process as study 2. All subjects with nocturnal urinary incontinence were excluded from the current study (n = 34).

All participants eligible for analyses (n = 183/245) completed a FVC during 24 hours (n = 13), 48 hours (n = 30) or 72 hours (n = 140). Therefore, they registered micturition frequency, volumes and time registrations of going to bed and getting up in the morning.

Ethical approval was obtained from the Ghent University Hospital ethics committee (EC/2011/565; EC/2013/950; EC/2014/0035; EC/2014/1241) The Declaration of Helsinki was followed and all subjects gave a written informed consent.

2.2 | Statistical analysis

2.2.1 | Determinants for nocturia

Nights with at least two nocturnal voids were considered as nights with nocturia, whereas nights with less than two nocturnal voids were defined as nights without nocturia. The selection of determinants was made a priori in order to include most of the determinants

anticipated to be relevant and in order to minimise the interdependence between determinants:

- general determinants: age (years), gender, body mass index (BMI; kg/m^2)
- determinants derived from each individual night of the FVC: sleep duration (hours), 24 hours urine output (mL/h), fluid intake during daytime (time between waking up and 6 PM), evening (time between 6 PM and going to sleep) and 24 hours (mL) and log odds of a modified NP index:

$$\log_{10} \frac{\text{nocturnal urine output (mL/h)}}{\text{24h urine output (mL/h)}}$$

- determinants derived by taking the average of all nights of the FVC: 24 hours maximum VV (mL), relative 24 hours mean urine output (= 24 hours mean VV/24 hours maximum VV), relative nocturnal urine output (= nocturnal mean VV/24 hours maximum VV) and log odds of nocturnal mean VV on 24 hours mean VV:

$$\log_{10} \frac{\text{nocturnal mean VV (mL)}}{\text{24h mean VV (mL)}}$$

The rationale for the log odds transformation in case of ratios is justified as ratios having a non-normal distribution while the hypotheses tests and predictive modelling (see below) make normality assumptions.

2.2.2 | Descriptive parameters

Median, interquartile range and frequency were recorded as descriptive parameters. Differences between groups were assessed using the area under the receiver operating curve (AUC-ROC) and Mann-Whitney-Wilcoxon tests. Holm corrections were applied for multiple statistical testing. A $P < 0.05$ was considered statistically significant.

2.2.3 | Development of a multivariate model

A multivariate model of nocturia was developed by combining: an algorithm for ranking all possible determinants of nocturia by decreasing relevance, the number of determinants to be used in the model and a classification algorithm modelling the presence or absence of nocturia from the selected determinants. Several variable ranking algorithms were evaluated: Wilcoxon tests, least angle regression (LARS, a linear method)[7] or random forest importance.[8] Similarly, several classification algorithms were evaluated: logistic regression (LR), random forest, ensemble of univariate logistic regressions (EULR)[9] or 5-nearest-neighbours (5NN).[10] The performance of each combination of algorithms was evaluated within a cross-validation procedure where predictive models are repeatedly learnt (200 times) from 80% data and tested on the remaining 20% data. This was applied for different numbers of descriptors.

The final model was chosen as the combination of algorithms and the number of determinants having the highest discrimination was determined by area under the curve – receiver operating curve (AUC-ROC). In addition, the stability of the feature selection was evaluated with the Kuncheva index, with a higher index indicating that selection of variables was similar in all resampling loops.[11]

2.2.4 | Determinants of the best logistic regression model

Determinants of the best LR model are reported based on the average ranking, which is the average of the variable ranking obtained by the random forest feature selection over 200 resampling iterations. The sign of the variable's weight in an LR is also reported. This LR was tuned on the whole dataset, after rescaling variables to average zero and unit standard deviation.

3 | RESULTS

A total of 183 subjects, 73 (35%) men and 138 (65%) women aged 50-67, with a median age of 57 years were enrolled in this study. Table 1 reports the descriptive parameters of all candidate determinants for the total number of nights (n = 493) and compares the nights with (n = 180) and without (n = 313) nocturia. These descriptive parameters are also detailed for each of the three datasets separately. On univariate analysis, 6 of the 13 considered determinants were significantly associated ($P < 0.05$) with nocturia symptoms: 24 hours maximum VV (AUC 0.73), log odds of nocturnal urine output/24 h urine output (AUC 0.70), relative nocturnal urine output (AUC 0.63), age (AUC 0.63), log odds of nocturnal mean VV on 24 hours mean VV (AUC 0.62) and gender (AUC 0.57).

Figure 1 shows how the LR performances were influenced by the number of determinants selected in the model. The best discrimination (AUC of 0.98, 95% CI 0.966-0.995) was obtained when all 13 determinants were included. However, a logistic regression model based on seven determinants selected with random forest had comparable discrimination with an AUC of 0.976 (95% CI 0.961-0.991), had optimal signature stability (Kuncheva index 0.944) and was able to discriminate almost perfectly between nights with and without nocturia. Table 2 provides an overview of the best combinations of determinant selection and classification algorithms with the corresponding performances. The linear weight of each of the seven selected determinants in the best LR model is described in Table 3 with the associated *P*-values of Wald tests. They are all significantly non-zero except for age and BMI. Using Table 3, the prediction of the probability of experiencing nocturia according to the LR model can be computed using the following formula:

$$P(\text{nocturia}|x) = \frac{1}{1+\exp\left(-\left(\text{Intercept}+\beta_1\frac{x_1-\mu_1}{\sigma_1}+\cdots+\beta_7\frac{x_7-\mu_7}{\sigma_7}\right)\right)}$$
$$= \frac{1}{1+\exp\left(-\left(-3.15+6.18\frac{x_1-(-0.098)}{0.28}+\cdots+0.35\frac{x_7-24.7}{3.9}\right)\right)}$$

TABLE 1 Univariate analysis of the determinants of nocturia

Group	Variable	Number of nocturnal nights						AUC (%)	p-value
		Overall n= 493	Meno study n= 102	N-LUTS study n= 16	Nocturia study n= 375	<2 n= 313	≥2 n= 180		
Pre-disposition	Age (years)	56 (49-67)	52 (50-54.75)	71 (69-72.25)	60 (48.00-67.50)	54 (47-65)	63 (51-68.25)	63	<0.001
	Gender (male/female)	199/294	0/102	0/16	199/176	111/202	88/92	57	0.028
	BMI (kg/m²)	24.30 (22.27-26.57)	24.17 (22.19-26.88)	23.54 (21.98-25.16)	24.34 (22.27-26.64)	24.16 (22.03-25.64)	24.68 (22.9-27.47)	57	0.099
FBC	24h maximum VV (mL)	450 (350-600)	550 (450-620)	400 (368.75-550)	420 (320-600)	525 (400-650)	380 (300-462.5)	73	<0.001
Diuresis	Log odds nocturnal urine output/24h urine output	−0.08 (−0.29-0.10)	−0.08 (−0.29-0.08)	−0.18 (−0.42-0.11)	−0.08 (−0.28-0.10)	−0.16 (−0.34-0.02)	0.06 (−0.16-0.20)	70	<0.001
	Relative nocturnal urine output	0.66 (0.50-0.79)	0.66 (0.48-0.80)	0.55 (0.49-0.78)	0.66 (0.52-0.79)	0.68 (0.53-0.87)	0.62 (0.46-0.72)	63	<0.001
	Log odds nocturnal mean VV/24h mean VV	0.13 (0.01-0.27)	0.17 (0.04-0.33)	0.12 (0-0.27)	0.12 (0.01-0.26)	0.15 (0.03-0.33)	0.09 (−0.02-0.20)	62	<0.001
	Relative 24h mean urine output	0.46 (0.37-0.57)	0.42 (0.32-0.53)	0.45 (0.40-0.53)	0.48 (0.38-0.58)	0.45 (0.36-0.57)	0.48 (0.38-0.58)	54	0.633
	24h urine output (mL/h)	80.21 (55.33-116.13)	86.61 (63.86-119.06)	75.20 (52.31-110.9)	77.84 (54.88-116.64)	81.31 (55.44-115.24)	77.82 (54.69-118.69)	52	1.000
Drinking/ sleeping habits	Daytime fluid intake (mL)	1300 (992.50-1700)	1350 (987.50-1900)	1100 (1000-1725)	1300 (987.50-1655)	1290 (950-1630)	1405 (1017.5-1750)	56	0.128
	Sleep duration (h)	8.50 (7.50-9.00)	8.38 (7.50-9.46)	9 (8-10)	8.50 (7.62-9)	8.25 (7.50-9.00)	8.50 (7.75-9.25)	55	0.326
	24h fluid intake (mL)	1870 (1450-2300)	2050 (1587.50-2550)	1500 (1112.50-2250)	1815 (1417.50-2240)	1850 (1450-2228.75)	1900 (1440-2460)	53	0.943
	Evening fluid intake (mL)	500 (305-737.50)	600 (400-800)	300 (225-506)	500 (300-715)	500 (350-737.5)	500 (300-735)	51	1.000

Data presented as Median (Range).
AUC: average area under the receiver operating curve; BMI: body mass index; FBC: functional bladder capacity; LUTS: lower urinary tract symptoms; VV: void volume

The median and first and third quartiles of each variable are reported for the overall number of nights and for subgroups based on the presence of nocturia. The area under the receiver-operating curve comparing both groups is reported, as well as the *P*-value of a Mann-Whitney-Wilcoxon test and the corrected *P*-value after applying the Holm correction for multiple statistical testing.

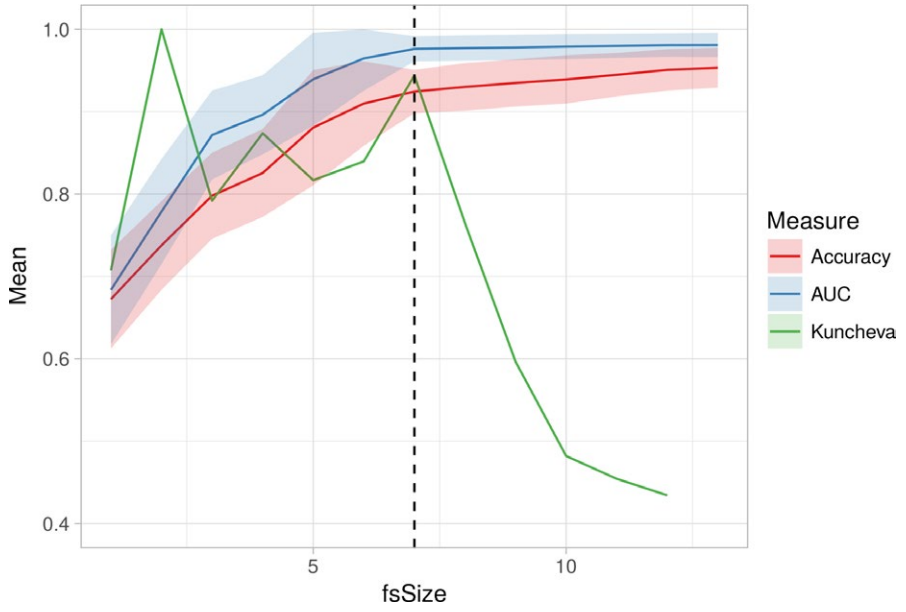

FIGURE 1 Variation of the performance of each model according to the number of selected determinants, with random forest importance as selection algorithm and logistic regression as classification algorithm

where x_1 is the log odds nocturnal urine output/24 hours urine output, x_2 is the 24 hours maximum voided volume (mL), x_3 is the log odds nocturnal mean voided volume/24 hours mean voided volume, x_4 is the relative nocturnal urine output, x_5 is the 24 hours urine output (mL/h), x_6 is the age (years) and x_7 is the body mass index (kg/m^2) and the β_i, μ_i and σ_i are the respective LR coefficients, average and standard deviations reported in Table 3.

4 | DISCUSSION

We developed an explanatory multivariate model that predicts for nocturia symptoms defined as two or more nocturnal voids. Our best fit logistic regression model based on 7/13 selected determinants, had a sensitivity of 91%, specificity of 93%, and AUC of 0.98 to discriminate male or female subjects aged 50-67 with nocturia

TABLE 2 Multivariate analysis of the determinants of nocturia

Selection of determinants	Number of determinants	Type of classification	AUC (%)	Sensitivity (%)	Specificity (%)	BCR (%)	Kuncheva
Random forest	7	Logistic regression	98 (96-99)	91 (86-97)	93 (89-98)	92 (90-95)	0.944
LARS	8	EULR	90 (85-94)	86 (77-95)	77 (69-85)	82 (77-86)	0.846
LARS	6	Random forest	93 (89-96)	69 (60-78)	93 (89-97)	81 (76-86)	0.847

BCR, balanced classification rate; EULR, ensemble of univariate logistic regressions; LARS, least angle regression.
Performance obtained with the best combinations of determinant selection and classification algorithms in the resampling-based evaluation procedure. The average performance measured on the test sets is reported along with a 95% confidence interval.

TABLE 3 Determinants included in the best logistic regression (LR) model

Determinants	Average (μ)	Standard deviation (σ)	Coefficient in logistic regression (β)	*P*-valueWald test
(Intercept)	—	—	−3.15	<0.001
Log odds nocturnal urine output/24 h urine output	−0.098	0.28	6.18	<0.001
24 h maximum voided volume (mL)	485	198	−5.07	<0.001
Log odds nocturnal mean voided volume/24 h mean voided volume	0.137	0.217	−1.00	0.012
Relative nocturnal urine output	0.653	0.211	−2.83	<0.001
24 h urine output (mL/h)	89.3	45.3	5.16	<0.001
Age (years)	55.5	15.3	−0.19	0.418
Body mass index (kg/m^2)	24.7	3.9	0.35	0.096

symptoms from those without nocturia. We also confirmed that an increased nocturnal urine production and reduced FBC are the main factors that determine the presence of nocturia during a specific night, while 24 hours urine output and fluid intake during daytime and 24 hours urine output had an inferior importance.

Limitations of our study include the fact that only data obtained from FVCs were included and that comorbidities were not recorded. The nocturia symptom may be because of underlying comorbidities such as diabetes and hypertension, which have to be excluded before the beginning of LUTS treatment. The length of recording in the FVC also varied in between studies, some were 24 hours only. Second, the age span of the included population is relative narrow and was observed to be a determinant for the multivariate model, so it still needs to be tested in a broader age range to validate an appropriate fit.

Our model can contribute to new insights into combination therapy for nocturia as it allows simulating the effect of different available treatment modalities and their combinations. This can be used to test several scenarios. For example, given the data of a single patient, one could test if modifying a given parameter to some extent could – or not– modify its nocturia status. The benefit is that the model, for each patient, will not only take into account the modification of that particular feature, but will also bear the impact of the other parameters, left unchanged. A modification of a given parameter to some value for one patient might thus not lead to the same impact as the same modification for another patient, because they might differ in the other parameters. Also renal function profile evaluation in NP screening could discriminate between water and solute diuresis as pathophysiological mechanisms complement the bladder diary and could facilitate optimal individualised treatment of patients with NP. However, it is much more complicated and therefore our model seems to be a good easy-to-use alternative.[12] Previous studies have reported that NP is the major cause of nocturia,[13] but prevalence varies widely across different studies because of the use of dozens of different definitions.[5,6]

The most widely used definition is based on the NP index (NPI), which is the ratio of nocturnal urine production (NUP) to 24 hours urine production. The guidelines issued by the International Continence Society (ICS) recommends that the limit should be >20% in younger adults, >33% in adults 65 years and older and somewhere in between for middle-aged adults. Analysis of FVCs showed that 76% (641/846) of European participants and 88% (806/917) of American participants with at least two nocturia episodes had an NPI greater than 33%.[13] The prevalence of NP increased with age but was high in all age groups regardless of gender, ethnicity, country and concomitant therapy for overactive bladder or BPE. However, the discriminative value to diagnose NP as a cause of nocturia is limited when an NPI greater than 33% is used as a cut-off value for NP.[14] In the Krimpen study, NP was diagnosed in 92% of men with nocturia ≥2, but also in 70% of those without nocturia.[15]

The ICS definition of NP is not based on normal distributions, not thoroughly validated and not able to discriminate patients with nocturia from those without nocturia. Therefore, this definition has been challenged and other definitions have been proposed such as NPI >53%, NPI >78%, NUP >90 mL/h or NUP >6.4 mL/kg.[5,6]

Although reduced FBC is also recognised as another underlying mechanism of nocturia, no uniform widely accepted definition is available, which is reflected by the various definitions used: mean voided volume <250 mL, maximum voided volume <300 mL).[16,17] There is also evidence that a major proportion of nocturia patients may benefit from combination therapy to address multiple mechanisms underlying nocturia.[2]

Analysis of FVCs obtained from 41 men with two or more nocturia episodes showed that 20% had isolated NP and 63% had NP in combination with another factor.[16]

FVCs obtained from 29 men and women with at least two nocturia episodes showed an isolated reduced FBC in 7%, isolated NP in 7%, isolated global polyuria in 28% and the combination of a reduced FBC and NP in 59% of subjects.[18]

Although a full range of treatments capable of meeting the needs of patients with NP or a reduced FBC are available, only a few studies have addressed the possible combinations.

The addition of desmopressin to α-blocker therapy of 123 men with BPE and nocturia reduced the number of nocturnal voids by 64%, which was significantly better that the 45% reduction of 125 men treated with α-blocker alone.[19]

Administration of solifenacin (5 mg and 10 mg) reduced the number of nocturia episodes in OAB patients with and without NP, but only showed a significant reduction in patients without NP, compared to placebo ($P = 0.006$ for 5 mg; $P = 0.026$ for 10 mg).[20]

5 | CONCLUSION

Based on a pooled analysis of frequency volume charts of 183 elderly subjects, for both men and women, we developed a multivariate logistic regression model that could differentiate nights with and without nocturia. The model could achieve a Kuncheva index of 0.944 (where 1 is the perfect match), an AUC of 98%, a sensitivity of 91% and specificity of 93%.

The following information is relevant to accomplish the excellent predictability of the model: functional bladder capacity, 24 hours urine output, nocturnal output, age, BMI.

By identifying the most important determinants for nocturia nights, the mixed aetiology of nocturia is recognised. In addition, the effect of influencing any of the parameters can lead to estimating the probability of nocturia-free nights using the multivariate model, which is of clinical benefit for the patients.

DISCLOSURE

None.

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REFERENCES

1. Weiss JP, Blaivas JG, Blanker MH, et al. The new England Research Institues, Inc. (NERI) Nocturia Advisory Conference 2012: focus on outcomes of Therapy. *BJU Int* 2013;111(5):700-716.
2. van Kerrebroeck P, Hashim H, Holm-Larsen T, Robinson D, Stanley N. Thinking beyond the bladder: antidiuretic treatment of nocturia. *Int J Clin Pract*. 2010;64(6):807-816.
3. Park HK, Kim HG. Current evaluation and treatment of nocturia. *Korean J Urol*. 2013;54(8):492-498.
4. Raskolnikov D, Friedman FM, Etwaru DJ, Weiss JP. The evaluation and management of persistent nocturia. *Curr Urol Rep*. 2014;15(9):439.
5. Bosch JR, Everaert K, Weiss JP, et al. Would a new definition and classification of nocturia and nocturnal polyuria improve our management of patients? ICI-RS 2014 *Neurourol Urodyn* 2016;35(2):283-287.
6. Madersbacher S, Cornu JN. Nocturnal polyuria: it's all about definition, and be Patient!. *Eur Urol*. 2013;63(3):548-550.
7. Efron B, Hastie T, Johnstone I, Tibshirani R. Least angle regression. *Ann Stat*. 2004;2:407-499.
8. Breiman L. Random forests. *Mach Learn*. 2001;45(1):5-32.
9. Sollich P, Krogh A. Learning with ensembles: how overfitting can be useful. In: Touretsky D, Mozer M, Hasselmo M, eds. *Advances in Neural Information Processing Systems*. Vol 8. Cambridge, MA: MIT Press.; 1996:190-196.
10. Altman NS. An introduction to kernel and nearest-neighbor nonparametric regression. *Am Stat*. 1992;46(3):175-185.
11. Kuncheva L. A stability index for feature selection. *Artificial intelligence and applications*. Anaheim, CA: ACTA Press. 2007:390-395.
12. Goessaert AS, Krott L, Hoebeke P, Vande Walle J, Everaert K. Diagnosing the pathophysiologic mechanisms of nocturnal polyuria. *Eur Urol*. 2015;67:283-288.
13. Weiss JP, van Kerrebroeck PE, Klein BM, Norgaard JP. Excessive nocturnal urine production is a major contributing factor to the etiology of nocturia. *J Urol*. 2011;186(4):1358-1363.
14. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn*. 2002;21(2):167-178.
15. van Doorn B, Blanker MH, Kok ET, Westers P, Bosch JL. Prevalence, incidence, and resolution of nocturnal polyuria in a longitudinal community-based study in older men: the Krimpen study. *Eur Urol*. 2013;63(3):542-547.
16. Klingler HC, Heidler H, Madersbacher H, Primus G. Nocturia: an austrian study on the multifactorial etiology of this symptom. *Neurourol Urodyn*. 2009;28:427-431.
17. Lukacz ES, Sampselle C, Gray M, et al. A healthy bladder: a consensus statement. *Int J Clin Pract*. 2011;65(10):1026-1036.
18. Goessaert AS, Krott L, Walle JV, Everaert K. Exploring nocturia: gender, age, and causes. *Neurourol Urodyn*. 2015;34(6):561-565.
19. Ahmed AF, Maarouf A, Shalaby E, Gabr AH, Shahin A, Ghobish A. The impact of adding low-dose oral desmopressin therapy to tamsulosin therapy for treatment of nocturia owing to benign prostatic hyperplasia. *World J Urol*. 2015;33(5):649-657.
20. Brubaker L, FitzGerald MP. Nocturnal polyuria and nocturia relief in patients treated with solifenacin for overactive bladder symptoms. *Int Urogynecol J Pelvic Floor Dysfunct*. 2007;18(7):737-741.

How to cite this article: Olesen TK, Denys M-A, Goessaert A-s, et al. Development of a multivariate prediction model for nocturia, based on urinary tract etiologies. *Int J Clin Pract*. 2019;e13306. https://doi.org/10.1111/ijcp.13306