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Original article

Mycoplasma genitalium and *Trichomonas vaginalis* in France: a point prevalence study in people screened for sexually transmitted diseases

S. Pereyre [1, 2, 3, *], C. Laurier Nadalié [1, 2], C. Bébéar [1, 2, 3], for the investigator group[4]

[1)] *University of Bordeaux, Bordeaux, France*
[2)] *INRA, Bordeaux, France*
[3)] *Bordeaux University Hospital, Bordeaux, France*

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ABSTRACT

Objective: *Mycoplasma genitalium* and *Trichomonas vaginalis* are common causes of sexually transmitted infections, but limited prevalence data are available in France. We aimed to evaluate the prevalence of *M. genitalium* and *T. vaginalis* infections and to assess prevalence by gender, age, sample collection sites and clinical symptoms. A multicentre collection of specimens was intended to obtain a nationwide overview of the epidemiology.

Methods: Between September 2014 and January 2015, a total of 2652 consecutive urogenital specimens submitted to the microbiology diagnostic departments of 16 French university hospitals for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* detection were collected. *M. genitalium* and *T. vaginalis* prevalence were evaluated using a commercial real-time PCR kit. Clinical data from patients were anonymously collected.

Results: *T. vaginalis* and *M. genitalium* prevalence were 1.7% (95% confidence interval 1.3–2.4) and 3.4% (95% confidence interval 2.8–4.2), respectively, and did not differ between gender or age groups, except *M. genitalium* prevalence between men and women in the 35- to 44-year age group (5.9 vs. 1.5%; p 0.03). *M. genitalium* prevalence was significantly higher in patients receiving care in sexually transmitted infection clinics, abortion centres, family planning clinics and prisons than in gynaecologic, obstetric and reproduction centres (4.0 vs. 1.7%, p 0.009). Among *M. genitalium*– and *T. vaginalis*–positive patients, 70.9 and 61.5% were asymptomatic, respectively.

Conclusions: The low *T. vaginalis* prevalence does not justify systematic screening for this organism in France. Conversely, selective screening for *M. genitalium* may be warranted in care settings that receive presumably high-risk sexual behaviour patients, regardless of symptoms. **S. Pereyre, CMI 2017;23:122.e1–122.e7**

Introduction

Mycoplasma genitalium and *Trichomonas vaginalis* are common causes of sexually transmitted infections (STIs). These microorganisms are responsible for nongonoccocal urethritis and dysuria in men [1,2]. In women, *T. vaginalis* is responsible for vaginitis with a profuse, frothy vaginal discharge, dysuria and cervicitis, whereas *M. genitalium* is responsible for cervicitis and pelvic inflammatory disease [2–4]. *M. genitalium* has also been associated with spontaneous abortion and preterm birth and may be involved in infertility [4].

T. vaginalis is the most prevalent nonviral STI worldwide, with strong disparities by age and ethnicity [2]. However, the African and American continents are much more affected than Europe, with 42.8 million and 57.8 million adults infected in Africa and America, respectively, versus only 14.3 million adults infected in Europe in 2008 [3]. In Europe, the prevalence of *T. vaginalis* infection was recently evaluated to be between 0.5 and 1.4% in patients visiting general practitioners and STI clinics in the Netherlands [5,6], but additional European prevalence data are needed. The prevalence of *M. genitalium* infection ranges from 1 to 3% in the general population worldwide and rises to 38% in African sex workers and STI

* Corresponding author. S. Pereyre, USC EA3671 Mycoplasmal and Chlamydial Infections in Humans, University of Bordeaux, Campus Bordeaux Carreire, 146 rue Léo Saignat, 33076 Bordeaux, France.
E-mail address: sabine.pereyre@u-bordeaux.fr (S. Pereyre).
[4] Members of the investigator group are listed in the Acknowledgements.

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testing centres [7–9]. In Europe, the prevalence of *M. genitalium* infection was 1.2% in men and 1.3% in women in the British general population [7] and 0.8% in French pregnant women [10]. The prevalence was reported to be between 4 and 5% in patients visiting STI clinics and general practitioners in Europe [5,11,12]. In addition, recent reports showed increasing resistance of *M. genitalium* to macrolides in Europe, which is the class of antibiotics used as the first line treatment [11,13,14]. This macrolide resistance may be associated with the widespread use of single-dose azithromycin therapy [15–17]. A precise evaluation of *M. genitalium* and *T. vaginalis* prevalence in different population groups is needed to set up targeted detection of *M. genitalium* and *T. vaginalis* in defined high-prevalence population categories. This targeted screening would help reduce the spread of the bacteria and unnecessary antibiotic prescriptions.

The detection of both microorganisms has long been hampered by the lack of a sensitive detection method. For *T. vaginalis*, the commonly used microscopic evaluation of genital secretions (wet mount) and culture have low sensitivity [2]. The culture for *M. genitalium* detection is extremely fastidious, and no serology exists for this bacterium [9]. Thus, to clarify the epidemiology of *M. genitalium* and *T. vaginalis,* newly available sensitive nucleic acid amplification tests (NAATs) are required. A few commercially available NAAT kits to detect *M. genitalium* alone or both *M. genitalium* and *T. vaginalis* have recently been approved and commercialized in Europe. These kits will facilitate the determination of the precise epidemiology.

Because limited *M. genitalium* and *T. vaginalis* prevalence data are available in France, the aim of the study was to evaluate the prevalence of *M. genitalium* and *T. vaginalis* infections in French patients undergoing *C. trachomatis* and *N. gonorrhoeae* molecular detection tests using the commercially available Conformité Européene (CE)-marked S-DiaMGTV real-time PCR kit (Diagenode, Belgium). The multicentre collection of specimens was intended to obtain a nationwide overview of the epidemiology of both microorganisms. The prevalence of *M. genitalium* and *T. vaginalis* infections was assessed by gender, age and sample collection sites. Clinical symptoms, the reason for consultation and coinfections were also assessed in *M. genitalium*− and *T. vaginalis*−positive patients.

Material and Methods

Patients, specimens and data collection

Between 1 September 2014 and 31 January 2015, a 1-month prospective collection of consecutive urogenital specimens submitted for *C. trachomatis* and *N. gonorrhoeae* detection to the medical microbiology diagnostic departments of 16 French university hospitals and regional laboratories distributed throughout the French territory was performed. Clinical data were anonymously collated from the patients by the microbiologist of each laboratory at the time he received the specimen for *C. trachomatis* and *N. gonorrhoeae* detection.

Specimen processing

M. genitalium and *T. vaginalis* detection was performed using nucleic acid extracts obtained from routine *C. trachomatis*/*N. gonorrhoeae* testing according to the routine extraction method of each centre (Supplementary Table S1). The *C. trachomatis* and *N. gonorrhoeae* NAAT results were collated from each participating centre. *M. genitalium* and *T. vaginalis* amplifications were performed in all centres using the CE-marked S-DiaMGTV real-time PCR kit, validated on urine samples and urogenital swabs, which targets the *mgPa* adhesin and the *mg219* genes of *M. genitalium* and a specific 2 kb repeat sequence of *T. vaginalis,* according to the manufacturer's instructions. The monoplex *M. genitalium* version of the kit targeting only the *mg219* gene was previously evaluated [18]. In the Bordeaux centre, *M. genitalium* detection was performed using the previously reported in-house PCR [18]. The PCRs were performed using the thermocyclers routinely used in each centre. Negative PCR results were validated only if an accurate amplification of the internal control was obtained.

Statistical analysis

In the present study, patients were only included once, at the date of the first *C. trachomatis*/*N. gonorrhoeae* detection. In case of concurrent specimens, patient status was determined in order to calculate the prevalence of infection. A patient was considered positive for a microorganism as soon as one specimen was positively detected. A patient was considered negative if all concurrent specimens were negative.

Categorical data are presented as frequencies (percentages), and the 95% confidence intervals (95% CI) of the infection prevalence were calculated using the exact binomial distribution. The frequencies were compared by the chi-square or Fisher's exact test, as appropriate. p values below 0.05 were considered significant.

Ethics statement

The present project is in compliance with the Helsinki Declaration (Ethical Principles for Medical Research Involving Human Subjects). The study was conducted in accordance with the guidelines of the 'Direction de la Recherche Clinique et de l'Innovation,' the research board of the Bordeaux university hospital. All patient data were anonymously reported, with no possibility of connecting the isolates and specimens to individual patients. Using the written welcome booklet or the analysis result sheet from microbiology laboratories, patients are explicitly informed at their admission to hospital that their samples could be used for research purposes and that they can oppose this use. Because specimens used in this study are part of routine patient management without any additional sampling, and because patients provided no objection for their samples to be used, article L1211-2 of the French Code of Public Health states that this study did not need to be examined by the ethical committee 'Comité de Protection des Personnes' and that patients' informed consent was not required.

Results

Population characteristics

A total of 2652 specimens from 2594 unique patients (68% women and 32% men) were collected from September 2014 to January 2015. The specimens from women included 83.3% cervicovaginal swabs (1481/1778) and 13.5% first-void urine samples (240/1778). The specimens from men comprised 73.2% first-void urine samples (635/867), 6.7% sperm samples (58/867), 6.8% throat swabs (59/867), 5.9% anal swabs (51/867) and 3.3% urethral swabs (29/867). The origin of 52 specimens (2.0%) was unknown, and the gender of seven patients was unknown.

The mean age of the patients was 28 years, and the median age was 25 years (range 1–90 years). The age of 73 patients was unknown. The percentages of the patients in the age groups <16 years, 16 to 24 years, 25 to 34 years, 35 to 44 years and >45 years were 0.5% (12/2521), 45.1% (1138/2521), 33.9% (855/2521), 14.2% (357/2521) and 6.3% (159/2521), respectively.

The sample collection sites were 40.9% STI centres (1060/2594), 14.0% gynaecologic practices (363/2594), 11.0% family planning centres (286/2594), 10.0% abortion centres (260/2594), 5.1% obstetric practices (131/2594), 4.3% penitentiary centres (111/2594), 3.6% reproduction centres (91/2594), 2.4% infectious disease practices (63/2594) and 8.8% various other practices (229/2594).

In the studied population, the reasons for consultation were 53.0% STI screening (1374/2594), 16.6% genital symptom complaints (431/2594), 1.3% STI in partner (35/2594), 1.2% nongenital symptom complaints (16/2594), 0.7% test of cure visit (18/2594) and 27% unknown reasons (701/2594).

Overall prevalence of M. genitalium and T. vaginalis infections

The overall prevalence of *M. genitalium* infection was 3.4% (95% CI 2.8–4.2), which was intermediate between the prevalence of *C. trachomatis* (9.6%; 95% CI 8.5–10.8) and *N. gonorrhoeae* (2.9%; 95% CI 2.3–3.7) infections. *M. genitalium* prevalence ranged from 0 to 8.3% according to the investigated centre, with the highest prevalences of 8.3 and 5.5% observed in two centres in Paris (Table 1). The percentage of *T. vaginalis*–positive patients calculated among the 2261 patients for whom *T. vaginalis* detection was performed was only 1.7% (95% CI 1.3–2.4), which was significantly lower than the percentage of *M. genitalium*–positive patients (p <0.001). *T. vaginalis* prevalence ranged from 0 to 4.4% in the investigated centres (Table 1).

M. genitalium and *T. vaginalis* prevalences were also assessed by specimen type (Table 2). There was no significant difference in the *M. genitalium* and *T. vaginalis* proportions of positive specimens between cervicovaginal swabs and first-void urine samples in women and between urethral swabs and first-void urine samples in men.

Prevalence of M. genitalium and T. vaginalis infections by gender and age

The prevalence of *M. genitalium* and *T. vaginalis* infections did not differ between gender, at 4.2 and 3.1% (p 0.15) for *M. genitalium* and 1.4 and 1.9% (p 0.33) for *T. vaginalis*, respectively (Table 3).

The percentages of *M. genitalium*– and *T. vaginalis*–positive patients were not significantly different between the age groups <16, 16 to 24, 25 to 34, 35 to 44 and >45 years regardless of gender (Table 3). Although differences were not statistically significant, we note that the percentage of *M. genitalium*–positive women tended to decrease with age, from 3.8% among the 16- to 24-year-old category to 1.5% among the 35- to 44-year-old category (Table 3). In contrast, the percentage of *M. genitalium*–positive men tended to increase with age, from 2.9% among the 16- to 24-year-olds to 5.9% among the 35- to 44-year-olds. In the 35- to 44-year age group, *M. genitalium* prevalence was significantly higher in men than in women (5.9 vs. 1.5%, p 0.03). Regarding *T. vaginalis* prevalence, the same nonsignificant increase was observed in men over the age groups, from 0 in the 16- to 24-year age group to 4.3% in the 35- to 44-year age group (Table 3).

Prevalence of M. genitalium and T. vaginalis infections by sample collection sites

Prevalences of *M. genitalium* and *T. vaginalis* infections were assessed according to sample collection sites. *M. genitalium* prevalence was more than 3% in penitentiary centres, family planning centres, STI centres and abortion centres (Table 4) (i.e. in care settings in France visited by patients presumably exhibiting higher-risk sexual behaviour than the general population). The prevalence of *M. genitalium* infection was below 2.5% in obstetric practices, reproduction centres and gynaecologic practices (i.e. in care settings visited by presumably low-risk sexual behaviour patients). According to this high-/low-risk behaviour sorting, *M. genitalium* prevalence was significantly higher in high-risk sexual behaviour care settings than in low-risk sexual behaviour care settings (4.0 vs. 1.7%, p 0.009; Table 4).

T. vaginalis prevalence was highest in abortion centres, family planning centres, penitentiary centres and STI centres and lowest in gynaecology practices, obstetric practices and reproduction centres (Table 4). However, *T. vaginalis* prevalence was not significantly different in presumed high-risk sexual behaviour patients and low-risk sexual behaviour patients (2.0 vs. 1.2%, p 0.24).

Clinical symptoms and reasons for consultation of M. genitalium– and T. vaginalis–positive patients

The reasons for consultation of *M. genitalium*– and *T. vaginalis*–positive patients were primarily STI screening (75.4% in *M. genitalium*–positive patients and 68.6% in *T. vaginalis*–positive patients) (Fig. 1A). Genital symptoms were the reason for consultation in 21.7 and 28.6% of the *M. genitalium*– and *T. vaginalis*–positive patients, respectively.

Table 1
Prevalence of various infections at 16 participating centres

Participating centre town (hospital or laboratory name)	Centre type	No. of tested patients	% (*n*) patients positive for:			
			Mg	Tv	Ct	Ng
Angers	University hospital laboratory	174	2.9 (5)	4.0 (7)	11.5 (20)	1.1 (2)
Besançon	University hospital laboratory	64	1.6 (1)	3.1 (2)	9.4 (6)	4.7 (3)
Bordeaux	University hospital laboratory	333	3.6 (12)	ND	7.8 (26)	3.0 (10)
Caen	University hospital laboratory	147	2.72 (4)	1.4 (2)	14.3 (21)	3.4 (5)
Grenoble	University hospital laboratory	72	0 (0)	2.8 (2)	1.4 (1)	2.8 (2)
Lyon (Croix Rousse)	University hospital laboratory	104	1.9 (2)	0 (0)	8.7 (9)	3.8 (4)
Marseille (LDA 13)	Regional Laboratory	180	3.9 (7)	4.4 (8)	6.1 (11)	5.6 (10)
Nantes	University hospital laboratory	215	1.4 (3)	0.5 (1)	8.8 (19)	2.3 (5)
Nîmes	University hospital laboratory	112	3.6 (4)	0.9 (1)	9.8 (11)	0 (0)
Paris (A. Béclère)	University hospital laboratory	145	8.3 (12)	0.7 (1)	13.1 (19)	3.4 (5)
Paris (Lariboisière)	University hospital laboratory	264	3.4 (9)	1.9 (5)	13.3 (35)	5.7 (15)
Paris (Tenon/St Antoine)	University hospital laboratory	307	5.5 (17)	1.6 (5)	12.4 (38)	0.7 (2)
Poitiers	University hospital laboratory	83	2.4 (2)	0 (0)	7.2 (6)	0 (0)
Saint Etienne	University hospital laboratory	166	3.0 (5)	2.4 (4)	4.8 (8)	0.6 (1)
Toulouse	University hospital laboratory	150	3.3 (5)	0.7 (1)	9.3 (14)	2.0 (3)
Troyes	Hospital laboratory	78	0 (0)	0 (0)	5.1 (4)	2.6 (2)
Total		2594	3.4 (88)	1.7 (39)	9.6 (248)	2.7 (69)

Ct, *Chlamydia trachomatis;* Mg, *Mycoplasma genitalium;* ND, not determined; Ng, *Neisseria gonorrhoeae;* Tv, *Trichomonas vaginalis.*

Table 2
Proportion of Mg- and Tv-positive specimens by gender and sample source

Specimen	Women		Men				
	Cervicovaginal swab	First-void urine	Urethral swab	First-void urine	Sperm sample	Throat swab	Anal swab
Mg positive	3.0 (45/1481)	3.3 (8/240)	3.4 (1/29)	4.6 (29/635)	1.7 (1/58)	1.7 (1/59)	5.9 (3/51)
Tv positive	1.8 (22/1236)	2.9 (7/240)	0 (0/18)	1.4 (8/569)	1.7 (1/58)	0 (0/59)	2.0 (1/51)

Data are presented as % (number of positive specimens/number of specimens tested).
Mg, *Mycoplasma genitalium;* Tv, *Trichomonas vaginalis.*

Table 3
Prevalence of Mg and Tv infections by gender and age group

Gender	Age group					
	<16 years	16–24 years	25–34 years	35–44 years	>45 years	All ages[a]
Mg prevalence						
Women	0 (0/11)	3.8 (34/899)	2.8 (16/565)	1.5* (3/203)	1.5 (1/66)	3.1 (54/1769)
Men	0 (0/1)	2.9 (7/238)	4.8 (14/289)	5.9* (9/152)	4.3 (4/92)	4.2 (34/819)
Total[b]	0 (0/12)	3.6 (41/1138)	3.5 (30/855)	3.4 (12/357)	3.1 (5/159)	3.4 (88/2594)
Tv prevalence						
Women	0 (0/9)	1.7 (14/803)	2.7 (13/481)	0.6 (1/161)	1.7 (1/58)	1.9 (29/1516)
Men	0 (0/1)	0 (0/231)	1.1 (3/281)	4.3 (6/141)	1.2 (1/83)	1.4 (10/739)
Total[b]	0 (0/10)	1.4 (14/1035)	2.1 (16/763)	2.3 (7/304)	1.4 (2/142)	1.7 (39/2261)

Data are presented as % (number of positive patients/number of patients tested).
Mg, *Mycoplasma genitalium;* Tv, *Trichomonas vaginalis.*
*Statistically significant difference between men and women (p 0.03, Fisher's exact test).
[a] In the group of patients for whom Mg detection was performed, the age of 73 patients was unknown (25 women, 47 men, 1 gender unknown). The age of 7 patients was unknown (4 women, 2 men, 1 gender unknown) among the 2261 patients for whom Tv detection was performed.
[b] The gender of six patients was unknown.

Table 4
Prevalence of Mg and Tv infections by sample collection site

Sample collection site	Mg	Tv
Care settings visited by presumably high-risk sexual behaviour patients	4.0 (68/1717)*	2.0 (29/1492)
STI centres	3.9 (41/1060)	1.5 (15/972)
Abortion centres	3.1 (8/260)	3.7 (6/162)
Family planning centres	4.2 (12/286)	2.4 (6/248)
Penitentiary centres	6.3 (7/111)	1.8 (2/110)
Care settings visited by presumably low-risk sexual behaviour patient	1.7 (10/585)*	1.2 (6/517)
Gynaecologic practices	2.5 (9/363)	1.3 (4/305)
Obstetric practices	0 (0/131)	0.8 (1/123)
Reproduction centres	1.1 (1/91)	1.1 (1/89)
Other[a]	3.4 (10/292)	1.6 (4/253)

Data are presented as % (number of positive patients/number of patients tested).
Mg, *Mycoplasma genitalium;* STI, sexually transmitted infection; Tv, *Trichomonas vaginalis.*
*Statistically significant difference (p 0.009, χ^2 test).
[a] Other includes internal medicine, infectious disease, psychiatry, rheumatology, geriatric practices and emergency departments.

The natures and frequencies of the genital clinical symptoms in the *M. genitalium*–positive and *T. vaginalis*–positive patients are presented in Fig. 1B. Most *M. genitalium* infections were asymptomatic; 70.9% of the *M. genitalium*–positive patients had no symptom, without significant difference between genders. A percentage of 61.5% of the *T. vaginalis*–positive patients were also asymptomatic. Abnormal vaginal or penile discharge was the most frequent symptom reported by 16.4% of the *M. genitalium*–positive patients and 26.9% of the *T. vaginalis*–positive patients, respectively. Among patients of the tested population presenting at least one STI symptom, only 3.8% (16/419) and 2.4% (10/419) were *M. genitalium* and *T. vaginalis* positive, respectively. These percentages were not significantly different from the percentages of *M. genitalium* and *T. vaginalis* infections in the asymptomatic patients, 3.7% (39/1058; p 0.98) and 1.5% (16/1058; p 0.25), respectively.

Prevalence of coinfections

The percentage of coinfections was high in the *M. genitalium*–positive and *T. vaginalis*–positive patients. A total of 38.6% (34/88) of *M. genitalium*–positive patients were coinfected with *C. trachomatis, N. gonorrhoeae* or *T. vaginalis,* and 46.2% (18/39) of *T. vaginalis*–positive patients were coinfected with *C. trachomatis*, *N. gonorrhoeae* or *M. genitalium*. The prevalence of *M. genitalium* and *T. vaginalis* infections was assessed according to *C. trachomatis* and *N. gonorrhoeae* positive or negative status (Table 5). *M. genitalium* prevalence was significantly higher in the *C. trachomatis*–positive patients than in *C. trachomatis*–negative patients (7.7 vs. 2.9%, respectively). *M. genitalium* prevalence was also three times higher in the *N. gonorrhoeae*–positive patients than in the *N. gonorrhoeae*–negative patients (10.1 and 3.3%, respectively). In contrast, the prevalence of *T. vaginalis* was not significantly different between the *C. trachomatis*– and *N. gonorrhoeae*–positive or –negative patients.

Discussion

In the present study, a multicentre collection of specimens was intended to obtain a nationwide overview of the prevalence of *M. genitalium* and *T. vaginalis* infections in France. The population

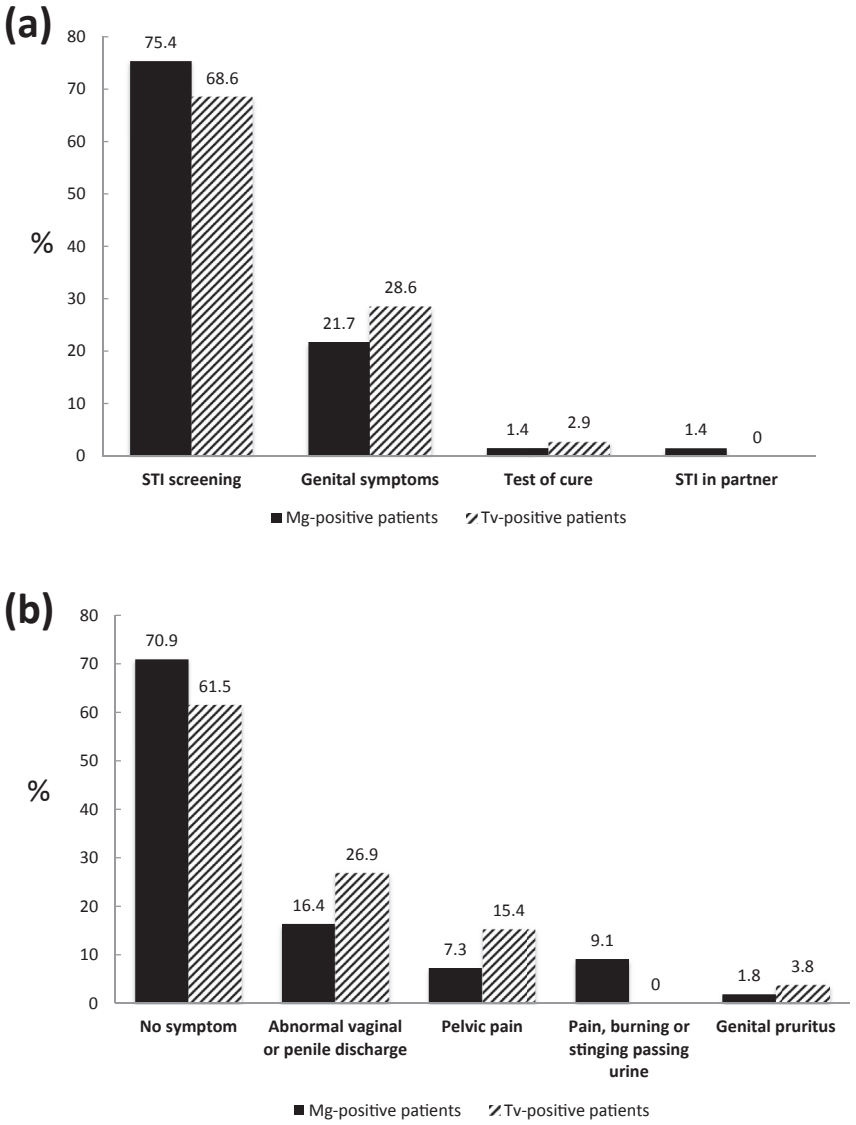

Fig. 1. Reason for consultation (A) and nature and percentage of genital clinical symptoms (B) in *Mycoplasma genitalium*– and *Trichomonas vaginalis*–positive patients.

undergoing *C. trachomatis* and *N. gonorrhoeae* screening was chosen as a preferential STI target population for screening of two other STI agents, *M. genitalium* and *T. vaginalis*. The same commercialized detection kit was used in 15 of 16 centres, but different commercialized extraction methods were used (Supplementary Table S1), which may have influenced the sensitivity of detection at each centre.

The prevalence of *T. vaginalis* infection was low, at 1.7% in the population of patients undergoing *C. trachomatis/N. gonorrhoeae* screening in France. This prevalence is in accordance with the prevalence in the Netherlands, which ranges between 0.6 and 1.5% [5,19]. In contrast, the American *T. vaginalis* prevalence has been reported to be higher (8.7%) based on NAAT in women undergoing screening for *C. trachomatis* and *N. gonorrhoeae* [20]. Other US studies reported a high *T. vaginalis* prevalence, ranging from 13 to 47% [2], confirming that the American prevalence of *T. vaginalis* infection cannot be generalized to European countries. Additionally, *T. vaginalis* prevalence was shown to greatly vary according to race/ethnicity in the United States, with a higher prevalence in black than in white people [2,20,21].

In the present study, *T. vaginalis* prevalence increased in men as they aged, from 0 in the 16- to 24-year age group to 4.3% in the 35- to 44-year age group, although this finding was not statistically significant. This result was in accordance with the greater isolation of *T. vaginalis* that is typically reported in men over 30 years of age [22]. In contrast, this trend was not observed in women. In the

Table 5
Prevalence of Mg and Tv infections in Ct- and Ng-positive and -negative patients

Infection	Ct			Ng		
	Positive-patients (%)	Negative-patients (%)	p	Positive-patients (%)	Negative-patients (%)	p
Mg prevalence	7.7	2.9	<0.001	10.1	3.3	<0.001
Tv prevalence	3.2	1.5	0.09	5.1	1.6	0.08

Ct, *Chlamydia trachomatis;* Mg, *Mycoplasma genitalium;* Ng, *Neisseria gonorrhoeae;* Tv, *Trichomonas vaginalis.*

United States, *T. vaginalis* infection was reported to increase with age in women and to peak among women aged ≥40 years [20].

Overall, the low prevalence of *T. vaginalis* infections in France and the absence of identification of a high-prevalence group of patients suggest that a systematic screening of this microorganism may not be considered. This finding is in contrast with the suggestions of the STI treatment guidelines from the US Centers for Disease Control and Prevention, where *T. vaginalis* prevalence is high and screening is recommended for women seeking care for vaginal discharge and might be recommended for persons receiving care in high-prevalence settings and persons at high risk of infection [21].

Regarding *M. genitalium* infection, the prevalence of 3.4% was higher than the prevalence of *N. gonorrhoeae* infection and twice as high as *T. vaginalis* prevalence in patients undergoing *C. trachomatis*/*N. gonorrhoeae* screening. This prevalence was not significantly different from the 3.1 and 4.5% *M. genitalium* prevalence reported in the Netherlands [5,6] but was slightly lower than the 4.9% prevalence reported in Denmark [11]. This percentage makes *M. genitalium* the second most prevalent sexually transmitted microorganism after *C. trachomatis,* as was previously reported in other European studies [5,6,22].

In the present study, the prevalence of *M. genitalium* infection was not significantly different in men and women, which was in agreement with previous reports [5]. A Danish study reported that *M. genitalium* prevalence was higher in men than in women, but this finding might have been due to the massive systematic screening by gynaecologists in this country, whereas *M. genitalium* testing was often restricted in men to symptomatic patients [11]. Although not statistically significant, two opposite trends were observed in women and men in our study when we analysed *M. genitalium* prevalence according to the age group (Table 3). In women, *M. genitalium* prevalence appeared to be the highest in the 16- to 24-year-old group, then decreased with age until the 35- to 44-year-old age group. This observation is in agreement with the literature [7,10,11]. Notably, in a national British survey, the prevalence was highest in 16- to 19-year-old women and decreased with age to the lowest value in 35- to 44-year-old women [7]. In a French study investigating pregnant women, a fivefold higher *M. genitalium* prevalence was found in 18- to 24-year-old women than in women over 25 years of age. Age <25 years old was associated with an increased risk of *M. genitalium* infection [10]. This finding is similar to the established knowledge of *C. trachomatis* epidemiology, in which youth is a factor that is strongly associated with *C. trachomatis* infection [23]. In contrast, we observed that *M. genitalium* prevalence in men seems to increase with age and peak in the 35- to 44-year age group. In the literature, *M. genitalium* prevalence was reported to peak later in men than in women in the 25- to 34-year age group [7,11], but a decrease in *M. genitalium* prevalence was usually reported in the 35- to 44-year age group [7,11]. Considering the small number of men in each age group in our study (range 92–289 men), additional large epidemiologic studies are needed to confirm either the increased prevalence of *M. genitalium* infections with age in men or the peak of infection in 25- to 34-year-olds.

Additionally, over 70% of *M. genitalium*–positive patients had no genital symptoms, and *M. genitalium* prevalence was similar between the asymptomatic patients and patients reporting genital symptoms. A high proportion of asymptomatic carriers among the infected patients was previously observed [24,25]. Additionally, Sonnenberg *et al.* [7] recently evaluated a majority of asymptomatic patients and did not find any association between reported STI symptoms and *M. genitalium* positivity. This finding suggests that testing only patients who are symptomatic will miss a large number of infections and thus is not a pertinent screening approach [7].

This study indicates that the public health significance of *M. genitalium* infections is not negligible. *M. genitalium* infection is quite common in people who engage in high-risk sexual behaviour but is frequently asymptomatic. The detection of *M. genitalium*–infected patients appears to be necessary because, beside the risk of transmission to sex partners, *M. genitalium* infections have been associated with an increased risk of HIV acquisition, HIV transmission, preterm labour and pelvic inflammatory disease [4,26,27]. We found that *M. genitalium* prevalence was significantly higher in patients receiving care in STI clinics, abortion centres, family planning centres and prisons. In agreement with this finding, *M. genitalium* was previously found to be strongly associated with the reporting of sexual risk behaviours [7]. As a consequence, these high-prevalence care settings visited by presumably high-risk sexual behaviour patients could be the preferred settings for systematic *M. genitalium* screening. This screening will be facilitated by the recent availability of commercial sensitive NAATs to detect this bacterium. This conclusion is in accordance with the recent European guidelines for *M. genitalium* infections [28] that recommend laboratory testing in persons who engage in high-risk sexual behaviour. In contrast, systematic screening in other care settings, such as reproduction centres, gynaecologic and obstetric practices, does not seem to be justified because *M. genitalium* prevalence is low. Testing in settings with a low prevalence is more likely to have low positive predictive values with false-positive results.

Epidemiologic data on *M. genitalium* and *T. vaginalis* infections are scarce across Europe, especially in France. The strength of this study is to present the overall epidemiology of these two infections in a large population of patients undergoing *C. trachomatis* and *N. gonorrhoeae* screening. The diversity of patients included in this study, including men and women from all age groups, from different geographical regions and from different types of medical settings, as well as symptomatic and asymptomatic patients with high- or low-risk sexual behaviours, gives a global overview of *M. genitalium* and *T. vaginalis* infections in France. These data will help to prepare national guidelines for the detection of *M. genitalium* and *T. vaginalis*. However, limitations of the study are the absence of data about men who have sex with men among the male patients tested and the absence of race/ethnicity data—although the recording of these latter data is not allowed in France. Another limitation of this study is the lack of multivariate analysis and of statistical power to confirm or infer differences of prevalence of infections by age group. Further and larger epidemiologic studies are thus needed.

Conclusions

In the present study, *M. genitalium* was the second most prevalent sexually transmitted microorganism after *C. trachomatis*, whereas the prevalence of *T. vaginalis* infection was low. The high proportion of asymptomatic *M. genitalium*–positive patients, the recent availability of *M. genitalium*–detecting commercially available CE-marked NAATs and the higher *M. genitalium* prevalence in high-risk sexual behavior patients may warrant selective screening in patients receiving care in STI centres, abortion centres, family planning centres and prisons, regardless of symptoms. In contrast, the low prevalence of *T. vaginalis* infection in France does not seem to justify systematic screening for this microorganism.

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Transparency Declaration

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.cmi.2016.10.028.

References

[1] Taylor-Robinson D, Jensen JS. *Mycoplasma genitalium*: from Chrysalis to multicolored butterfly. Clin Microbiol Rev 2011;24:498–514.
[2] Meites E, Gaydos CA, Hobbs MM, Kissinger P, Nyirjesy P, Schwebke JR, et al. A review of evidence-based care of symptomatic trichomoniasis and asymptomatic *Trichomonas vaginalis* infections. Clin Infect Dis 2015;61(Suppl. 8): S837–48.
[3] World Health Organization. Global incidence and prevalence of selected curable sexually transmitted infections, 2008. Geneva: World Health Organization; 2012.
[4] Lis R, Rowhani-Rahbar A, Manhart LE. *Mycoplasma genitalium* infection and female reproductive tract disease: a meta-analysis. Clin Infect Dis 2015;61: 418–26.
[5] de Jong AS, Rahamat-Langendoen JC, van Alphen P, Hilt N, van Herk C, Pont S, et al. Large two-centre study into the prevalence of *Mycoplasma genitalium* and *Trichomonas vaginalis* in the Netherlands. Int J STD AIDS 2016;27:856–60.
[6] van der Veer C, van Rooijen MS, Himschoot M, de Vries HJ, Bruisten SM. *Trichomonas vaginalis* and *Mycoplasma genitalium*: age-specific prevalence and disease burden in men attending a sexually transmitted infections clinic in Amsterdam, the Netherlands. Sex Transm Infect 2016;92:83–5.
[7] Sonnenberg P, Ison CA, Clifton S, Field N, Tanton C, Soldan K, et al. Epidemiology of *Mycoplasma genitalium* in British men and women aged 16–44 years: evidence from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). Int J Epidemiol 2015;44:1982–94.
[8] Napierala Mavedzenge S, Weiss HA. Association of *Mycoplasma genitalium* and HIV infection: a systematic review and meta-analysis. AIDS 2009;23:611–20.
[9] Cazanave C, Manhart LE, Bébéar C. *Mycoplasma genitalium*, an emerging sexually transmitted pathogen. Med Mal Infect 2012;42:381–92.
[10] Peuchant O, Le Roy C, Desveaux C, Paris A, Asselineau J, Maldonado C, et al. Screening for *Chlamydia trachomatis, Neisseria gonorrhoeae*, and *Mycoplasma genitalium*: should it be integrated into routine pregnancy care in French young pregnant women? Diagn Microbiol Infect Dis 2015;82:14–9.
[11] Salado-Rasmussen K, Jensen JS. *Mycoplasma genitalium* testing pattern and macrolide resistance: a Danish nationwide retrospective survey. Clin Infect Dis 2014;59:24–30.
[12] Le Roy C, Henin N, Pereyre S, Bébéar C. Emergence of fluoroquinolone-resistant *Mycoplasma genitalium* in France. Emerg Infect Dis 2016;22:1677–9.
[13] Touati A, Peuchant O, Jensen JS, Bébéar C, Pereyre S. Direct detection of macrolide resistance in *Mycoplasma genitalium* isolates from clinical specimens from France by use of real-time PCR and melting curve analysis. J Clin Microbiol 2014;52:1549–55.
[14] Pond MJ, Nori AV, Witney AA, Lopeman RC, Butcher PD, Sadiq ST. High prevalence of antibiotic-resistant *Mycoplasma genitalium* in nongonococcal urethritis: the need for routine testing and the inadequacy of current treatment options. Clin Infect Dis 2014;58:631–7.
[15] Lau A, Bradshaw CS, Lewis D, Fairley CK, Chen MY, Kong FY, et al. The efficacy of azithromycin for the treatment of genital *Mycoplasma genitalium*: a systematic review and meta-analysis. Clin Infect Dis 2015;61:1389–99.
[16] Anagrius C, Lore B, Jensen JS. Treatment of *Mycoplasma genitalium*. Observations from a Swedish STD clinic. PLoS One 2013;8:e61481.
[17] Ito S, Shimada Y, Yamaguchi Y, Yasuda M, Yokoi S, Nakano M, et al. Selection of *Mycoplasma genitalium* strains harbouring macrolide resistance–associated 23S rRNA mutations by treatment with a single 1 g dose of azithromycin. Sex Transm Infect 2011;87:412–4.
[18] Le Roy C, Pereyre S, Bébéar C. Evaluation of two commercial real-time PCR assays for detection of *Mycoplasma genitalium* in urogenital specimens. J Clin Microbiol 2014;52:971–3.
[19] Geelen TH, Hoebe CJ, Dirks A, Dukers-Muijrers NH, van Bergen JE, Wolffs PF. Low positivity rate after systematic screening for *Trichomonas vaginalis* in three patient cohorts from general practitioners, STI clinic and a national population-based chlamydia screening study. Sex Transm Infect 2013;89: 532–4.
[20] Ginocchio CC, Chapin K, Smith JS, Aslanzadeh J, Snook J, Hill CS, et al. Prevalence of *Trichomonas vaginalis* and coinfection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in the United States as determined by the Aptima *Trichomonas vaginalis* nucleic acid amplification assay. J Clin Microbiol 2012;50: 2601–8.
[21] Workowsky KA, Bolan GA. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(RR-03):1–137.
[22] Horner P, Blee K, O'Mahony C, Muir P, Evans C, Radcliffe K, et al. 2015 UK national guideline on the management of non-gonococcal urethritis. Int J STD AIDS 2016;27:85–96.
[23] Bébéar C, de Barbeyrac B. Genital *Chlamydia trachomatis* infections. Clin Microbiol Infect 2009;15:4–10.
[24] Falk L, Fredlund H, Jensen JS. Signs and symptoms of urethritis and cervicitis among women with or without *Mycoplasma genitalium* or *Chlamydia trachomatis* infection. Sex Transm Infect 2005;81:73–8.
[25] Anagrius C, Lore B, Jensen JS. *Mycoplasma genitalium*: prevalence, clinical significance, and transmission. Sex Transm Infect 2005;81:458–62.
[26] Mavedzenge SN, Van Der Pol B, Weiss HA, Kwok C, Mambo F, Chipato T, et al. The association between *Mycoplasma genitalium* and HIV-1 acquisition in African women. AIDS 2012;26:617–24.
[27] Vandepitte J, Weiss HA, Bukenya J, Nakubulwa S, Mayanja Y, Matovu G, et al. Alcohol use, *Mycoplasma genitalium*, and other STIs associated with HIV incidence among women at high risk in Kampala, Uganda. J Acquir Immune Defic Syndr 2013;62:119–26.
[28] Jensen JS, Cusini M, Gomberg M, Moi H. 2016 European guideline on *Mycoplasma genitalium* infections. J Eur Acad Dermatol Venereol 2016;30:1650–6.