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High prevalence of lymphogranuloma venereum detected in MSM through an enhanced European surveillance pilot study

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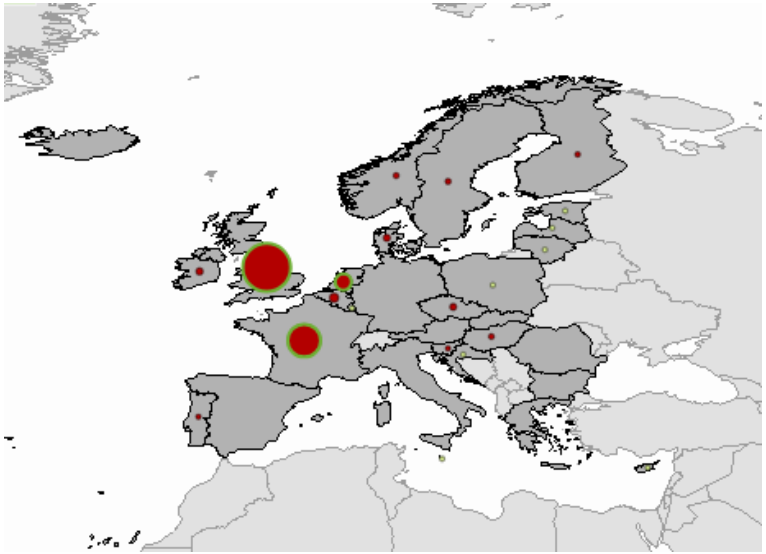
Background

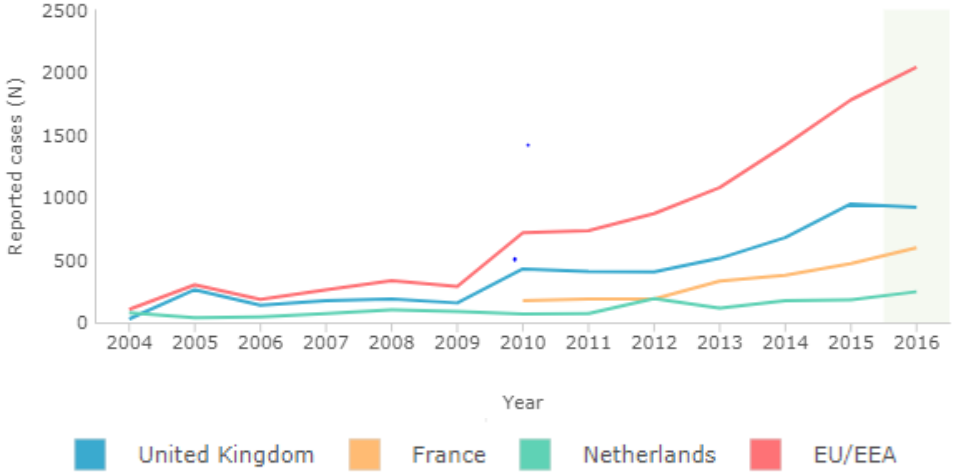
LGV epidemics in men who have sex with men (MSM) have been reported in Europe, North America, Australia and Canada

Infection can manifest as severe proctitis, although it may be asymptomatic

LGV transmission is strongly associated with HIV-positive status, high turnover of sexual partners and dense sexual networks

Surveillance Atlas of Infectious Diseases





Some under-diagnosis and/or under-reporting

2016 EU/EEA = 2043

- UK = 919
- France = 596
- Netherlands = 245

Aims

ECDC funded study

1. Undertake a pilot study to determine the feasibility of establishing and expanding enhanced LGV sentinel surveillance across Europe

2. Investigate the epidemiology of LGV where little current evidence exists

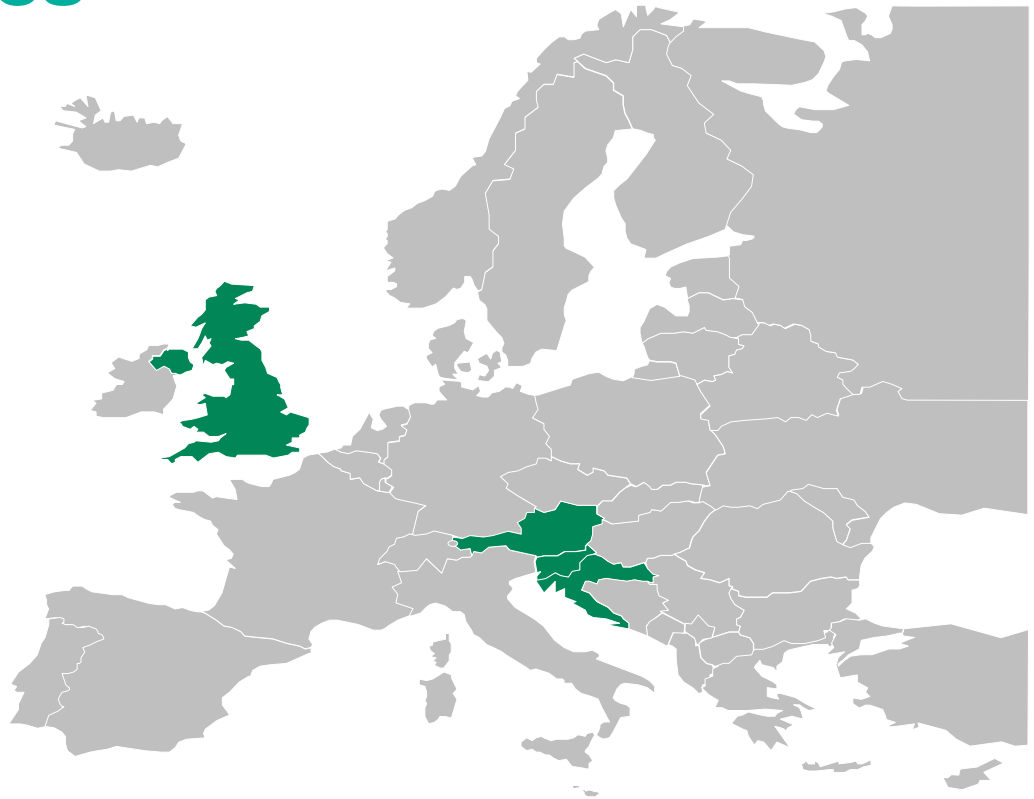
Participating countries

Vienna, Austria

Ljubljana & Maribor, Slovenia

Zagreb, Croatia

London, UK



Methods

Between October 2016 and May 2017, rectal swabs from MSM positive for CT by nucleic acid amplification tests (Austria=19, Croatia=14, Slovenia=6, UK=162) were sent to PHE

Stored rectal swabs from Austria (2015-2016, n=147) and one lymph-node punctate from Croatia (2014) were also tested

CT/LGV multiplex RT-PCR performed*

The *omp*A gene of LGV-positive specimens was sequenced

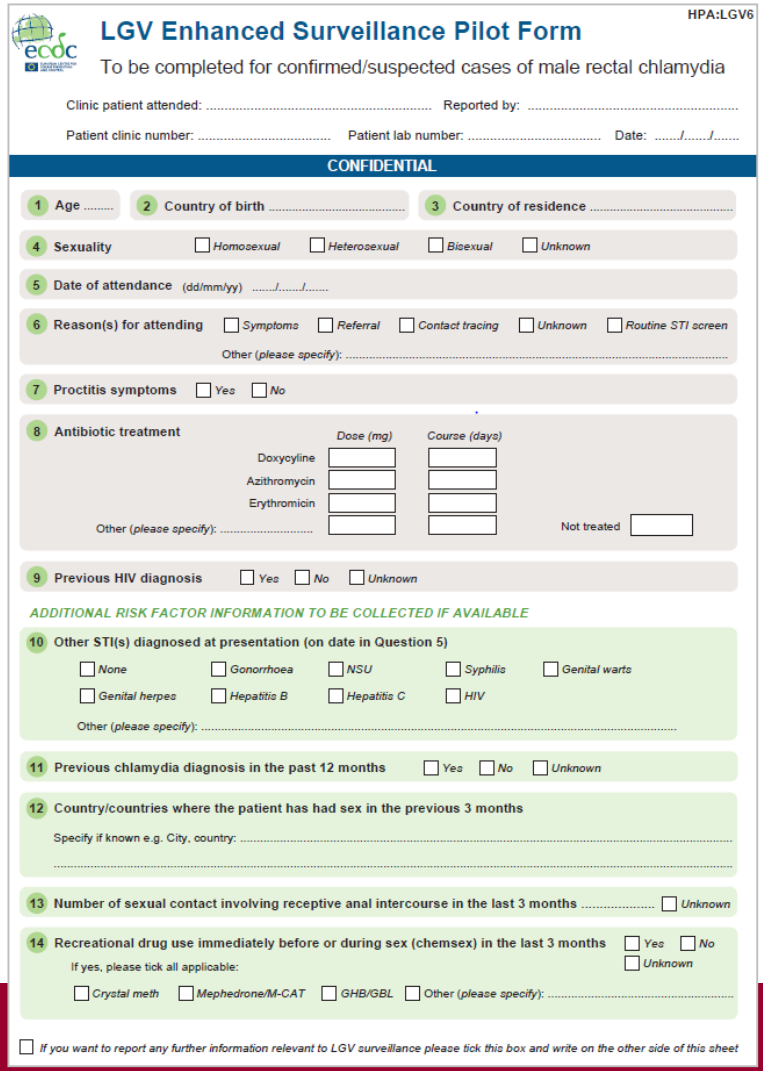
* CT - 88 bp region of the CT cryptic plasmid; LGV - 36 bp deletion of the polymorphic membrane protein H gene (*pmpH*)

Methods

Enhanced clinical and behavioral surveillance data were collected

Patient characteristics associated with LGV infection were investigated* when variable completion was >80%

*using univariate logistic regression, expressed as odds ratios (OR) with 95% confidence intervals (CI). A Pearson χ2-test, Fisher's exact or Mann-Whitney tests were used to test for statistical significance ($p<0.05$).



HPA:LGV6

LGV Enhanced Surveillance Pilot Form

To be completed for confirmed/suspected cases of male rectal chlamydia

Clinic patient attended: ..... Reported by: .....

Patient clinic number: ..... Patient lab number: ..... Date: ...../...../.....

CONFIDENTIAL

1 Age ..... 2 Country of birth ..... 3 Country of residence .....

4 Sexuality ☐ Homosexual ☐ Heterosexual ☐ Bisexual ☐ Unknown

5 Date of attendance (dd/mm/yy) ...../...../.....

6 Reason(s) for attending ☐ Symptoms ☐ Referral ☐ Contact tracing ☐ Unknown ☐ Routine STI screen

Other (please specify): .....

7 Proctitis symptoms ☐ Yes ☐ No

8 Antibiotic treatment

	Dose (mg)	Course (days)
Doxycyline		
Azithromycin		
Erythromicin		
Other (please specify):		

Not treated ☐

9 Previous HIV diagnosis ☐ Yes ☐ No ☐ Unknown

ADDITIONAL RISK FACTOR INFORMATION TO BE COLLECTED IF AVAILABLE

10 Other STI(s) diagnosed at presentation (on date in Question 5)

☐ None ☐ Gonorrhoea ☐ NSU ☐ Syphilis ☐ Genital warts

☐ Genital herpes ☐ Hepatitis B ☐ Hepatitis C ☐ HIV

Other (please specify): .....

11 Previous chlamydia diagnosis in the past 12 months ☐ Yes ☐ No ☐ Unknown

12 Country/countries where the patient has had sex in the previous 3 months

Specify if known e.g. City, country: .....

.....

13 Number of sexual contact involving receptive anal intercourse in the last 3 months ..... ☐ Unknown

14 Recreational drug use immediately before or during sex (chemsex) in the last 3 months ☐ Yes ☐ No ☐ Unknown

If yes, please tick all applicable:

☐ Crystal meth ☐ Mephedrone/M-CAT ☐ GHB/GBL ☐ Other (please specify): .....

☐ If you want to report any further information relevant to LGV surveillance please tick this box and write on the other side of this sheet

Results

Among 349 CT-positive specimens collected from MSM in the four countries, the overall LGV positivity rate was 30.1% (105/349, 95% CI 25.5% - 35.1%)

	MSM with LGV-CT compared to those with non-LGV-CT			
	Austria (n=166)	**Croatia (n=15)**	**Slovenia (n=6)**	**UK (n=162)**
LGV positivity among CT-positive MSM	**47.6%** (40.1-55.2)	**20%** (7.1-45.2)	**16.7%** (3.0-56.4)	**13.6%** (9.1-19.7)
Age	37 vs. 35 yrs	**34 vs. 26 yrs**		**44 vs. 37 yrs**
Proctitis	**91.8% vs. 40.5%**	**100% vs. 25%**		**52.4% vs. 11.7%**
STI co-infection		33.3% vs. 30.0%		**63.2% vs. 36.6%**
Previous CT infection	**35.8% vs. 20.0%**			33.3% vs. 22.6%
HIV positive	85.1% vs. 76.0%	100% vs. 36.4%		81.8% vs. 63.5%

Cells in **bold** are significant; $p < 0.05$

Blank cells – insufficient data for analysis

Results – *ompA* sequencing

	Austria		Croatia		Slovenia		UK		Total	
LGV ompA sequences [Accession number] :	No.	%	No.	%	No.	%	No.	%	No.	%
No. LGV positive	79		3		1		22		105	
L2/434/BU [AM884176]	48	67.6	2	66.7	-	-	1	8.3	51	58.6
L2b/UCH-1/proctitis [AM884177]	5	7.0	1	33.3	1	100	5	41.7	11	12.6
L2bV1 [JX971936]	16	22.5	0	0.0	-	-	0	0.0	16	18.4
L2bV1 & L2/434/BU	1	1.4	0	0.0	-	-	0	0.0	1	1.1
L2bV5 [MH253040] (new; most similar to L2bV4 [KU518892] with G-A @ 271 bp)	0	0.0	0	0.0	-	-	4	33.3	4	4.6
L2bV6 [MH253041] (new; most similar to L2b [AM884177] with G-A @ 998 bp)	0	0.0	0	0.0	-	-	1	8.3	1	1.1
L2h [MH253042] (new; most similar to L2 [AM884176] with A-G @ 997 bp)	1	1.4	0	0.0	-	-	1	8.3	2	2.3
LGV sequence not obtained*	8	10.1	0	0.0	0	0.0	10	45.5	18	17.1

*Includes one patient from Austria with genotype G according to *ompA* sequencing; possible dual LGV and non-LGV CT infection

Study limitations

Very small numbers in Slovenia and Croatia; 95% CIs overlap

Differences in;

- selection criteria
- clinic formats
- testing algorithms
- case mix

Majority of MSM in Austria and Croatia had symptoms – bias for detecting LGV

Some poor variable completion

*omp*A sequencing - high level of CT recombination which compromises genotype assignment

Discussion

LGV surveillance feasible? Yes but challenging

Dependent on availability of rectal CT testing

Yes - can adapt clinical, testing and surveillance pathways, but dependent on availability of local LGV testing

No - insurance / changes to patient pathways / limited resources

Consider representativeness

Need close collaborations between clinicians, microbiologists & epidemiologists

Discussion

High frequency of LGV infection in some MSM populations, with almost a third of CT-positive MSM infected with an LGV genotype

Similar epidemiology to previous studies – although decreased association with HIV

LGV diagnostics were only routinely available in the UK - systematic under-diagnosis in other countries

Potential under-treatment – esp. Austria single dose azithromycin/cefixime

Asymptomatic infections are of concern

More *ompA* sequence diversity vs. the initial clonal spread of the L2b genovar *ompA* sequence

To conclude…

LGV continues to spread through high-risk networks of MSM across Europe.

To improve the sexual health of MSM, unified efforts are needed;

- overcome barriers to testing & diagnostics
- establish effective surveillance
- optimise prevention, diagnosis & treatment

Acknowledgements

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