Global burden of recurrent vulvovaginal candidiasis: a systematic review

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Supplementary Material

Search terms:

Population-based studies on the prevalence of recurrent VVC were sought, with the British Society for Medical Mycology (BSMM) recommended search terms as follows: (vulvovaginal candidiasis, vaginal candidosis, vaginal candida) AND (epidemiology OR prevalence). The search string was: ((("candidiasis, vulvovaginal"[MeSH Terms] OR ("candidiasis"[All Fields] AND "vulvovaginal"[All Fields]) OR "vulvovaginal candidiasis"[All Fields] OR ("vulvovaginal"[All Fields] AND "candidiasis"[All Fields])) AND ("candidiasis, vulvovaginal"[MeSH Terms] OR ("candidiasis"[All Fields] AND "vulvovaginal"[All Fields]) OR "vulvovaginal candidiasis"[All Fields] OR ("vaginal"[All Fields] AND "candidosis"[All Fields]) OR "vaginal candidosis"[All Fields]) AND ("candidiasis, vulvovaginal"[MeSH Terms] OR ("candidiasis"[All Fields] AND "vulvovaginal"[All Fields]) OR "vulvovaginal candidiasis"[All Fields] OR ("vaginal"[All Fields] AND "candida"[All Fields]) OR "vaginal candida"[All Fields])) AND (("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "epidemiology"[MeSH Terms]) OR ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms])). In addition we searched EMBASE and Web of Science. .

Table S1: Papers included and evaluated using modified GRADE criteria.

Reference	Type of study	Countries included	Patient number	mean age (range)	Definition of rVVC	Diagnostics	Incidence	Main limitations (number)
1	Retrospective online omnibus opinion poll / survey	USA, France, Germany, UK, Italy, Spain	6,010 (app 1,000 per country)	(16-65)	≥4 episodes/y	Questionnaire (self-reporting)	9% (variation between age groups)	No medical assessment or diagnostics to confirm self-reporting, retrospective study model, no data from developing countries. (4)
2	Retrospective telephone survey (random digit dialling)	USA	2000	(18-65+)	≥4 episodes/y	Questionnaire (self-reporting of physician diagnosed disease)	8%	No medical assessment or diagnostics to confirm self-reporting, retrospective study model, no data from developing countries. (4)
3	Prospective survey at 8 obstetrics & gynecology clinics	Italy	767	34.6 (15-94)	≥4 episodes/y	Interview, single assessment and culture	10%	Done at obstetrics & gynecology clinics thus semi-selected population and likely to have higher than average proportion of symptomatic patients. Single assessment, RVVC incidence based on self-reporting retrospectively, no data from developing countries. (3)
4	Prospective descriptive study at obstetrics & gynecology clinic	Turkey	495	36.4 (18-51)	≥4 episodes/y	Interview, single assessment and culture	10.7% at the time of study, 19.8% with a prior history of rVVC	Done at obstetrics & gynecology clinics, only patients on hormonal contraceptives included thus semi-selected population and likely to have higher than average proportion of symptomatic patients. Single assessment, RVVC incidence based on self-reporting retrospectively, no data from developing countries. (3)
5	Prospective longitudinal (12 month) study	USA	1248 (709 completed)	(18-30)	≥4 episodes/y	Structured questionnaire, single assessment, culture	4%	Focus on vaginal yeast colonisation, association of presistent colonisation with symptoms not reported. 7.5% of women included were on antifungal therapy and thus culture negative. Young patients thus semi-selected population, no data from developing countries. (4)
6	Retrospective questionnaire based study at 16 general practises	Australia	1298	39.5 (18-70)	not defined	Questionnaire (self-reporting)	34.8% had had VVC after antibiotics	Focus on post-antibiotc VVC, no time-frame, no medical assessment or diagnostics to confirm self-reporting, retrospective study model, no data from developing countries. (6)
7	Retrospective online questionnaire	France, Germany, Netherlands, Sweden, UK, USA	6010	34 (16-55)	not defined	Questionnaire (self-reporting)	5-20 times = 29%; >20 times = 6%	No medical assessment or diagnostics to confirm self-reporting, no time-frame for the frequency, retrospective study model, no data from developing countries. (6)
8	Cross sectional study at 2 general practises	Australia	76	23.9	Monthly or more often	Questionnaire (self-reporting)	6%	No medical assessment or diagnostics to confirm self-reporting, small patient number, young patients thus semi-selected population, no data from developing countries. (6)
Total		11	17365					

Table S2: GRADE scores

Reference	GRADE/ type of evidence	GRADE/ quality	GRADE/ Consistency of incidence*	GRADE/ Directness	GRADE/ Population size**	GRADE Score
1	2	-2	1	0	2	**3**
2	2	-2	1	-1	1	**1**
3	2	-2	1	-2	1	**0**
4	2	-2	0	-2	0	**-2**
5	2	-2	0	-2	1	**-1**
6	2	-3	-1	-1	1	**-2**
7	2	-3	-1	0	2	**0**
8	2	-2	1	-1	0	**0**

Methodology for estimating productivity losses

Data for annual hours actually worked and average annual wages were obtained from the Organization for Economic Co-operation and Development (OECD) 2010 dataset.[9] GDP output in 2010 per country was obtained from the World Bank 2010 dataset.[10] Data on wages was unavailable for 47 countries or territories. We divided the average annual wages (national currency units) by the average hours actually worked per worker to obtain the average hourly wage. This was converted to US$ using the mid-market exchange rates as of 31/12/2010. The average hourly wage in US$ was reduced by the gender gap in each country using 2010 data, defined as the difference between male and female median wages in a specific nation divided by median male wage for that country (with respect to full-time employees only).[11] This figure was multiplied using the number of lost hours per year by rVVC as determined by Aballea *et al* to produce a monetary equivalent of productivity loss per person.[12] Finally the figure was then multiplied by our base case estimate in each country to determine the total cost of productivity loss in 2010.

Figure S1. Examples of rVVC showing marked erythema (redness) and swelling of the labia and some vaginal discharge on the left and right images.

Figure S2. Projected case burdens (2010-2030) in 15-54 year old females using the base model.

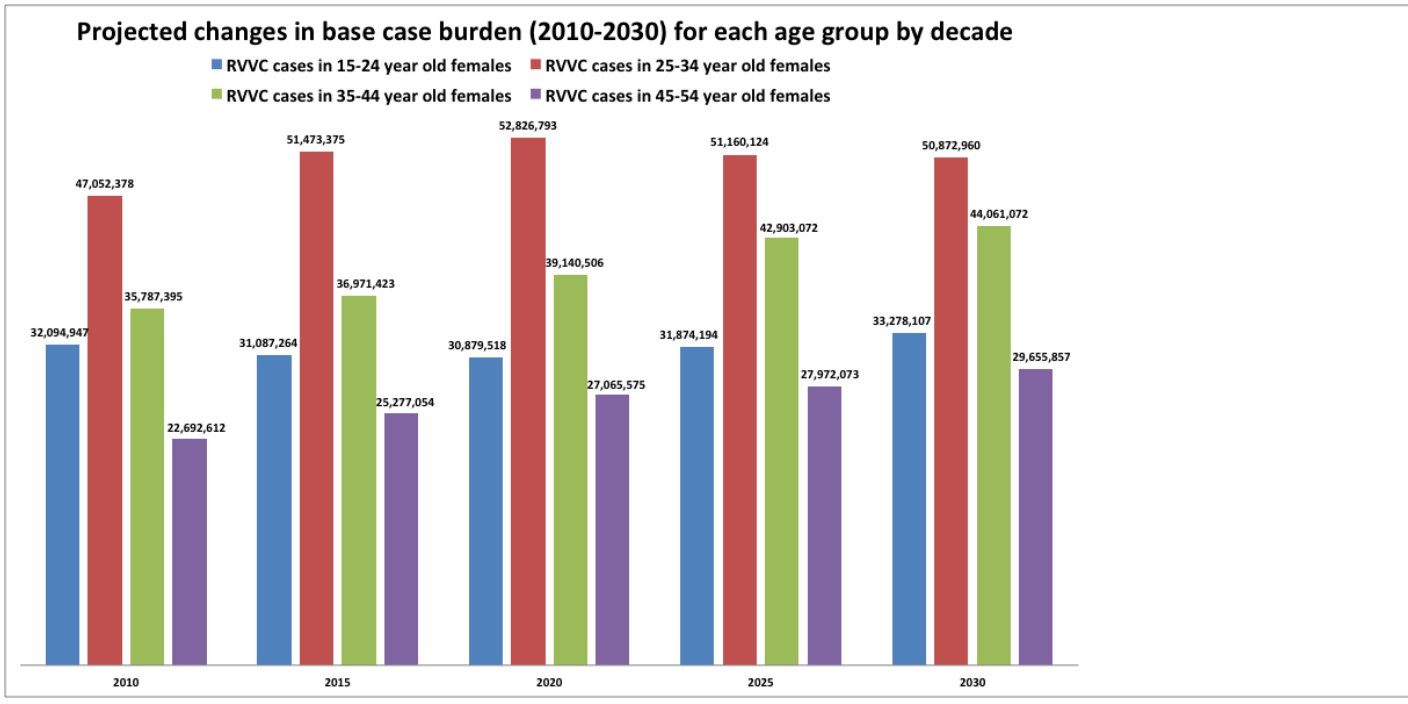

Figure S3. Projected case burdens (2010-2030) in 15-54 year old females using the alternative flat 6% model.

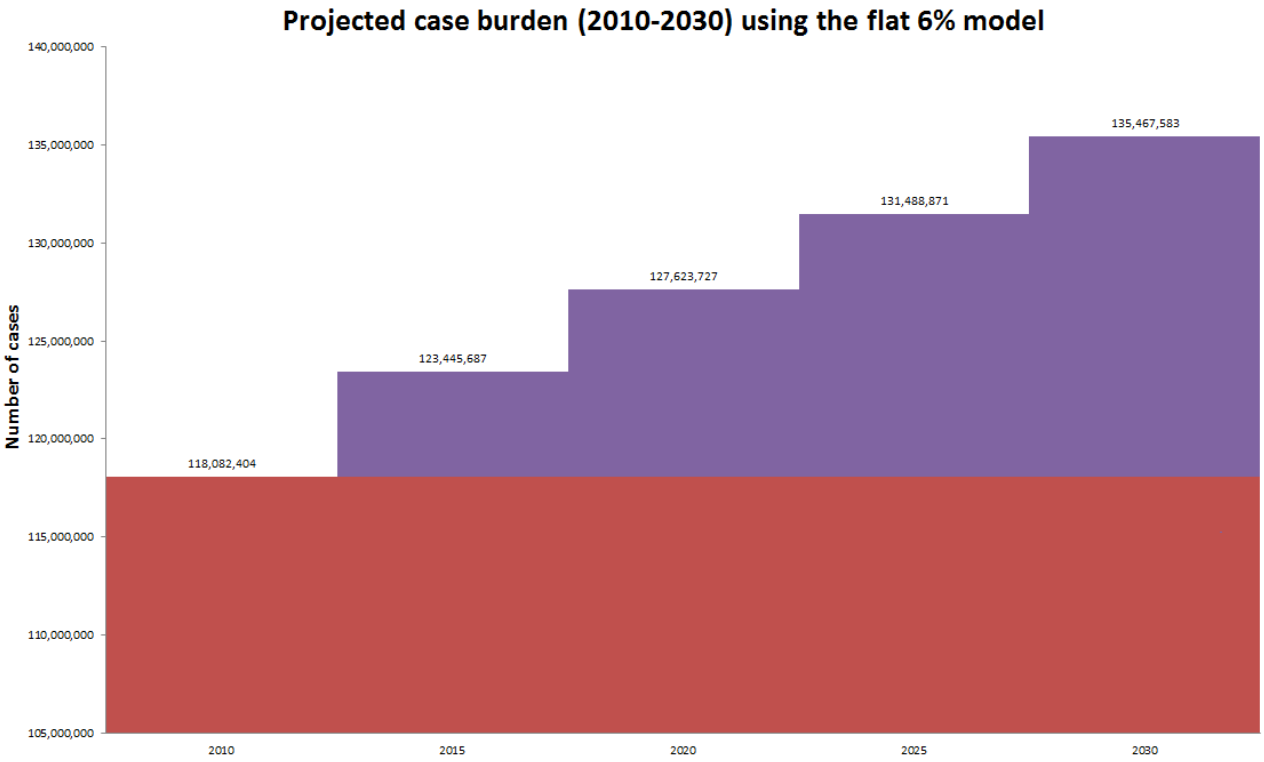

Table S3. RVVC productivity losses by country. The estimates of economic loss for countries with data on average wages, hours worked per week, GDP output and number of working women in high income countries (>$12,616 USD). Daily wages have been reduced by the OECD Gender Gap in order to help mitigate the disparity in wages between men and women.

High income (>US$ 12616) countries	GDP (current US$, millions, 2010)	Total base case	Average hourly wages as of 31-12-2010 after gender gap reduction (US$)	Loss per person (US$)	Total country cost in 2010 (US$)
Australia	1,141,794	439,994	37.99	1,253.59	551,570,628
Austria	377,680	164,263	23.83	786.27	129,155,826
Belgium	471,218	203,401	31.22	1,030.19	209,541,183
Canada	1,614,072	670,239	26.14	862.66	578,186,721
Czech Republic	198,494	206,247	7.40	244.34	50,393,651
Denmark	312,949	100,331	43.17	1,424.61	142,932,129
Estonia	19,033	24,986	5.26	173.59	4,337,493
Finland	236,706	94,656	23.90	788.63	74,648,795
France	2,565,039	1,157,014	25.93	855.65	989,997,226
Germany	3,304,439	1,532,162	26.39	870.94	1,334,427,379
Greece	294,223	211,330	12.35	407.71	86,162,027
Hungary	129,583	195,382	6.28	207.12	40,467,219
Ireland	209,387	92,360	31.03	1,024.03	94,578,854
Israel	231,674	137,997	13.45	444.00	61,270,889
Italy	2,055,355	1,136,805	18.67	616.18	700,471,691
Japan	5,495,387	2,192,838	20.21	666.91	1,462,421,857
Korea, Rep.	1,094,499	1,047,141	7.18	237.03	248,204,704
Luxembourg	52,147	10,195	39.92	1,317.26	13,429,150
Mexico	1,051,129	2,494,530	3.34	110.08	274,603,681
Netherlands	777,158	309,529	30.26	998.61	309,097,014
Norway	420,946	90,650	49.01	1,617.19	146,599,324
Poland	469,799	779,999	6.46	213.33	166,400,728
Portugal	228,939	206,613	9.97	329.06	67,987,965
Slovakia	87,077	114,176	6.89	227.44	25,968,473
Slovenia	46,908	39,381	16.16	533.44	21,007,273
Spain	1,384,845	926,162	19.40	640.19	592,923,788
Sweden	463,062	168,013	26.80	884.32	148,576,902
Switzerland	549,105	152,592	44.65	1,473.44	224,834,444
United Kingdom	2,295,523	1,169,168	23.34	770.10	900,381,211
United States	14,958,300	5,991,927	23.97	790.93	4,739,176,150
Sum GDP	42,536,472			Total cost (US$)/year	14,389,754,376

References for supplementary material

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