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# BMJ Open Cost and outcomes of the ultrasound screening program for birth defects over time: a population-based study in France

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## ABSTRACT

**Objective** To assess trends in the average costs and effectiveness of the French ultrasound screening programme for birth defects.

**Design** A population-based study.

**Setting** National Public Health Insurance claim database.

**Participants** All pregnant women in the 'Echantillon Généraliste des Bénéficiaires', a permanent representative sample of 1/97 of the individuals covered by the French Health Insurance System.

**Main outcomes measures** Trends in the costs and in the average cost-effectiveness ratio (ACER) of the screening programme (in € per case detected antenatally), per year, between 2006 and 2014. Incremental cost-effectiveness ratio (ICER) from 1 year to another were also estimated. We assessed costs related to the ultrasound screening programme of birth defects excluding the specific screening of Down's syndrome. The outcome for effectiveness was the prenatal detection rate of birth defects, assessed in a previous study. Linear and logistic regressions were used to analyse time trends.

**Results** During the study period, there was a slight decrease in prenatal detection rates (from 58.2% in 2006 to 55.2% in 2014;  $p=0.015$ ). The cost of ultrasound screening increased from €168 in 2006 to €258 per pregnancy in 2014 ( $p=0.001$ ). We found a 61% increase in the ACER for ultrasound screening during the study period. ACERs increased from €9050 per case detected in 2006 to €14 580 per case detected in 2014 ( $p=0.001$ ). ICERs had an erratic pattern, with a strong tendency to show that any increment in the cost of screening was highly cost ineffective.

**Conclusion** Even if the increase in costs may be partly justified, we observed a diminishing returns for costs associated with the prenatal ultrasound screening of birth defects, in France, between 2006 and 2014.

## INTRODUCTION

Screening and prevention are not necessarily cost saving or more cost effective than treatment for existing conditions. A review of the cost-effectiveness literature found that 'distributions of cost-effectiveness ratios

## Strengths and limitations of this study

- We observed the chronological trend of the average cost-effectiveness ratio of the French ultrasound birth defect screening programme.
- We used two large data sources: national registries of birth defect and the national claims database.
- Almost all costs related to the screening were included.
- We used a unique effectiveness criterion: the prenatal detection rate of birth defects.
- Costs and prenatal detection rates had to be extrapolated from different samples because nationwide data are not available in France.

for preventive measures and treatments are very similar—in other words, opportunities for efficient investment in healthcare programmes are roughly equal for prevention and treatment'.<sup>1</sup>

Screening and prevention can reduce morbidity and mortality by allowing earlier diagnosis; however, this would not necessarily reduce costs if only a small part of the population targeted for prevention is at risk to be affected by a disease or in the absence of treatment. Screening a large population requires important resources, which may be better used to support other healthcare actions.<sup>2</sup>

All industrialised countries organise programmes for prenatal birth defects screening.<sup>3</sup> Indeed, congenital abnormalities represent one of the leading cause of infant mortality, morbidity and long-term adverse developmental outcomes.<sup>4-6</sup>

So far, medico economic studies of prenatal screening for congenital anomalies have mostly focused on Down's syndrome screening. Studies of prenatal screening for structural fetal anomalies are rare. Several reviews<sup>7,8</sup> have highlighted the limits of the



current literature on the subject, whether in comparisons of different modalities of screening<sup>9,10</sup> or screening versus no screening.<sup>11,12</sup> Moreover, while screening programmes for birth defects are organised in all industrialised countries, the cost-effectiveness (using global costs and prenatal detection rates) of such programmes was never evaluated at a national level. The available data in France suggest that detection rates of birth defects remain stable since the early 2000.<sup>13,14</sup>

Using national cost claims data and registry-based prenatal detection rates, our objective was to assess trends in the costs and effectiveness (cost per birth defect detected) of the French ultrasound screening programme for birth defects, by estimating both annual average cost-effectiveness ratio (ACER) and incremental cost-effectiveness ratio (ICER) from 1 year to another.

## DATA AND METHODS

We assessed time trends for costs, efficacy and ACER of the French ultrasound screening programme for structural birth defects, between 2006 and 2014. In France, three ultrasound screening examinations are recommended for singleton pregnancies at 11–14, 20–25 and 30–35 weeks of gestation.<sup>15</sup> A screening for birth defects is performed during these examinations, in addition to other analysis (placenta localisation, fetal growth estimation). The scans are performed by certified practitioners and examinations' reports must include images of standard views following the French guidelines.<sup>15</sup> Both public and private centres must comply with these guidelines. When a fetal anomaly is suspected, further examinations are performed by specialists and the parents are referred to prenatal referral centres.<sup>16</sup> There are 48 referral centres for prenatal diagnosis in France and its overseas territories, providing full diagnostic workup, parents counselling and fetal treatments. When a severe fetal anomaly is confirmed, termination of pregnancy for fetal abnormality (TOPFA) can be authorised, regardless of the gestational age, according to the French regulations.<sup>17</sup> TOPFA may be considered at the request of the parents, if the continuation of the pregnancy seriously endangers the mother's health, or if there is a high probability for the future born infant to be affected by a severe and incurable disease. In addition to ultrasound screening examinations, a first trimester combined test is offered to all pregnant women for the evaluation of the risk of Down's syndrome. This combined testing is based on maternal age, maternal biochemical markers and nuchal translucency measurement.<sup>18</sup>

The outcome for effectiveness was the prenatal detection rate of fetuses with birth defects. Details of the methodology for data sources, definition of cases, exclusion criteria, in particular for cases detected by other modalities than ultrasound and calculation methods have been reported elsewhere.<sup>13</sup> The prenatal detection rate was defined as the ratio of the number of cases detected prenatally (positive screening) on the total number of cases

per year. A case was defined as a fetus with at least one abnormality whatever the pregnancy outcome was (live birth or fetal loss after 20 WG or following a TOFPA). The screening was considered positive if the fetal anomaly was suspected by ultrasound during the pregnancy regardless the precise diagnosis after birth. For multiple abnormalities, the screening was considered positive if at least one had been detected prenatally. Fetal anomalies where the ones listed by European surveillance of congenital anomalies; EUROCAT (which excludes some minor abnormalities with very low medical or aesthetic impact).<sup>19</sup>

Cases detected following the first combined test were excluded from the analysis for both costs and efficacy as our aim was to focus on the ultrasound screening programme. However, increased nuchal translucency cases (>99th percentile) were included as these cases are related to the ultrasound screening (high risk for Down's syndrome and other fetal anomalies, whatever the results of maternal biochemical markers). We used data from three French regional registries of birth defects. These public organisations identify cases with congenital anomalies over a predefined area (usually an administrative region). We included three registries: Auvergne, Paris and La Reunion, all members of EUROCAT, the European network for registries of birth defects<sup>20</sup> and using the standards recommended for this purpose. We included the population of women who gave birth (live birth or fetal loss after 20 WG) or following a TOFPA in the areas covered by these three registries, during the study period (2006–2014). We excluded women not resident in those areas. Cost calculations included all procedures performed as part of the screening programme (number of ultrasound screening examinations), further examinations performed following the suspicion of a fetal abnormality and the operating costs of the referral centres. TOPFA costs were not included. We used the public healthcare system perspective and the time horizon of the pregnancy.

Data sources for calculation of costs were as follows:

### 1. Costs of procedures

The annual number of procedures for the screening and diagnosis of structural fetal anomalies and their costs were extracted from the national claims database, using the Echantillon Généraliste des Bénéficiaires (EGB), a permanent representative sample of 1/97 of the individuals covered by the French Health Insurance System for employees. This public insurance covered 85% of the total population.<sup>21</sup> This claims database is exhaustive and covers the entire French population. The database contains information about procedures' fees (including extra billing (or balance billing)), either performed in free-standing clinics or in hospital facilities, and cost sharing: costs for the healthcare system, both compulsory and complementary health insurance and out-of-pocket costs for patients. After the third month of pregnancy, all healthcare costs (including transportation) are covered by the statutory health insurance, the only out of pocket costs for patients are the extra billing which

private practitioners may charge. Each episode of care is identified by a code. We identified pregnant women using delivery codes. Multiple codes are used for ultrasound examinations performed during the pregnancy, depending on the indication. We included procedures related to the detection of fetal anomalies (systematic first, second and third trimester ultrasound examinations, ultrasound examinations for the monitoring of a known fetal anomaly, fetal echocardiography, and amniocentesis, chorionic villus sampling). Procedures unrelated to the prenatal detection of fetal anomalies (dating ultrasound examinations before 11 WG, ultrasound examinations for fetal growth monitoring including Doppler, fetal well-being evaluation) were excluded. We excluded other imaging procedures (MRI or tomodesitometric examination), due to their very low occurrence in the population.

## 2. Infrastructure costs

In addition to the income resulting from their activity (ultrasound examinations, invasive tests and so on), referral centres in charge of prenatal diagnosis and genetic counselling are funded through a specific governmental grant. The annual amount of this grant was retrieved in official governmental data.<sup>22</sup>

Costs related to the specific screening for Down's syndrome were excluded from the total costs of the programme. Cost of blood tests using maternal biochemical markers were not included, as well as invasive tests performed after a positive first trimester combined test. Costs of the first-trimester ultrasound scan were included in our cost-effectiveness analysis, even if the screening for Down's syndrome was a part of these procedures.

We extrapolated the annual costs of procedures computed from the database to the entire population using the ratio of the total number of annual deliveries (data from the official governmental office for statistics, INSEE<sup>23</sup>) with the annual number of deliveries in the EGB sample. By adding the infrastructure costs, we estimated the total annual costs of the screening programme.

The ACER was estimated in € per case detected antenatally, for each year, as follow:

$$ACER_t = C_t / (N_t * R_t * p)$$

Where:

- t was the year.
- C were costs of the ultrasound screening programme for birth defects.
- N was the number of deliveries.
- R was the prenatal detection rate for birth defects.
- p was the prevalence of birth defects.

N was extracted from the official governmental office for statistics, INSEE.<sup>23</sup> R and p were estimated from the dataset of the birth defects registers and previously published.<sup>13</sup> p was the average prevalence of birth defects for the study period in the areas covered by the birth defects registers.

In addition to the ACERs, we estimated ICERs by comparing the costs and detection rates from 1 year to the next:  $ICER_t = (C_t - C_{t-1}) / ((N_t * R_t * p) - (N_{t-1} * R_{t-1} * p))$ .

We used a simple linear regression to assess time trends in the costs of ultrasound screening and in the cost-effectiveness ratios. We used logistic regression for looking at trends in the odds of prenatal diagnosis. All analyses were conducted using Stata V.14.0 software (StataCorp, College Station, Texas, USA).

## RESULTS

In the 1/97 sample of the national claims database, we included a total number of 57 104 pregnant women for the 2006–2014 period, ranging from 5888 to 6882 per year (0.7% to 0.8% of the total number of deliveries in France). The mean maternal age in our sample was similar to that of the national population of pregnant women with the same trend of increase age during the study period (from 29.5 to 29.8 years old).<sup>24</sup> In our sample, the proportion of multiple pregnancies was 1.6% during the study period.

The number of ultrasound screening examinations increased by approximately 20%, from 2.47 per pregnancy in 2006 to 2.98 in 2014 ( $p=0.005$ ). We observed an increase of all types of ultrasound examinations, especially for the surveillance of fetal anomalies, which increased by three folds during this period (from 0.07 to 0.26 per pregnancy during the study period;  $p=0.003$ ). The number of fetal echocardiographies increased from 0.01 to 0.03 per pregnancy ( $p<0.001$ ). The average rate of invasive prenatal diagnosis procedures related to ultrasound screening was 0.016, and this rate did not change significantly over time ( $p=0.38$ ). This absence of change resulted from two opposite trends: the total number of invasive procedures decreased during the study period (from 0.08 to 0.04 per pregnancy,  $p<0.001$ ) but the estimated proportion of invasive procedures related to the ultrasound screening progressively increased over time (from 22% to 38% of the total number of invasive tests).

Ultrasound procedures were performed either in the private sector (by self-employed sonographers or in private for profit hospitals) or in public hospitals in 82% and 18%, respectively. Invasive procedures were mostly performed in public hospitals (65% of the total number).

The official fee for screening ultrasound was revised between 2007 and 2008, leading to a 19%, 15% and 27% increase in costs for the first, second and third trimester ultrasound scans, respectively. In addition, the proportion of the first, second and third trimester ultrasound procedures with extra billing increased during the study period from 40.5% to 46.5%, 40.9% to 47.1% and 42.8% to 44.6%, respectively. The average value of extra billing also increased for all ultrasound procedures during the study period. Consequently, the overall ultrasound screening procedures cost progressively increased during the study period from €139 685 270 in 2006 to €195 310 309 in 2014 (table 1). Detailed costs for first, second and third trimester screening ultrasound scans are available as online supplementary data.

The specific governmental grant to referral centres was created in 2007, accounting for 6.7% of the total cost of

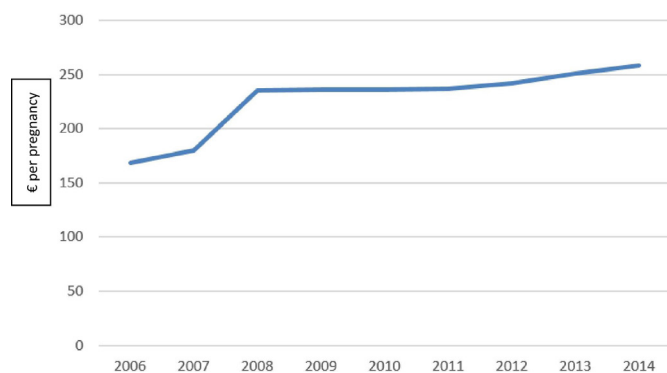
**Table 1** Estimated total cost (and its repartition between procedures cost and infrastructure cost) and cost per pregnancy of the French ultrasound screening programme for birth defect between 2006 and 2014

	Total cost (€)	Including		Cost per pregnancy (€)
		Procedures cost (€)	Infrastructure cost(€)	
2006	139 685 270	139 685 270	0	168
2007	147 545 154	137 655 154	9 890 000	180
2008	194 943 053	185 053 053	9 890 000	235
2009	194 453 720	184 563 720	9 890 000	236
2010	196 517 392	186 627 392	9 890 000	236
2011	195 435 422	185 545 422	9 890 000	237
2012	198 731 955	186 161 955	12 570 000	242
2013	203 869 909	188 959 909	14 910 000	251
2014	210 790 309	195 310 309	15 480 000	258

the screening programme. Due to an increase since 2012, this grant accounted for 7.3% of the total costs in 2014 (table 1).

The overall cost of the screening programme in France was estimated to be €210 790 000, in 2014. Ultrasound examinations accounted for 99.5% of the total procedural costs (0.5% for invasive procedures). Seventy seven per cent of the total cost was covered by the public health insurance and 23% by patients (out-of-pocket or complementary insurance). Costs per pregnancy, total costs and their distribution are detailed in table 1, for the 2006–2014 period. The cost of screening increased from €168 in 2006 to €258 per pregnancy in 2014 ( $p=0.001$ ) (figure 1).

We identified 15 989 cases of fetal anomalies (average: 1777 per year (range: 1661–1869)) from the registries between 2006 and 2014. The prevalence of birth defects during the study period was 3.2% and was fairly stable. The overall prenatal detection rate of birth defects following ultrasound screening during the study period was 57.0%, ranging from 53.9% (in 2012) to 58.7% (in 2008). The logistic regression found a small declining trend for the overall prenatal detection rate during the study period (OR=0.985; 95% CI 0.972 to 0.997;  $p=0.015$ ).



**Figure 1** Chronological evolution of the cost per pregnancy (€) of the French ultrasound screening programme for birth defects.

ACER's and ICER's values for the 2006–2014 period are presented in table 2. Prevalence for birth defects was considered as stable during the study period (3.3%). We found a 61% increase in the ACER for ultrasound screening during the study period. ACER increased from €9050 per case detected in 2006 to €14 580 per case detected in 2014 ( $p=0.001$ ). ICERs had an erratic pattern, with a strong tendency to show that any increment in the cost of screening was highly cost ineffective.

## DISCUSSION

Our study represents this first analysis of the French prenatal screening programme for structural birth defects (excluding Down's syndrome). We found a trend of decreasing cost-effectiveness from €9050 in 2006 to €14 580 in 2014 (+62%) per case detected. This decrease in efficiency was essentially explained by the increase in costs even if we also found a small decrease in prenatal detection rates. Screening costs per pregnancy increased from €168 in 2006 to €258 in 2014, which was due to an increase in both the number and in the unit costs of ultrasound scans performed for prenatal detection of birth defects. Both the frequency and amounts of extra billing (or balance billing) also increased during the study period. To our knowledge, this is the first study to report on the efficiency of a national ultrasound screening programme for birth defects.

We chose to use both ACERs and ICERs. Indeed, our objective was not to compare the current screening policy to alternatives in order to maximise health benefits but to provide information on how much money is expected to be spent on average per identification of congenital anomaly. The use of ACER allowed simple comparisons from 1 year to another.

We have previously reported the prenatal detection rate of birth defects in France, between 2006 and 2014, using data from regional birth defects registers,<sup>13</sup> all members of EUROCAT, the European network for registries of birth defects.<sup>20</sup> This detection rate was 57.0%,

**Table 2** Evolution of the average cost-effectiveness ratio (ACER) and incremental cost-effectiveness ratio (ICER) of the French ultrasound screening programme for birth defect between 2006 and 2014, and parameters used for its calculation

	Total costs (€)	Detection rate (%)	Number of deliveries	ACER (€/detected case)	Difference in costs (€)	Difference in detected cases (n)	ICER (€/detected case)
2006	139 685 270	58.2	829 352	9050			
2007	147 545 154	57.9	818 705	9723	7 859 884	-259	Dominated
2008	194 943 053	58.7	828 404	12 518	47 397 899	398	119 111
2009	194 453 720	57.2	824 641	12 886	-489 333	-482	1016
2010	196 517 392	57.2	832 799	12 901	2 063 672	142	14 549
2011	195 435 422	57.8	823 394	12 843	-1 081 970	-16	66 599
2012	198 731 955	53.9	821 047	14 026	3 296 533	-1048	Dominated
2013	203 869 909	57.3	811 510	13 713	5 137 954	699	7355
2014	210 790 309	55.2	818 565	14 580	6 920 400	-409	Dominated

ACERs calculation using the formula:  $ACER_t = C_t / (N_t * R_t * p)$ . Where: t was the year, C were costs of the ultrasound screening programme for birth defects (total costs), N was the number of deliveries, R was the prenatal detection rate for birth defects (detection rate), p was the total prevalence of birth defects (p=3.3%, for all the study period). ICERs calculation using the formula:  $ICER_t = (C_t - C_{t-1}) / ((N_t * R_t * p) - (N_{t-1} * R_{t-1} * p))$ .

and is covered the cases prenatally detected by ultrasound scans only (other screening modalities such as first trimester combined test with NT<99th were systematically excluded). The logistic regression even found a decreasing trend for the overall prenatal detection rate during the study period (OR=0.985; 95% CI 0.972 to 0.997; p=0.015). In parallel, the costs of the ultrasound screening programme for birth defects sharply increased from €168 in 2006 to €258 in 2014. Several factor could account for the increase in the costs of the ultrasound screening programme. The creation of a governmental grant for the referral centres of prenatal diagnosis in 2007 (and its revaluation since 2012) accounted for 21% of this increase. The official fee for screening ultrasounds was re-evaluated in 2008, which comprised 60% of the increase in costs. The remaining 19% were mostly due to the progressive increase in the number of ultrasound examinations per pregnancy, as well as the increase in extra billing practices. We observed a 51% increase of the total costs of the screening programme, comparatively, the healthcare spending increased by 24% between 2006 and 2014.<sup>25</sup>

As for all screening programmes, prenatal screening for fetal anomalies raises two issues, that is, its relevance and its cost effectiveness. The relevance of ultrasound screening programmes for birth defects is no longer a matter of debate. For certain birth defects, a prenatal diagnosis allows for optimal surveillance of pregnancies and perinatal management, in particular a delivery in an adequate maternity unit to improve postnatal management,<sup>26–30</sup> and for some birth defects, administration of prenatal treatments (eg, fetal surgery).<sup>31–32</sup> Moreover, in cases of severe fetal anomalies, parents may opt for termination of pregnancy, depending on their country's legislation.<sup>33</sup> Our goal was not to present results which could be directly extrapolated to other countries, with different screening programmes or even to countries with a three-scan strategy, because the uptake and performance of

screening would differ. We suggest, however, that the cost-effectiveness of such programmes must be investigated. The number and timing of recommended screening ultrasound scans during pregnancy is the main difference between screening programmes across countries. In Europe, up to three screening ultrasound scans are usually reimbursed to low-risk pregnant women, but some countries recommend one (eg, Denmark, Finland and Sweden), two (eg, England, Belgium and Switzerland) and others three (eg, France, Italy and Spain) scans.<sup>3</sup> In our study, the ultrasounds accounted for the majority of the screening programme costs. Hence differences in the number and fees of ultrasounds can result in substantial differences in the costs of one screening programme from another. In addition, several parameters may impact the number of ultrasound and overall programmes cost, including population coverage, false positive rates and care pathways for positive screenings. Detection rates may also vary from one programme to another. Indeed, several studies have shown significant variations among countries in prenatal detection rates for specific birth defects.<sup>34–37</sup> To our knowledge, only one cost-effectiveness study attempted to compare different programmes of routine antenatal ultrasound screening, by modelling the number and the time of ultrasound screening examinations offered during pregnancy.<sup>10</sup> However, the authors acknowledged that, due to uncertainty about both costs and effectiveness of ultrasound examinations, their model had important limitations.

There are several limitations to our study that should be addressed. First, the methodological choice of ACER is not recommended in economic evaluations. We justified our choice by the absence of a decisional policy context. We complemented the ACERs by an estimate of ICERS, which are not exactly a decision tool since no decision was planned, but rather an observation of how unplanned decisions by professionals resulted in highly ineffective allocation of resources. Second, costs and prenatal

detection rates had to be extrapolated from different samples because nationwide data are not available in France. However, we do not believe that this difference between our study populations could have biased our results. Thus, prenatal diagnosis practices and policies are decided at a national level. Moreover, referral centres for prenatal diagnosis are equitably distributed across the country. Third, due to a modification in the calculation of the hospital's funding between 2006 and 2009, the number of ultrasound examinations performed during this period in public hospitals was not recorded and had to be estimated. However, when we applied our estimation method on the 2010–2014 period and compared the estimated total costs to the real total cost (computed with the database), we noticed only small differences (between –2.7% and +0.8% depending on the year). In addition, public hospitals accounted for less than 20% of all ultrasound examinations performed, thus limiting a potential bias resulting from the estimation. Fourth, some inputs related to the screening were not included in the costs estimation. Some procedures indicated after a positive screening (fetal MRI and fetal treatment) do not have specific codes and could therefore not be identified. Consequently, our global cost estimation is slightly underestimated. Nevertheless, according to the French Agency of Biomedicine reports, such procedures are performed infrequently and the related cost should be insignificant.<sup>38</sup> Fifth, the ultrasound prenatal screening not only focuses on the detection of fetal anomalies. Thus, other complications such as multiple gestation, placenta praevia or fetal growth anomalies might be found and contribute to the overall benefit of the screening. Some of these anomalies are more severe than others and their detection will radically change the management of the pregnancy. Our data does not allow identification these cases and therefore a precise quantification of the potential benefits in relation to costs. Sixth, we did not include the costs of subsequent decisions following the detection of birth defects, as we did not want to assume that the objective of the screening programme was to increase the number of terminations or to reduce the costs associated with postnatal care. And finally, although not specifically monitored, the increase in ultrasound scans is likely to increase non healthcare costs to women, with additional travel cost, time costs and missed days of work.

## CONCLUSION

In France, between 2006 and 2014, the increase in costs of the ultrasound screening for birth defects was not associated to an increase in its efficacy. The observational design of our study limits the interpretation of the observed trends, especially for the increase in costs, which may be partly justified. Official fees for screening ultrasounds need to be reevaluated to obtain fair pricing. However, we observed a clear diminishing returns for costs associated with prenatal ultrasound screening of birth defects, in France. An international comparison of

ultrasound screening programmes for birth defects could be conducted if similar studies were performed in other countries.

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**Contributors** CF, BK, J-MJ and ID-Z conceptualised the study and designed the analysis. FD was certified for the EGB database access. CF, FD, BK, HR and IP collected the data. All authors contributed to perform the analysis. CF, FD, BK, J-MJ and ID-Z wrote the final manuscript. J-MJ and ID-Z were the guarantor of the study.

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**Ethics approval** It was a time-trend observation on aggregated data, provided by an analysis on anonymised individual data, and didn't require ethical approval. The EGB analysis, part of the SNIIRAM and property of the CNAMTS, was performed after INSERM approval and is covered by the Commission Nationale de l'Informatique et des Libertés (CNIL) (accords CNIL AT/CPZ/SVT/JB/DP/CRO52220 du 14/06/2005 et DP/CRO71761 du 28/08/2007).

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**Data availability statement** Data are available upon reasonable request. The data that support the findings of this study are available from the corresponding author upon reasonable request.

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