

ORIGINAL REPORT

Health problems most commonly diagnosed among young female patients during visits to general practitioners and gynecologists in France before the initiation of the human papillomavirus vaccination program

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ABSTRACT

Purpose Background rates for common health problems have seldom been estimated to facilitate interpretation of signals that may occur after a new public health intervention. Background rates of diagnoses from general practitioners (GPs) and gynecologists (GYNs) were assessed before the implementation of human papillomavirus (HPV) immunization program.

Methods This cross-sectional study used data collected in 2006 in France. All visits of women (aged 11–23 years) to a GP or a GYN participating in the longitudinal patient data (LPD) network were considered. Diagnoses and symptoms were retrieved and classified according to the International Classification of Primary Care. Only diagnoses made in $\geq 1\%$ of visits were reported in primary analyses. Independent analyses were performed for visits to GPs and GYNs and for adolescents and young adults. Finally, the rates of pre-specified health problems of interest (e.g., because of their potential identification as signals after HPV immunization) were computed from processed diagnostic data, using time windows consistent with HPV vaccination scheme.

Results About 380 813 GP and 36 329 GYN visits were analyzed. Acute upper respiratory infections were the most frequently recorded diagnoses by GPs, accounting for 11 783 per 100 000 visits per year. Visits related to the respiratory system accounted for 10 of the 23 most frequent diagnoses by GPs. Genital candidiasis was the most frequent GYN diagnosis, accounting for 4746 per 100 000 visits per year. Most GYN visits were for pregnancy-related issues or menstrual problems. The main diagnoses were similar in adolescents compared with young adults in both GP and GYN settings. Pre-specified health problems occurred at high rates, as exemplified by acne that was diagnosed in 0.8% of patients during time windows consistent with HPV immunization.

Conclusion Diagnostic data processed from electronic health records identified the rates of common health events experienced by young female patients routinely visiting their GP or GYN before HPV immunization. Such rates may prove useful in interpreting adverse events reported after the launch of new medical interventions. Copyright © 2011 John Wiley & Sons, Ltd.

KEY WORDS—vaccines; adverse events; health problems; electronic health records

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INTRODUCTION

In June 2006, the Food and Drug Administration and, in September 2006, the European Medicines Agency have given marketing approval of the first

human papillomavirus (HPV) vaccine for young girls, adolescents, and young women to prevent diseases because of the HPV.¹ Specific post-marketing activities have been launched by the manufacturers of the vaccines, in agreement with regulators, in the context of risk management programs, in addition to the usual pharmacovigilance procedures.² Up to now, neither specific programs nor spontaneous reports have produced information of concern.^{3,4}

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Vaccine coverage has a major impact on the success of a vaccination program.⁵ However, once a vaccine is widely distributed, it is likely that reports of adverse events will be released as a result of their occurrence “by chance” in temporal association with immunization. Distinguishing causality from coincidence may be difficult when immunization coverage is high and reported health problems are frequent. The availability of background rates of health problems diagnosed before the implementation of a vaccination program may facilitate such causal assessment. For instance, using hospital data and background rates in the USA, Siegrist *et al.* have demonstrated that a considerable number of autoimmune-mediated conditions would be reported in close temporal association with a three-dose immunization program.⁶ To further confirm that more data are needed in the assessment of vaccine-related events, Douglas has critically reviewed reported associations between HPV vaccine and various events, concluding that many signals were not valid.⁷ In the USA, Slade *et al.* have shown that in the 18 months after HPV vaccine implementation, adverse report rates were similar to the expected background rates, except for syncope and venous thromboembolic events.⁸ However, syncopes were probably not because of the HPV vaccine itself but of the vaccination process, and thromboembolic events probably reflected the fact that 90% of women undergoing HPV vaccination had at least one underlying risk factor for thromboembolism (i.e., oral contraception, smoking, or obesity).^{9,10}

In line with these concerns, the International Conference of Harmonisation E2E guidelines has recommended the assessment of background rates of adverse events as well as frequently diagnosed conditions or diseases before a product or a public health program was initiated. This would identify upper threshold rates, whose crossing might signal intervention-related events.¹¹

At present, such background rates for the most common health problems diagnosed during a physician's encounter with young female patients are lacking in most countries. Given that the majority of patients' health problems are managed on an outpatient basis, it is important to assess their frequency in that setting. This is of particular importance in the context of HPV vaccines, as this intervention targets a new, specific, and large population, that is, young female patients aged 14–23, while being used primarily to prevent long-term consequences of exposure to HPV. As such, perceived benefits and risks may differ from those related to older vaccines and may lead to the occurrence of new, atypical complaints.

To facilitate the assessment of any possible report of association with the HPV vaccine, knowledge of background rates of new health problems diagnosed in young women by general practitioners (GPs) and gynecologists (GYNs) is therefore essential. We investigated electronic health records to verify whether the background rates of health problems diagnosed by GPs and GYNs in France in 2006 could be identified before the national HPV vaccination program was initiated.

METHODS

This was a multicenter study using data recorded in France in 2006, before the initiation of the national HPV vaccination program. All visits to GPs and GYNs participating in the longitudinal patient data (LPD) network during the study period were considered. No other medical specialty was considered because GPs and GYNs are the physicians most frequently consulted by young women. Only visits of female patients between the ages of 11 and 23 years of age, which includes the age range targeted for the HPV vaccination in France (14–23 years), were considered.

Study population—longitudinal patient data network

This network consists of 1200 GPs and 750 various medical specialists who continuously and voluntarily provide anonymized and coded patients' data. Data are downloaded in a centralized database using the Doc'Ware software. This procedure has obtained ethical approval from the French National Data Protection Authority in 2002. Physicians included in the LPD network are a representative sample of the practices in the continental France regions (personal communication, CSD). LPD database contains diagnoses, signs, and symptoms, as well as prescription data, on approximately 1.5 million patients.

Definition and classification of the most common diagnoses made during general practitioner and gynecologist visits

Diagnoses for each visit included in the LPD database were analyzed, regardless of the triggering symptoms. Indeed, a diagnosis was recorded for 90% of GP visits, and the diagnoses made by physicians are usually more valid than the complaints and symptoms presented by the patients as the reasons for encounter.¹²

To standardize data recorded by physicians, the diagnoses were recoded and classified according to the International Classification of Primary Care, second

version (ICPC-2) by two translators, using its French translation, under the supervision of an expert in primary care classifications (L.L.). The ICPC-2 is mapped with the International Classification of Diseases and is a member of the World Health Organization Family of International Classifications.¹³ The use of the ICPC-2 classification limits the list of diagnostic rubrics to approximately 700. This classification is considered as an efficient tool for coding diagnosis in primary care, although not completely exhaustive.¹⁴

For the purpose of this study, all diagnoses were analyzed. In addition to visits related to prespecified procedures, visits with no specific reasons as well as visits labeled "no disease (ICPC-2, A97)," "health maintenance/prevention (A98)," "post-coital contraception (W10)," "oral contraception (W11)," "intrauterine contraception (W12)," "sterilization (W13)," and "other contraception (W14)" were all considered as procedures. They were included in the denominators but not in the numerator for calculating the background rates of diagnoses.

Only diagnoses made in at least 1% of visits of either adolescents or adults by either GPs or GYNs were considered as common and were reported in the primary analyses.

All diagnoses gathered by body systems (ICPC-2 chapters) are presented in the Appendices and are put in context in the Results section. Based on the sampling coefficients used *a priori* in the selection of the participating physicians, extrapolations of the expected number of visits for a given diagnosis were calculated at the national level considering geographical region, physicians' and patients' age and sex, and medical specialty (GP/GYN). These extrapolations are presented in the Appendices.

Patients' age was stratified as follows: 11–16 (adolescents) and 17–23 years of age (young adults).

Statistical analyses

1 Background rates of most common diagnoses

Independent analyses were performed for GP and GYN visits, for adolescents and young adults separately. Background rates of diagnoses per 100 000 visits in 2006 along with 95%CI were calculated. Sensitivity analyses were performed, stratifying on the season of the diagnosis to take into account seasonal trends. In addition, analyses were performed taking only one visit per specific diagnosis per woman in the event a woman consulted her physician several times for the same problem during the study period. In this case, procedures and visits for non-specific problems were not considered in the denominator because it better reflects rates of new health problems. For example, a woman visiting her

physician twice for a migraine during the study year was only counted once in the numerator; the denominator considered all of her visits except those for procedures or with no reason or missing data, which were excluded, hence not counted.

Sensitivity analyses were performed to compare the overall background rates of the most common health problems diagnosed by GPs and GYNs in 2005 with those found in 2006, to see whether there was inter-calendar year variation.

2 Background rates of specific diagnoses in adolescent girls

With a methodology used in similar studies,^{6,15,16} we estimated the expected number of specific diagnoses occurring in temporal relationship (within 6 weeks after each injections) to HPV vaccination purely by chance, under the following conditions: increased risk of being diagnosed with the specific types of diagnoses after HPV vaccination: yes or no, and a HPV vaccination schedule of three doses administered at 0–2–6 months. This was specifically performed by converting the diagnoses rates (in 100 000 visits per year) to rates in units relevant to the temporal relationship under evaluation (6 weeks). These rates were then multiplied by 3 (for three doses of vaccine to be fully vaccinated) and then further multiplied by 100 000 to obtain the number of theoretical new diagnoses per 100 000 fully vaccinated adolescent girls in the specific study year.

To do this, we first identified the following diagnoses: weakness/tiredness general (A04), feeling anxious/nervous/tense (P01), acne (S96), and menstrual problems [combination of menstrual pain (X02), intermenstrual pain (X03), menstruation absent/scanty (X05), menstruation excessive (X06), menstruation irregular/frequent (X07), and postponement of menstruation (X10)]. These diagnoses were selected for their likeliness of being attributed to the vaccine, given their subjective nature and their multiple or unknown causes (weakness, tiredness, and anxiety) or because they are related to pathologies of the anatomic site targeted by the vaccine (gynecological health problems) or linked to health problems (acne) that are frequently encountered in the vaccine's target population.

Next, we selected two diagnoses that are documented to occur after immunization, that is, fever (A03) and syncope (A06).³

All analyses were performed using SAS, 9th edition.

RESULTS

Overall, 380 813 visits to participating GPs and 36 329 visits to participating GYNs of female patients aged

11–23 years in 2006 were considered. For GPs and GYNs, the majority of visits (71%) concerned young adults (aged 17–23 years), and approximately 10% and 24% of visits had missing diagnosis data, respectively. These missing diagnosis data included genuine missing data (approximately 7% for GPs and 9% for GYNs) and reasons for encounter (approximately 3% for GPs and 15% for GYNs).

Table 1 presents all diagnoses made by participating GPs and GYNs, stratified according to ICPC-2 chapters, regardless of the 1% cutoff. Visits to GPs were essentially prompted by respiratory (28.4%) and digestive (10.2%) problems. Gynecological problems, and pregnancy diagnosis or follow-up accounted for 3.6%, and 1.6% of GP visits, respectively. Most common diagnoses identified by GYNs were gynecological problems (19.1%) and pregnancy diagnosis and follow-up (4.5%).

According to the 1% cutoff, Table 2 presents the frequencies and rates per 100 000 visits along with their 95%CI for the most frequent diagnoses made by GPs, stratified according to the age category. Acute upper respiratory infection and acute tonsillitis were the most commonly diagnosed health problems in both adolescents and adults. Overall, occurrence of new

health problems was similar in both age groups (Table 2).

When considering all women combined, visits to GPs for infections and respiratory diagnoses were common (Appendix I). Indeed, an acute upper respiratory infection (ICPC-2, R74) was the most frequent diagnosis, accounting for 11 783 diagnoses per 100 000 visits per year. Visits related to the respiratory system (ICPC-2, Chapter R) accounted for 10 of the 23 most frequent diagnoses made by GPs in 2006. Other common diagnoses included back pain syndrome (L84), urinary infections (U71), gastrointestinal infections (D70), acne (S96), pregnancy, and anxiety/nervousness/tension feeling (P01). Gynecological diagnoses were seldom diagnosed by GPs, and they were mostly related to menstruation, for instance, menstrual pain (1.1%; 203 140 estimated visits).

Table 3 presents the frequencies and rates per 100 000 visits along with their 95%CI for the most frequent diagnoses made by GYNs in 2006, stratified according to age category. Adolescents and adult visits were, for similar reasons, related to menstruation or genital infections, except that adolescents more frequently visited their GYNs for acne or general pain and adults for pregnancy-related issues (Table 3).

Table 1. Frequencies and rates with corresponding 95%CIs for all health problems diagnosed by participating general practitioners and gynecologists in 2006 (adolescents and adults)

ICPC-2 chapter	Body system	GPs (380 813 overall visits)				GYNs (36 329 overall visits)			
		Frequency (n)	%	Rate per 100 000 visits	95%CI	Frequency (n)	%	Rate per 100 000 visits	95%CI
R	Respiratory	108 142	28.4	28 398	28 228–28 567	44	0.1	121	85–157
D	Digestive	38 809	10.2	10 191	10 090–10 292	179	0.5	493	421–565
L	Musculoskeletal	36 108	9.5	9482	9384–9580	44	0.1	121	85–157
S	Skin	30 813	8.1	8091	8001–8182	648	1.8	1784	1646–1921
P	Psychological	14 516	3.8	3812	3750–3874	12	0.04	33	
X	Female genital	13 673	3.6	3590	3530–3651	6945	19.1	19117	18 667–19 567
N	Neurological	12 507	3.3	3284	3227–3342	74	0.2	204	157–250
A	General and unspecified	12 159	3.2	3193	3136–3250	372	1.0	1024	920–1128
U	Urological	9478	2.5	2489	2439–2539	342	0.9	941	842–1041
H	Ear	7760	2.0	2038	1992–2083	0	0	0	0
W	Pregnancy, childbearing, family, planning	6135	1.6	1611	1571–1651	1638	4.5	4509	4290–4727
T	Endocrine/metabolic and nutritional	5893	1.5	1547	1508–1587	178	0.5	490	418–562
K	Cardiovascular	4978	1.3	1307	1271–1344	106	0.3	292	236–347
F	Eye	3355	0.9	881	851–911	0	0	0	0
B	Blood, blood forming organs and immune mechanism	2995	0.8	786	758–815	96	0.3	264	211–317
Y	Male genital	90	0.02	24	19–29	6	0.02	17	
Z	Social problems	11	0.003	3		0	0	0	0

GPs, general practitioners; GYNs, gynecologists; CPC-2, International Classification of Primary Care, second version.

Table 2. Frequencies and rates with corresponding 95% CIs for the most common health problems diagnosed by participating GPs in 2006 (adolescents and adults)

ICPC-2 codes	Description	Adolescents only (11–16 years) (138 001 overall visits)				Adults only (17–23 years) (242 812 overall visits)			
		Frequency (n)	%	Rate per 100 000 visits	95% CI for rate	Frequency (n)	%	Rate per 100 000 visits	95% CI for rate
R74	Upper respiratory infection acute	18 926	13.7	13 714	13 519–13 910	25 946	10.7	10 686	10 556–10 816
R76	Tonsillitis acute	6917	5.0	5012	4894–5130	9477	3.9	3903	3824–3982
R77	Laryngitis/tracheitis acute	3768	2.7	2730	2643–2818	4983	2.1	2052	1995–2109
R80	Influenza	3543	2.6	2567	2483–2652	3731	1.5	1537	1487–1586
S96	Acne	3106	2.3	2251	2172–2330	3833	1.6	1579	1529–1629
R96	Asthma	3098	2.2	2245	2166–2324	4634	1.9	1908	1854–1963
D01	Abdominal pain/cramps general	2944	2.1	2133	2056–2210	3595	1.5	1481	1432–1529
R78	Acute bronchitis/bronchiolitis	2871	2.1	2080	2004–2157	4342	1.8	1788	1735–1841
D70	Gastrointestinal infection	2825	2.0	2047	1972–2123	4689	1.9	1931	1876–1986
R97	Allergic rhinitis	2752	2.0	1994	1920–2069	5395	2.2	2222	2163–2281
D73	Gastro-enteritis	2604	1.9	1887	1814–1959	4679	1.9	1927	1872–1982
R75	Sinusitis acute/chronic	2043	1.5	1480	1416–1545	5125	2.1	2111	2053–2168
H71	Acute otitis media/myringitis	2006	1.5	1454	1390–1517	1463	0.6	603	572–633
L84	Back syndrome without radiating pain	1960	1.4	1420	1357–1483	6202	2.6	2554	2491–2618
R05	Cough	1847	1.3	1338	1277–1399	2170	0.9	894	856–931
L77	sprain/strain of ankle	1668	1.2	1209	1151–1267	1496	0.6	616	585–647
R83	Respiratory infection other	1610	1.2	1167	1110–1224	2255	0.9	929	890–967
S88	Dermatitis contact/allergic	1607	1.2	1164	1108–1221	3117	1.3	1284	1239–1329
X02	Menstrual pain	1577	1.1	1143	1086–1199	2776	1.1	1143	1101–1186
U71	Cystitis/urinary infection other	1186	0.9	859	811–908	6812	2.8	2805	2739–2872
A04	Weakness/tiredness general	1002	0.7	726	681–771	4016	1.7	1654	1603–1705
P01	Feeling anxious/nervous/tense	949	0.7	688	644–731	3864	1.6	1591	1541–1642
N89	Migraine	983	0.7	712	668–757	3744	1.5	1542	1493–1591
P76	Depressive disorder	317	0.2	230	204–255	3643	1.5	1500	1452–1549
X72	Genital candidiasis female	280	0.2	203	179–227	2509	1.0	1033	993–1074
W78	Pregnancy	89	0.1	64	51–78	5287	2.2	2177	2119–2236

When considering all women combined, the main diagnoses by GYNs were female genital infections, pregnancy, and menstruation problems (Appendix II). More specifically, genital candidiasis (ICPC-2, X72) was the most frequent diagnosis, accounting for 4746 diagnoses per 100 000 visits. Visits related

to genital problems (ICPC-2, Chapter X) accounted for seven of the eight most common GYN diagnoses. Pregnancy-related diagnoses (ICPC-2, W78) were the second most frequent diagnoses, accounting for 3325 diagnoses per 100 000 GYN visits per year.

Table 3. Frequencies and rates with corresponding 95% CIs for the most common health problems diagnosed by participating GYNs in 2006 (adolescents and adults)

ICPC-2 codes	Description	Adolescents only (11–16 years) (2494 overall visits)				Adults only (17–23 years) (33 835 overall visits)			
		Frequency (n)	%	Rate per 100 000 visits	95%CI for rate	Frequency (n)	%	Rate per 100 000 visits	95%CI for rate
X02	Menstrual pain	199	8.0	7979	6871–9088	585	1.7	1729	1589–1869
X72	Genital candidiasis female	95	3.8	3809	3043–4575	1629	4.8	4815	4581–5048
X07	Menstruation irregular/frequent	88	3.5	3528	2791–4266	263	0.8	777	683–871
X06	Menstruation excessive	86	3.4	3448	2719–4177	130	0.4	384	318–450
S96	Acne	59	2.4	2366	1762–2969	276	0.8	816	719–912
X05	Menstruation absent/scanty	56	2.2	2245	1657–2833	422	1.2	1247	1128–1366
X16	Vulval symptom/complaint	54	2.2	2165	1588–2743	887	2.6	2622	2449–2794
X14	Vaginal discharge	45	1.8	1804	1277–2332	638	1.9	1886	1739–2032
A01	Pain general/multiple sites	29	1.2	1163	740–1586	283	0.8	836	739–934
X81	Genital neoplasm	29	1.2	1163	740–1586	195	0.6	576	495–657
X08	Intermenstrual bleeding	24	1.0	962	577–1347	366	1.1	1082	971–1193
W78	Pregnancy	15	0.6	601		1193	3.5	3526	3326–3726

Table 4 presents the expected rates of coincidental diagnoses of acne, weakness/tiredness, feeling anxious/nervous/tense, problems related to the menstrual cycle, fever, and syncope within the 6-week time window after each injection of a three-dose vaccination regimen in adolescent girls. As an example, acne was identified commonly by GPs in this young female population, at rates close to 800 per 100 000 visits per year, whereas GYNs commonly identified problems related to menstruation, at rates higher than 6% of visits.

Sensitivity analyses on seasonal variations showed that GP diagnoses for allergic rhinitis were more frequent in the spring and fall and that acute respiratory tract infections were more common in winter, whereas other diagnoses remained fairly stable during the year (data not shown). Overall, almost no seasonal variation was observed for the most frequent health problems diagnosed by GYNs.

Finally, the overall background rates of the most common health problems diagnosed by GPs and

Table 4. Expected rates of specific diagnoses occurring in temporal relationship (within 6 weeks after each injection) to human papillomavirus vaccination purely by chance in adolescent girls visiting GPs or GYNs

ICPC-2 codes	Description	Expected rates of coincidental events after a 3-dose regimen of HPV vaccine in GPs' visits		Expected rates of coincidental events after a 3-dose regimen of HPV vaccine in GYNs' visits	
		Rate per 100 000 visits	95%CI	Rate per 100 000 visits	95%CI
S96	Acne	779	700–858	819	215–1423
A04	Weakness/tiredness general	251	206–296	55	
P01	Feeling anxious/nervous/tense	238	194–282	0	
X02 or X03 or X05 or X06 or X07 or X10	Combination of diagnoses related to menstruation	497	434–560	6288	4615–7961
A03	Fever	69	46–92	—	—
A06	Syncope	166	129–203	—	—

HPV, human papillomavirus.

GYNs were similar in 2005 and 2006, except for the flu/colds, which were more frequent in 2005 than in 2006 (data not shown).

DISCUSSION

To our knowledge, this is the first study to estimate the background rates of diagnosed health problems in women aged 11–23 years visiting GPs or GYNs in France. We were able to identify acute and non-acute problems of the respiratory tract as the most common health problems in young adults and adolescents visiting GPs. Visits to GYN were mainly for pregnancy and menstruation-related problems in adults and for acne in adolescents. These specialists never diagnosed anxiety nor fever and syncope as health problems managed during the consultation, which can be explained by the French reimbursement scheme restricted to screening, contraception, pregnancy, and abortion care.¹⁷ Few differences were observed between adolescents and young adults overall. Seasonal variations were observed for seasonal allergies and acute respiratory infections, following the expected seasonality and thus providing supportive evidence of the capacity of the methodology to identify differences in background rates.

Our data suggest that, as a result of their frequent occurrence, many health problems could be diagnosed by chance alone following an immunization. This was demonstrated again during the influenza A/H1N1/09 immunization campaign.¹⁵ As illustrations, we computed the expected rates of coincidental diagnoses of acne, weakness/tiredness, feeling anxious/nervous/tense, problems related to the menstrual cycle, fever, and syncope within the 6-week time window after each injection of a three-dose vaccination regimen in adolescent girls. Among these diagnoses, the most common one in GPs was acne (nearly 1% of visits). In GYNs, menstruation problems occurred in more than 6% of visits. These figures confirm that as expected, new diagnoses of “potential concern” could be commonly made by chance alone after the implementation of a new vaccination program. This is of interest, as common, benign, events that would be reported as occurring at increased rates following mass immunization would probably also lead to reassessment of the benefit:risk ratio of HPV vaccines. From this assumption, access to historical data from electronic health records and computations of expected rates and 95%CI, could be of major interest.

Our study results are difficult to compare with others that focused on incidence rates in hospital settings or on rare adverse events. For instance, new diagnoses of asthma would occur more seldom in the health records

that we assessed, and they would be more complex to assess than typical health problems such as acne, as a result of the complexity to diagnose asthma in primary care.

It is nevertheless interesting to highlight the fact that asthma that has been identified as being a frequent condition diagnosed in a hospital or an emergency department setting^{5,6,8} could also be identified in GP records in our study. We nonetheless believe that electronic GP or GYN records would not be the best tool to directly identify new cases of rare or complex diagnoses without review of complete clinical charts or hospital files.

This study focused on annual frequency rates of the most common medical diagnoses recorded by GPs or GYNs in female patients aged 11–23 years. It had one of the largest sample sizes for a study estimating background rates, hence ensuring robustness of the overall and specific frequency rates. All data on diagnoses were collected as part of an ongoing collaboration between French participating physicians and the LPD network. Participating physicians were representative of the general medical practice of continental France. However, as data collection within the LPD database is not standardized, all diagnoses made during a visit to a GP or GYN by female patients aged 11–23 years during 2006 were recoded using the ICPC-2 classification. Nevertheless, the validity of the original diagnoses made by the participating physicians could not be formally assessed, as is often the case in primary care. In addition, in the ICPC system, a distinction is made between health problems diagnosed as a consequence of presenting signs or symptoms (“diagnoses”), and visits where healthcare professionals perform preventive procedures, such as refill prescriptions for oral contraceptives or immunizations. In the young and generally healthy population that was studied, a significant proportion of visits related to preventive procedures rather than to health problems. Diagnosis data were frequently missing in GYNs’ files, mainly because of the recording of data related to reasons for encounter (instead of diagnoses), such as follow-up visits and requests for various preventive procedures. This should, however, not substantially alter computed background rates of main diagnoses.

The cutoff for the most frequent diagnoses was arbitrarily set at 1%. Hence, a problem diagnosed in at least 1% of physician visits was considered frequent and was reported here. As this threshold is arbitrary, we have provided the full list of frequency rates of diagnosed health problems in the two appendices. In addition, CIs can be computed from sets of data from successive years; they could then take account of changes in the occurrence of health problems, such as new epidemics.

In conclusion, the background rates presented in this study should facilitate the interpretation of potential

vaccine-related events after the introduction of new vaccines into a young female population. More generally, we believe that this method applies not only to the specific introduction of HPV vaccine but is of interest to interpret signals appearing after the launch of any new, and common, intervention—vaccine or pharmacological product—in that age group. As such, automated exploration of electronic health records could be considered as a new, and efficient, tool for active post-marketing surveillance, as illustrated by recent initiatives.¹⁸

CONFLICT OF INTEREST

The authors declare no conflict of interest.

KEY POINTS

- Background frequency rates for common health problems remain poorly documented, notably for young female patients visiting their general practitioners (GPs) or gynecologists.
- Our descriptive study showed that visits related to the respiratory system accounted for most frequent diagnoses by GPs. In gynecology, genital candidiasis was the most frequent diagnosis, and most visits were for pregnancy-related issues or menstrual problems.
- These data can facilitate interpretation of signals that occur after a new public health intervention, such as the human papillomavirus immunization program.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

APPENDIX: Frequencies, rates and extrapolation to the French population for the most common conditions

diagnosed by participating GPs (Appendix I) and gynecologists (Appendix II) in 2006 stratified by ICPC-2 chapters and codes.

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