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## Fournier's Gangrene: Management and Mortality Predictors in a Population Based Study

## Mathew D. Sorensen<sup>\*</sup>, John N. Krieger, Frederick P. Rivara, Matthew B. Klein, and Hunter Wessells

Harborview Injury Prevention and Research Center (MDS, FPR), Department of Urology (MDS, JNK, HW) and Division of Plastic Surgery, Department of Surgery (MBK), University of Washington School of Medicine, Seattle, Washington

## Abstract

**Purpose**—The Fournier's gangrene literature comes almost exclusively from tertiary referral centers. We used a population based database to evaluate variations in management and outcomes.

**Materials and Methods**—Inpatients with Fournier's gangrene who underwent surgical débridement or died were identified from select states in the State Inpatient Databases. Multivariate logistic regression analysis was done to evaluate patient and hospital related predictors of mortality.

**Results**—We identified 1,641 males with Fournier's gangrene treated at a total of 593 hospitals. At teaching hospitals more Fournier's gangrene cases were treated per year, and more surgical procedures, débridements and supportive care were reported. Patients treated at teaching hospitals had longer length of stay, greater hospital charges and a higher case fatality rate. Patient related predictors of mortality were increasing age (adjusted OR 4.0 to 15.0), Charlson comorbidity index (adjusted OR 1.20 per additional comorbidity), preexisting conditions, ie congestive heart failure (adjusted OR 2.1), renal failure (adjusted OR 3.2) and coagulopathy (adjusted OR 3.4), and hospital admission via transfer (adjusted OR 1.9), after adjusting for hospital factors and Fournier's gangrene experience. Teaching hospitals had higher mortality due primarily to more acutely ill patients (adjusted OR 1.9). Hospitals where more than 1 Fournier's gangrene case per year were treated had 42% to 84% lower mortality after adjusting for patient age, race, Charlson comorbidity index and admission via transfer (p <0.0001).

**Conclusions**—Teaching and nonteaching hospitals differ substantially in the populations, case definitions, and severity and management of Fournier's gangrene. Hospitals where more patients with Fournier's gangrene were treated had lower mortality rates, supporting the rationale for regionalized care for this rare disease.

## Keywords

penis; fasciitis, necrotizing; hospitals; mortality; genitalia, male

Fournier's gangrene is a rare necrotizing infection of the external genitalia or perineum.<sup>1</sup> Early recognition with aggressive surgical débridement, resuscitation and broad-spectrum antibiotics remain the cornerstones of therapy.<sup>2-5</sup> Previous attempts to predict mortality in

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<sup>&</sup>lt;sup>\*</sup> Correspondence: Department of Urology, University of Washington School of Medicine, 1959 Northeast Pacific St., Box 356510, Seattle, Washington 98195 (telephone: 206-543-3640; FAX: 206-543-3272; mathews@u.washington.edu)..

patients with Fournier's gangrene include the Fournier gangrene severity index, and patient vital signs and laboratory tests to calculate a score that could be used to monitor therapy and predict mortality.<sup>6,7</sup> This index, developed using clinical data on 30 patients presenting to a tertiary referral center in a 15-year period, has variable accuracy for predicting death.<sup>7-12</sup>

The literature on Fournier's gangrene comes almost exclusively from tertiary referral centers. To our knowledge no population based study has been done to evaluate whether differences in populations and management affect mortality in patients with Fournier's gangrene. Our earlier observations suggest that tertiary referral centers and community hospitals differ significantly in case definition and diagnosis of, and management for Fournier's gangrene.<sup>13</sup> Thus, the existing literature on death from Fournier's gangrene may be incomplete or inaccurate.

We examined differences in case severity and management between teaching and nonteaching hospitals, and determined predictors of death in patients with Fournier's gangrene in a large, population based data set. We hypothesized that more acutely ill patients would be cared for at teaching hospitals, and patient and hospital associated factors would prove important predictors of mortality.

## MATERIALS AND METHODS

#### **Study Populations**

SID, established by the Healthcare Cost and Utilization Project, includes data collected from 100% of admissions and discharges from all civilian hospitals in participating states.<sup>14</sup> SID is the largest hospital care data set in the United States. We analyzed data purchased from 13 states for 2001 and from 21 states for 2004. In 2001 data were purchased from Colorado, Florida, Iowa, Massachusetts, Maryland, Maine, North Carolina, New Jersey, New York, Oregon, Utah, Washington and West Virginia. For 2004 data were purchased from Arizona, Kentucky, Michigan, Nebraska, Nevada, Rhode Island, South Carolina, Vermont and Wisconsin but data on Maine were not available.

#### **Case Definition**

We used the ICD-9 diagnosis code for Fournier's gangrene (608.83) to identify cases.<sup>13</sup> Early, aggressive surgical débridement is essential in patients with Fournier's gangrene.2<sup>-5</sup> Thus, patients were required to have undergone genital or perineal débridement unless they died in the hospital. Débridement in the anatomical area of interest was defined by ICD-9 procedure codes 48.8–48.82, 48.9, 49.0, 49.01, 49.02, 49.04, 49.39, 49.93, 54.0, 54.3, 61.0–61.99, 62.0–62.19, 62.2–62.42, 63.3, 63.4, 64.0, 64.2, 64.3, 64.92, 64.98, 83.0–83.09, 83.19, 83.21, 83.3–83.39, 83.4, 83.42, 83.44–83.49, 86.0, 86.04, 86.09, 86.22, 86.28, 86.3, 86.4, 86.9 and 86.99.

Of the 1,641 cases identified 995 (61%) were from states reporting the number of distinct operating room visits. Using the ICD-9 procedure codes listed the average number of genital/perineal débridements per hospital admission was determined. To investigate surgical management for Fournier's gangrene we determined the frequency of suprapubic tube placement (codes 57.1–57.19), penectomy (code 64.3), orchiectomy (codes 62.3–62.42), colostomy (codes 46.0, 46.01, 46.03, 46.1–46.13, 46.2–46.23, 46.3, 46.39) and surgical wound closure with or without skin grafting (codes 61.49, 64.43, 64.44 and 86.60).

To evaluate the potential influence of medical comorbidities on outcome the Charlson comorbidity index was calculated in each patient based on 17 weighted comorbid conditions. This index is the most extensively studied index for risk adjustment and mortality prediction with proven reliability in a wide range of patient populations ranging

from critically ill individuals to those undergoing radical cystectomy.<sup>15-18</sup> To more specifically examine the effect of specific comorbidities as potential predictors of death individual covariates were analyzed, including preexisting obesity, diabetes, congestive heart failure, peripheral vascular disease, chronic pulmonary disease, hypertension, renal failure, liver disease, AIDS, coagulopathy, peptic ulcer disease and anemia.

#### **Data Analysis**

Most patient and hospital demographic variables were obtained from SID. However, some variables were obtained by linking hospital identification numbers with National Inpatient Sample, a separate database also operated by the Healthcare Cost and Utilization Project. Urban vs rural hospital classification was provided by National Inpatient Sample, as determined by Metropolitan Statistical area or Core Based Statistical Area from 2000 Census data. Teaching hospital status, determined by National Inpatient Sample, required that the institution have an American Medical Association approved residency program, be a member of the Council of Teaching Hospitals or have a ratio of full-time equivalent interns and residents to beds of 0.25 or greater. Bed size was classified by National Inpatient States region, urban vs rural site and teaching center status.<sup>14</sup>

Because patient age was not linearly associated with mortality, it was categorized as less than 40, 40 to 49, 50 to 59, 60 to 69 and 70 years or greater. The number of Fournier's gangrene cases treated per year was categorized as 0, 1, 2 to 4, 5 to 9, or 10 or greater due to nonnormal case distribution. The chi-square test was used to evaluate binary variables, the Student t test allowing for unequal variance was used to evaluate continuous variables and the Wilcoxon rank sum test was used to compare medians.

Multivariate logistic regression analysis with robust SEs was used to determine predictors of inpatient mortality on 3 analyses. 1) We evaluated patient related predictors of death, including age, race, Charlson comorbidity index, specific comorbidities, number of surgical débridements and admission via transfer vs primary presentation with a priori adjustment for all hospital factors, such as site, United States region, size, teaching center status, ownership and experience with Fournier's gangrene cases. 2) We evaluated hospital related predictors of death, including site (urban vs rural), United States region (North-east, South, Midwest or West), bed size (small, medium or large), teaching center status, ownership (nonprofit, private, public or government/other) and number of Fournier's gangrene cases treated per year with a priori adjustments for patient age, race, Charlson comorbidity index and patient admission via transfer. 3) To further explore the impact of disease severity we reevaluated hospital factors with additional adjustment for the number of surgical débridements.

Analysis was done using StataIC 10.0 (Stata®) or SAS® 9 with 2-tailed p values and significance considered at <0.05. The University of Washington institutional review board approved this study.

### RESULTS

#### **Hospital Demographics**

We identified 1,641 male patients with Fournier's gangrene treated at a total of 593 hospitals. Patients with Fournier's gangrene were treated most often at large urban hospitals (table 1). Although only 18% of the 1,720 hospitals analyzed from SID were designated as teaching hospitals, 57% of Fournier's gangrene cases were treated at these institutions. Overall at least 1 Fournier's gangrene case was treated at 215 of the 304 teaching hospitals (71%) while at least 1 was treated at only 362 of the 1,197 non-teaching hospitals (30%).

#### **Clinical Management**

Patients underwent an average  $\pm$  SD of  $2.2 \pm 1.6$  surgeries (median 2, range 0 to 11), including an average of  $1.5 \pm 1.0$  genital/perineal débridements (median 1, range 0 to 8) per hospital admission (table 2). Many patients required additional procedures, eg suprapubic tube, colostomy, orchiectomy, penectomy etc. Of the patients 10% required mechanical ventilation and 1.4% underwent dialysis. Overall 7% of patients underwent a primary closure or surgical wound coverage procedure with or without skin grafting during hospitalizations.

Median hospital stay was 8 days (table 3). Median hospital charges were \$27,646. Charges were more than 50% higher in patients who died than in those who survived (median \$40,871 vs \$26,574, p = 0.0001). Of survivors 51% were discharged home without the need for additional services, while 30% required home health care or a skilled nursing facility stay and the remainder had other dispositions, including intermediate care facility, discharged to an unknown site, transfer to another health facility, left against medical advice, hospice care or missing. The overall patient mortality rate was 7.5% (124 of 1,641).

#### **Teaching vs Nonteaching Hospitals**

Teaching hospitals were more likely to be larger and urban (table 2). At teaching hospitals more patients with Fournier's gangrene were treated per year than at nonteaching hospitals and they were younger, more likely to be nonwhite and more often admitted via transfer. Several markers of disease severity proved more common in patients with Fournier's gangrene treated at teaching hospitals, including more surgeries (especially genital/perineal débridement), surgical wound closures and mechanical ventilation. Patients treated at teaching hospitals had longer stays with higher total hospital charges. The patient mortality rate at teaching vs nonteaching hospitals was 8.9% vs 6.4% (unadjusted p = 0.06). In contrast, patients treated at teaching hospitals were less likely to undergo orchiectomy.

#### **Mortality Predictors**

On univariate analysis increasing patient age was associated with increased mortality (OR 4.0 to 18.8, table 4). Each 1-point increase in the Charlson comorbidity score was associated with a 50% increased risk of mortality (p < 0.001). Four specific comorbidi-ties evaluated were associated with increased mortality risk, including hypertension (OR 1.5), congestive heart failure (OR 3.7), renal failure (OR 5.3) and coagulopathy (OR 4.4). Each operation that a patient required also increased the unadjusted odds of death by 27%, likely reflecting more severe Fournier's gangrene. Patients were at increased risk for death when they required certain procedures during admission, including colostomy (OR 1.9), penectomy (OR 3.2), mechanical ventilation (OR 8.2) and dialysis (OR 10.1). In contrast, requiring orchiectomy was associated with a 70% decreased mortality risk.

On univariate analysis hospital ownership and admission via transfer were associated with mortality (table 4). Mortality was higher with increased length of stay (OR 1.6% per day). Cases presenting to urban institutions and teaching hospitals showed increased mortality (each p = 0.06). The number of Fournier's gangrene cases treated per year did not predict mortality on unadjusted analysis.

On multivariate analysis patient factors that independently predicted death were increasing age category (aOR 4.0 to 15.0), Charlson comorbidity index (aOR 1.20 per point), congestive heart failure (aOR 2.1), renal failure (aOR 3.2), coagulopathy (aOR 3.4) and admission via transfer (aOR 1.9) after adjusting for hospital site, size, ownership, United States region, teaching center status and number of patients with Fournier's gangrene treated per year (table 5). Race and number of surgeries did not predict mortality.

In a separate model evaluating hospital associated predictors mortality was 42% to 84% lower at hospitals where more than 1 case of Fournier's gangrene was treated per year after adjustments for patient age, race, Charlson comorbidity index and admission via transfer (p <0.0001). Patients treated at teaching hospitals had higher mortality (aOR 1.9) than those at nonteaching hospitals. However, when the model was adjusted for the number of surgeries, teaching hospital status was not an independent predictor of death from Fournier's gangrene.

### DISCUSSION

A disproportionate number of patients with Fournier's gangrene were treated at a relatively small group of teaching hospitals. Less than 18% of the 1,720 hospitals analyzed were considered teaching hospitals but 57% of Fournier's gangrene cases were managed at these hospitals. In contrast, patients with Fournier's gangrene were treated at only 30% of nonteaching hospitals (p < 0.0001). Patients treated at teaching hospitals were more acutely ill and required more surgical procedures (especially genital/perineal débridement), more mechanical ventilation and other supportive care, likely accounting for the longer stay, greater hospital charges and higher mortality rate.

In this population based study increasing patient age was the strongest independent predictor of mortality (aOR 4.0 to 15.0, p < 0.0001). Patients treated at hospitals where more individuals with Fournier's gangrene were treated had 42% to 84% lower mortality than hospitals where only 1 patient per year was treated after adjusting for other important patient and hospital factors (p < 0.0001). This may reflect more aggressive diagnosis of and management for Fournier's gangrene at more experienced hospitals. Patients admitted via transfer were also at higher independent risk for death (aOR 1.9). This may reflect more severe illness in transferred patients, lack of critical care facilities at transferring hospitals, or delayed management. These findings support increased regionalization of care for patients with Fournier's gangrene. Because patients often require care from urological surgeons, general surgeons, intensivists and plastic surgeons, a multidisciplinary approach provided at facilities where there is greater experience may improve patient outcomes.

Patients treated at teaching hospitals had a higher mortality rate (aOR 1.9). This may reflect differences in severity, management or supportive care, or diagnostic criteria for Fournier's gangrene at teaching hospitals may differ from criteria at nonteaching hospitals. After adjusting for the number of surgeries required by a patient during hospitalization teaching center status as a marker of disease severity was not an independent predictor of death. Higher mortality at teaching hospitals likely reflects a more severely ill population. Patient race and other hospital related factors assessed, including site, size, ownership and United States region, did not independently predict mortality.

Death tended to occur late during hospitalization. Patients who died had slightly longer median length of stay and greater hospital charges (median 40,871 vs 26,574, p = 0.0001). These findings may reflect a more indolent course of Fournier's gangrene after initial therapy in severely ill patients. Death may also reflect in hospital complications but we have no data on these events.

The Charlson comorbidity index performed well in this patient population. However, congestive heart failure, renal failure and coagulopathy added significantly to the comorbidities characterized in the Charlson index. Future studies of the mortality risk in patients with Fournier's gangrene should consider providing additional attention to these comorbidities.

The morbidity rate due to Fournier's gangrene was high. As in other reports, patients often required many operations, especially genital/perineal débridement, orchiectomy, cystostomy

and/or colostomy.19<sup>-22</sup> Overall 30% of survivors required ongoing care after hospital discharge. Given the rarity of surgical wound closure (7%) during the initial hospitalizations evaluated, ongoing care was necessary to facilitate open wound closure in many cases.

This study has important limitations. We did not have access to important clinical, laboratory or microbiological culture data so that we could not determine infection severity by skin surface area involvement or evaluate the performance of the Fournier's Gangrene Severity Index in our large patient cohort. The number of distinct visits to the operating room were determined in 61% of cases, potentially limiting use of this variable as a marker of disease severity. Data collection was retrospective, involving administrative data. Differential morbidity coding, coding errors or misclassifications are possible. The ICD-9 code for Fournier's gangrene (608.83) is found under the diseases of the male genital organs subheading and no comparable diagnosis code exists for females. Thus, our search strategy did not identify females with Fournier's gangrene.

To our knowledge we provide the first comparison of outcomes in patients treated at different hospital types and the first population based study of predictors of death. Findings support earlier observations from tertiary care referral centers documenting the frequent need for surgical procedures and supportive care. The large number of cases identified provided a unique opportunity to identify patient and hospital associated factors predictive of mortality.

#### CONCLUSIONS

Hospitals where more patients with Fournier's gangrene are treated had lower mortality rates, supporting the need to regionalize care for patients with this rare disease. Patients treated at teaching hospitals showed more surgical procedures, more supportive care, longer length of stay, greater hospital charges and higher death rates, reflecting a more severely ill population. Our findings indicate the need for more detailed studies of referral trends and institutional differences in care to improve clinical management and outcomes in patients with Fournier's gangrene.

## Acknowledgments

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## Abbreviations and Acronyms

SID State Inpatient Databases

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Characteristics of hospitals where patients with Fournier's gangrene are treated

Hospital Demographics	No. Pts (%)*
Site:	
Urban	1,404 (86)
Rural	126 (8)
Bed size:	
Small	128 (8)
Medium	364 (22)
Large	1,038 (63)
Ownership:	
Nonprofit	532 (32)
Private	163 (10)
Public	117 (7)
Government	718 (44)
Teaching:	
Yes	820 (50)
No	710 (43)

Numbers may not total 100% due to missing values.

Demographic characteristics of hospitals where patients were Fournier's gangrene are treated

	Teaching	Nonteaching	p Value
No. pts (%)*	820 (50)	710 (43)	
Pts			
Age range (years)			0.05
No. 40 or less (%)	25	22	
No. 40–49 (%)	22	19	
No. 50–59 (%)	24	25	
No. 60–69 (%)	16	15	
No. 70+ (%)	14	19	
Mean ± SD	$49.7 \pm 18.8$	$52.1 \pm 18.7$	
No. race/ethnicity (%):			< 0.001
White	59	72	
Black	28	17	
Hispanic	8	9	
Other	5	2	
Mean $\pm$ SD Charlson comorbidity index	$1.2 \pm 1.4$	$1.2 \pm 1.4$	0.96
% Admission source:			< 0.001
Primary presentation	89	98	
Transferred from elsewhere	11	2	
Hospital			
% Site:			< 0.001
Urban	98	85	
Rural	2	15	
% Bed size:			0.03
Small	7.7	9.2	
Medium	21.5	26.5	
Large	70.9	64.4	
% Ownership:			< 0.001
Nonprofit	26	45	
Private	0.4	23	
Public	7	9	
Government/other	67	24	
No. Fournier's cases/yr:			< 0.001
1	9	26	
2–4	53	71	
5–9	26	4	
10 +	12	0	
Mean ± SD	$2.4 \pm 2.1$	$1.5 \pm 0.8$	

Mean  $\pm$  SD No. admission:<sup>†</sup>

-

Teaching	Nonteaching	p Value
$2.3\pm1.7$	$1.9\pm1.3$	< 0.001
$1.6\pm1.0$	$1.4\pm0.9$	0.001
7	8	0.49
10	8	0.09
24	30	< 0.01
1	1	0.98
11	4	< 0.001
13	8	< 0.01
0.7	1.8	0.06
10	7	< 0.0001
31,900	22,862	< 0.0001
8.9	6.4	0.06
	$2.3 \pm 1.7$ $1.6 \pm 1.0$ 7 10 24 1 11 13 0.7 10 31,900	$2.3 \pm 1.7$ $1.9 \pm 1.3$ $1.6 \pm 1.0$ $1.4 \pm 0.9$ 7       8         10       8         24       30         1       1         11       4         13       8         0.7       1.8         10       7         31,900       22,862

No information on teaching status was available for 16 hospitals (3%) where 111 patients (7%) were treated.

 $^{\dagger}\textsc{Based}$  on 995 patients (61%) with reported surgical intervention dates.

Fournier's gangrene clinical management and outcomes

Mean ± SD No. admission:*	
Surgeries	$2.2 \pm 1.6$
Genital/perineal débridements	$1.5 \pm 1.0$
No. additional surgical procedures (%)	:
Suprapubic tube placement	119 (7)
Colostomy	145 (8)
Orchiectomy	429 (26)
Penectomy	15 (1)
Wound closure	115 (7)
No. supportive care (%):	
Mechanical ventilation	167 (10)
Dialysis	23 (1.4)
Median stay (days):	8
Survivors	8
Deaths	9.5
Median total hospital charges (\$):	27,646
Survivors	26,574
Deaths	40,871
No. surviving disposition (%):	
Ongoing needs at discharge	451 (30)
Home health care	353 (23)
Skilled nursing facility	98 (6)
Home	770 (51)
Left against medical advice	7 (0.5)
Other	287 (19)

\*Based on 995 patients (61%) with reported surgical intervention dates.

Unadjusted in hospital mortality risk in 1,641 patients with Fournier's gangrene

	OR (95% CI)	p Value
Pts		
Age:		< 0.001
Less than 40	Referent	
40–49	4.0 (1.3–12.3)	
50–59	7.5 (2.6–21.4)	
60–69	13.8 (4.8–39.4)	
70+	18.8 (6.7–53.1)	
Race/ethnicity:		0.60
White	Referent	
Black	0.70 (0.41-1.20)	
Hispanic	1.01 (0.49–2.10)	
Other	0.73 (0.22–2.43)	
Charlson comorbidity index (per point increase)	1.5 (1.3–1.6)	< 0.001
Specific comorbidities:		
Diabetes	0.94 (0.64–1.37)	0.74
Obesity	0.64 (0.32–1.30)	0.22
Hypertension	1.5 (1.0-2.1)	0.05
Congestive heart failure	3.7 (2.3–5.8)	< 0.001
Renal failure	5.3 (3.2-8.7)	< 0.001
Coagulopathy	4.4 (2.4-8.1)	< 0.001
Hospitals		
Bed size:		0.88
Small	Referent	
Medium	1.19 (0.55–2.58)	
Large	1.09 (0.53–2.23)	
Urban	2.68 (0.97-7.38)	0.06
Ownership:		0.02
Private nonprofit	Referent	
Private for profit	1.7 (0.8–3.4)	
Public	1.4 (0.6–3.2)	
Government/other	2.1 (1.3–3.4)	
Teaching	1.4 (0.98–2.12)	0.06
Transferred from elsewhere	1.9 (1.1–3.4)	0.04
No. Fournier's cases/yr:		0.55
1	Referent	
2-4	0.8 (0.5–1.3)	
5–9	1.1 (0.6–1.9)	
10+	0.6 (0.2–1.8)	
Additional length of stay/day	1.6 (0.7–2.5)	0.001

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	OR (95% CI)	p Value
Management		
Per surgical débridement	1.27 (1.1–1.5)	0.001
Surgical procedures:		
Suprapubic tube placement	1.3 (0.8–2.3)	0.29
Colostomy	1.9 (1.2–3.2)	0.01
Orchiectomy	0.31 (0.16-0.58)	< 0.001
Penectomy	3.2 (1.1–9.9)	0.04
Wound closure	0.63 (0.27–1.47)	0.29
Supportive care:		
Mechanical ventilation	8.2 (5.5–12.1)	< 0.001
Dialysis	10.1 (4.3–23.6)	< 0.001

## Multivariate predictors of death from Fournier's gangrene

	aOR (95% CI)	p Value
Pt		
Age:		< 0.0001
Less than 40	Referent	
40–49	4.0 (1.1–14.1)	
50–59	7.3 (2.2–24.7)	
60–69	11.0 (3.1–38.9)	
70+	15.0 (4.5–49.7)	
Charlson comorbidity index/point	1.20 (1.0–1.4)	0.04
Comorbidities:		
Congestive heart failure	2.1 (1.1–3.8)	0.02
Renal failure	3.2 (1.6-6.4)	0.001
Coagulopathy	3.4 (1.6–7.4)	0.002
Admission via transfer	1.9 (1.0–3.7)	0.048
Hospital		
No. Fournier's cases/yr:		< 0.0001
1	Referent	
2–4	0.53 (0.30-0.95)	
5–9	0.58 (0.27–1.24)	
10+	0.16 (0.04–0.66)	
Teaching center	1.9 (1.1–3.1)	0.01