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Évaluation des coûts de la prématurité en France

Cost-of-illness analysis of preterm births in France

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RÉSUMÉ

- **Objectifs**

Évaluer les coûts associés à la prise en charge médicale des grands prématurés (≤ 32 semaines d'aménorrhée : SA) en France, dans la première année de vie, du point de vue de l'Assurance Maladie. Comparaison aux coûts associés aux autres naissances prématurées (33-37 SA) et à terme (≥ 37 SA).

- **Méthode**

Extraction des données médicales et de remboursements issus du système d'information national de l'Assurance Maladie (SNIIRAM) de l'ensemble des naissances en 2009-2010. Description et comparaison des distributions de coûts à l'aide du test statistique Mann-Whitney.

- **Résultats**

Extraction de 467 106 naissances au final, dont 0,71 % de grands prématurés, sur 4,96 % de prématurés au total (< 37 SA). Les séjours hospitaliers des grands prématurés (resp. l'ensemble des prématurés) représentaient 14 % (resp. 26 %) du coût total hospitalier. Les coûts moyens associés étaient 25 fois supérieurs (resp. 7) à ceux des naissances à terme. L'ensemble des soins non-hospitaliers des grands prématurés représentaient 3 % (resp. 10 %) du coût total non-hospitalier. Les coûts moyens associés étaient 5 fois supérieurs (resp. 2 fois) à ceux des naissances à terme. Les résultats révèlent une relation inverse significative entre les coûts et l'âge gestationnel à la naissance, et d'importantes différences en termes de consommation de soins des grands prématurés comparés aux naissances à terme.

- **Conclusion**

Cette étude du coût de la prématurité en France constitue un premier travail permettant de justifier sur le plan médico-économique la nécessité d'améliorer la prévention de la prématurité et de ses conséquences.

Mots-clés : *Prématurité ; Analyse économique ; Coûts médicaux ; Prévention ; Bases de données médico-administratives.*

ABSTRACT

- **Objectives**

To evaluate the average direct medical costs of very preterm births (≤ 32 wGA) during the first year of life, within the framework of the French health insurance system. Comparison with other preterm (33-37 wGA) and term births (≥ 37 wGA).

- **Methods**

Extraction from the French national health insurance information system (SNIIRAM) of all hospital stays and non-hospital care, and the amounts paid by the public insurance system, detailed for each birth in the 2009-2010 period. Mann Whitney tests were used for descriptive and comparative analyses.

- **Results**

Extraction of 467,106 single births, among which 0.71 % were very preterm (and 4.96 % were preterm (< 37 wGA)). For very preterm births (and all preterm), the hospital stays accounted for 14 % (and 26 %) of the total hospital costs in the total population. The average hospital costs in the whole first year of life were 25 (and 7) times higher than those for term births. The non-hospital care accounted for 3 % (and 10 %) of the total non-hospital costs in the total population. The average non-hospital costs were 5 (and 2) times higher than those for term births.

- **Conclusion**

Our work presents the first economic study of prematurity in France. It could be used to justify the implementation of the improved strategies to prevent prematurity and its consequences.

Keywords : *Prematurity ; Cost Analysis ; Medical costs ; Prevention ; Medico-administrative database.*

INTRODUCTION

Because of its consequences in terms of mortality and morbidity, preterm birth, defined as childbirths at less than 37 completed weeks or 259 days of gestation, is a public health problem worldwide [1,2]. In France, the rate of prematurity increased steadily from 6.8 % in 1998 to 7.2 % in 2003 and 7.4 % in 2010. The same pattern is observed in other industrialized countries since the early 1980s [1,3,5]. The rate in the USA is higher and has steadily increased to the current level of 12.3 % [6]. The rate of very preterm birth (≤ 32 completed weeks) in France was estimated at 1.6 %, 2.0 %, and 1.9 %, respectively [3,7]. This evolution can mostly be attributed to the increased use of assisted reproduction [7,8] but also to increased obstetric interventions, such as induced labour and caesarean section for maternal/foetal medical reasons or non-medical reasons [5,9], and to increased maternal age. Changes in other

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factors that influence this rate have also been observed. These include higher body mass index, increased gestational diseases [9, 11], as well as behavioural characteristics (smoking/drinking alcohol, other addictions) and socioeconomic conditions (single mother and/or unemployment and/or living in rural areas without a driver's license). These socioeconomic characteristics are often associated with irregular and inadequate monitoring of pregnancy [3,9,11,13]. The contribution of all of these factors varies according to the gestational age (GA) at birth [14].

Prematurity is also associated with a higher risk of adverse consequences for health in the short and long term compared with term births, and therefore requires specific and expensive health, education and social services [1,2,14,15]. In the short term, children born prematurely are mostly affected by adverse neonatal outcomes, including chronic lung disease, severe brain injury, retinopathy of prematurity, necrotizing enterocolitis, and neonatal sepsis. In the long term, they have an increased risk of motor and sensory impairment, learning difficulties, behavioural problems and pulmonary dysfunction [2,16]. The incidence and severity of these morbidities are inversely related to GA [17,18]. It has also been estimated that half of the children with severe disabilities were born prematurely [14]. Prematurity is also the leading cause of death in the first four years of life, and the second in children under 5 years in the World according to the World Health Organization (WHO), and it is responsible for 70 % of neonatal deaths in industrialized countries [2]. In France, the stillbirth rate was assessed at 21.0 % at 24 – 32 weeks of GA (wGA) and the survival rate in the first month of life was assessed at 85.0 % of live births at 24 – 32 wGA (and 67.0 % of all births at 24 – 32 wGA). Stillbirth and survival rates are closely associated with GA [19].

To justify the amount of resources allocated to health strategies, it is crucial to assess the economic burden of prematurity and to identify the main costs associated with its management. However, the cost of prematurity remains unknown in France. Only two French studies were published on this topic in 1984, but they cannot be extrapolated to the current French health system [20]. The lack of studies for France was recently confirmed by a European report, which otherwise highlighted the definite and undeniably underestimated economic impact of prematurity in Europe, and a general lack of data for a real cost estimate [21].

Several reviews in the non-French literature have analysed the economic consequences of preterm birth. They principally reported an inverse relationship between costs and GA at birth [12, 22, 25]. A previous review of non-French literature we published [26] on costs with regard to estimated GA underlined a clear relationship between costs and GA in all of the studies, but also variability in contexts, objectives, populations, methodologies and considerable variability in costs and results between studies. It was suggested that extrapolation to the French context and meta-analyses were not feasible. This review clearly suggested the need for a specific study in France and its multiple components. Such a study would provide useful information for the public decision-making process, by targeting the allocation of resources or any budget and by providing process in the planning of care [27] at different levels of the health care organization [28].

The objective of our study was to assess the costs of preterm births in France. Because very preterm birth is regarded as the main risk factor for medical complications and long-term handicap [16, 22, 29, 31], we hypothesized that birth below 33 wGA would be associated with the highest medical costs.

We therefore aimed to evaluate direct hospital and non-hospital costs incurred because of prematurity during the first year of life in France, from the public health insurance system's point of view (the main funder of care in the first year of life). This study includes the cost distributions according to GA and also comparisons of costs between preterm and term infants with special attention paid to very preterm infants (GA ≤ 32 wGA).

MATERIALS AND METHODS

• Database

Our study used data extracted in 2012 from the "National Health Insurance Inter-Regime Information System" (SNIIRAM), managed by the National Health Insurance Fund for Salaried Workers (CNAMTS) for the early 2000s. It contains linked and anonymized detailed information on healthcare consumption and reimbursements for insurance beneficiaries, i.e. main insured and other persons covered (e.g. children) [32]. These data concern all mandatory health insurance schemes (the general social insurance scheme, that covers 86 % of the French population ; but also the scheme for agricultural workers and farmers ; this for the self-employed and 12 additional other specific health insurance schemes). The SNIIRAM database collects all hospital and non-hospital care data, which come from different other sources of our French health system.

Hospital data, concerning all French public and private hospitals, come from a national database called "The French Medical Information System Program in Medicine, Surgery and Obstetrics" (PMSI-MCO), managed by the "French Agency for Information on Hospital Care" (ATIH), before being transmitted to the CNAMTS and included in the SNIIRAM. For 20 years, hospital data have been used for medical research purposes and the quality of the French hospital database has been confirmed in recent studies. It provides a huge amount of epidemiological information concerning hospitalized patients in France [33,34].

Non-hospital care data come from the all regional primary health insurance funds, before being transmitted to the CNAMTS and included in the SNIIRAM, particularly in the "Inter Health Insurance Institutions Consumption Data" database (DCIR).

In order to reconstruct the whole care pathway for each individual, the CNAMTS uses an algorithm that ensures the chaining of all anonymous care consumption data, collected from various sources, for the same individual, while respecting anonymity [35]. Further explanations on data sources and their configuration in the SNIIRAM are given in *appendix 1*.

• Cost calculations for hospital and non-hospital care

The study distinguishes between hospitalizations and all other care services that do not require hospitalization (non-hospital care).

Concerning hospital costs, the study distinguishes both public and private sectors: For public sector, amounts paid by the public health insurance were estimated using the official hospitalization prices, the medical and administrative characteristics of stays, and the characteristics of the mother's insurance status. For private sector, as it is well known that some information may be missing, we systematically revised and completed information on related costs regarding admissions, using the usual calculation method *(appendix 2)*.

Concerning non-hospital costs, reimbursements of amounts paid by the public health insurance system to patients for non-hospital services (including external services) are directly available in the SNIIRAM.

The study population

The study population included all live births in France from January 1st, 2009 to February 28th, 2010 which were clearly identified in the Anonymized Abstracts of Stays (RSA) tables in the PMSI-MCO, with a clear GA, with all hospitalizations costed, and a successful chronological reconstruction of the anonymous hospital admissions pathway *(Figure 1)*. The choice of the period of inclusion is explained by the fact that GA has systematically been recorded in the PMSI – MCO since March 1st, 2009, and it was possible to extract births over a period of one year. Furthermore, it was also interesting to extract births in January and February 2009 for which the information on GA was available. Finally, the current availability of the data allowed follow-up until February 28th, 2011 and thus follow-up during the first year of life of the infants.

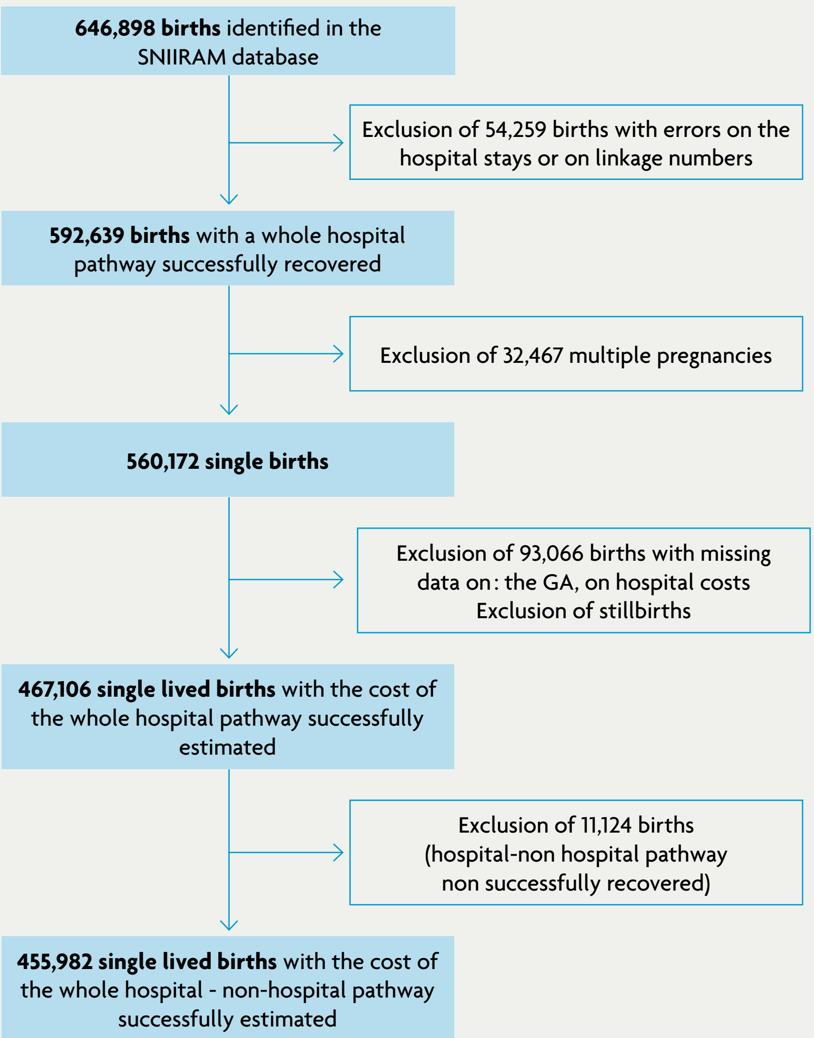
The studied population was restricted to single births clearly identified in the first year of life *(Figure 1)*. For the descriptive analyses, the population was stratified according to GA: the population of very preterm births was defined by a GA ≤ 32 wGA; the population of other preterm births (33 – 36 wGA) was stratified into two subgroups: moderate preterms (33 – 34 wGA) and late preterms (35 – 36 wGA).

For the comparative analyses, the population of very preterm births was compared with moderate and late preterms, and with term newborns (≥ 37 wGA). The overall population of preterm births (< 37 wGA) was compared with term newborns.

Statistical analyses

Retrospective analyses of comprehensive data were carried out. The analyses refer to direct medical costs of hospitalizations and non-hospital care of preterm and term infants during their first year of life.

Figure 1 ➢ DESCRIPTION OF THE POPULATION INCLUSION PROCESS



Legend

This figure illustrates the population inclusion process according to five steps.

1st step: From births extracted from the National Health Insurance Inter-Regime Information System (SNIIRAM) database: exclusion of those with errors in the hospital information or with errors in the linkage number production.

2nd step: From the 592,639 births for which the linkage numbers allowed us to reconstruct the whole hospital care pathway in the first year of life: exclusion of multiple pregnancies because of technical limitations.

3rd step: From the 560,172 remaining single births: exclusion of births for which information on the gestational age (GA) was missing; exclusion of those for which information on the costs estimations was unavailable; exclusion of stillbirths.

4th step: From the 467,106 remaining single live births, it was possible to estimate the hospital costs.

5th step: From the 467,106 single live births: exclusion of those for which the whole hospital – non hospital care pathway was not fully recovered.

The descriptive analyses concern the distributions of the cumulative hospital costs of each subgroup of GA. These analyses were initially carried out for the first period of hospitalization (from birth until the first discharge/until death), and secondly for the entire first year of life (including the initial period and readmissions until the first anniversary). We then considered the distributions of the cumulative non-hospital costs of each subgroup of GA during the first year of life. These analyses include all non-hospital care from a population of births with a successful chronological reconstruction of the hospital-non-hospital care pathway. Finally, we considered the distributions of the cumulative total (hospital + non-hospital) costs of each subgroup of GA during the first year of life and assessment of the proportions of each expenditure item in the cumulative total costs.

The comparative analyses by GA concern the distributions of:

- cumulative hospital costs, in the first period and in the entire first year of life;
- cumulative non-hospital costs;
- cumulative total costs;
- each expenditure item in the cumulative costs.

All costs were described as mean (± SD). All comparisons of costs were carried out with an analysis of variance (ANOVA) and a Mann Whitney test, under the conditions of application. Comparisons of the proportions of each expenditure item in total costs between GA categories were carried out with a Chi-square test.

Software

The management of databases and statistical analyses were performed with SAS (9.3) software ("Statistical Analysis System" software, SAS Institute Inc.).

RESULTS

Population

A total of 592,639 births were clearly identified in the PMSI-MCO between January 1st, 2009 and February 28th, 2010, from which the chronological reconstruction of the anonymous hospital care pathway was successful. Of these 560,172 (94.52 %) births were identified as singleton, and for 467,106 (83.38 %) of them there was clear information on GA at birth, a successful assessment of hospitalization costs, and clear identification of live births status *(Figure 1)*. Among these 467,106 births, 23,147 (4.96 %) were preterm (< 37 wGA): 3,318 (0.71 %) were very preterm (≤ 32 wGA) (particularly, 475 at 24 – 27 wGA and 2,843 at 28 – 32 wGA); 4,176 (0.89 %) were moderate preterm (33 – 34 wGA) and 15,653 (3.35 %) were late preterm (35 – 36 wGA). A total of 443,959 (95.04 %) were born at term (≥ 37 wGA).

Average length of stay and average hospital costs in the first period of hospitalization

The average length of stay (LOS) in the first period was highest for low GA births and decreased significantly with increasing GA *(table I)*. The average LOS for births at ≤ 32 wGA were 2.4 times higher than at 33 – 34 wGA, 6.3 times higher than at 35 – 36 wGA, and 11.1 times higher than at ≥ 37 wGA.

Table I ➢ Average LOS (days) and hospital costs (€) in the first period according to GA categories. Comparisons between the ≤ 32 wGA category and the other preterm and term births categories, and comparisons between all preterms (< 37 wGA) and terms (≥ 37 wGA)

GA[a] category	N	Length of stay (days)		Hospital costs (€)	
		Mean (± SD[c])	P	Mean (± SD[c])	P
≤ 32 wGA[b]	3,318	48.87 (29.46)	Ref.	40,043 (34,843)	Ref.
33 – 34 wGA[b]	4,176	20.30 (14.60)	< 0.01	12,627 (15,919)	< 0.01
35 – 36 wGA[b]	15,653	7.81 (8.07)	< 0.01	3,947 (6,675)	< 0.01
≥ 37 wGA[b]	443,959	4.40 (2.86)	< 0.01	1,317 (2,242)	< 0.01
Preterms	23,147	15.95 (20.26)	Ref.	10,687 (20,119)	Ref.
Terms	443,959	4.40 (2.86)	< 0.01	1,317 (2,242)	< 0.01

aGA: Gestational Age - bwGA: Weeks of gestation - cSD: Standard Deviation

The average cost of hospitalization in the first period was also higher among low GA births and decreased significantly with increasing GA *(table I)*. Those incurred for births at ≤ 32 wGA were 3.2 times higher than at 33 – 34 wGA, 10.1 times higher than at 35 – 36 wGA, and 30.4 times higher than at ≥ 37 wGA.

Admission to a Neonatal Intensive Care Unit (NICU) during the stay led to additional costs *(appendix 1)*. The lower the GA, the greater the likelihood of admission to an NICU (p-value < 0.01). The rate of NICU admission during the first period was: 62.65 % for births at ≤ 32 wGA (85.05 % at 24 – 27 wGA and 58.99 % at 28 – 32 wGA), 15.01 % at 33 – 34 wGA, 3.64 % at 35 – 36 wGA, and 0.32 % at ≥ 37 wGA.

Average cumulative length of stay and average cumulative hospital costs in the first year of life

The likelihood of at least one readmission during the first year of life was higher among low GA infants and decreased significantly with increasing GA (p-value < 0.01): 43.96 % for infants born at ≤ 32 wGA (48.42 % at 24 – 27 wGA and 42.95 % at 28 – 32 wGA); 30.03 % at 33 – 34 wGA, 22.78 % at 35 – 36 wGA, and 14.59 % at ≥ 37 wGA.

The average cumulative LOS during the first year of life was higher among low GA infants and decreased significantly with increasing GA *(table II)*. For infants born at ≤ 32 wGA the average cumulative LOS was 2.4 times higher than at 33 – 34 wGA, 5.9 times higher than at 35 – 36 wGA, and 10.6 times higher than at ≥ 37 wGA.

The average cumulative cost of hospitalization during the first year of life was also higher among low GA infants and decreased significantly with increasing GA *(table II)*. The average cumulative cost of hospitalization for infants born at ≤ 32 wGA was 3.1 times higher than at 33 – 34 wGA, 8.9 times higher than at 35 – 36 wGA, and 24.9 times higher than at ≥ 37 wGA.

Average cumulative non-hospital costs in the first year of life

It was impossible to reconstruct the whole care pathway for 9,687 (2.07 %) of the 467,106 births included in the study. The amount paid by the health insurance agency was available for 455,982 (99.68 %) of the remaining births *(Figure 1)*. The average cumulative cost of non-hospital care was assessed for 22,791 (5 % of the 455,982) newborns at < 37 wGA, for 3,279 (0.72 %) at ≤ 32 wGA, for 4,128 (0.91 %) at 33 – 34 wGA, for 15,384 (3.37 %) at 35 – 36 wGA, and for 433,191 (95.00 %) at ≥ 37 wGA. The average cumulative cost was also higher among low GA births and decreased significantly with increasing GA *(table III)*. For births at ≤ 32 wGA, it was 2.2 times higher than at 33 – 34 wGA, 3.2 times higher than at 35 – 36 wGA, and 4.7 times higher than at ≥ 37 wGA.

Table II ➢ Average cumulative LOS (days) and cumulative hospital costs (€) during the first year of life according to GA categories. Comparisons between the ≤ 32 wGA category and the other preterm and term births categories, and comparisons between all preterms (< 37 wGA) and terms (≥ 37 wGA)

GAa category	N	Length of stay (days)		Hospital costs (€)	
		Mean (± SDc)	P	Mean (± SDc)	P
≤ 32 wGAb	3,318	52.63 (31.40)	Ref.	43,041 (36,668)	Ref.
33 – 34 wGAb	4,176	22.28 (16.97)	< 0.01	14,077 (17,163)	< 0.01
35 – 36 wGAb	15,653	8.95 (10.30)	< 0.01	4,826 (8,627)	< 0.01
≥ 37 wGAb	443,959	4.96 (4.55)	< 0.01	1,728 (3,913)	< 0.01
Preterms	23,147	17.59 (22.23)	Ref.	11,973 (21,676)	Ref.
Terms	443,959	4.96 (4.55)	< 0.01	1,727 (3,906)	< 0.01

aGA: Gestational Age - bwGA: Weeks of gestation - cSD: Standard Deviation

Table III ➢ Average costs (€) of non-hospital care during the first year of life according to GA categories. Comparisons between the ≤ 32 wGA category and the other preterm and term birth categories, and comparisons between all preterms (< 37 wGA) and terms (≥ 37 wGA)

GAa category	N	Non-hospital costs (€)	
		Mean (± SDc)	P
≤ 32 wGAb	3,279	3,373 (4,614)	Ref.
33 – 34 wGAb	4,128	1,566 (2,462)	< 0.01
35 – 36 wGAb	15,384	1,043 (1,715)	< 0.01
≥ 37 wGAb	98,109	717 (910)	< 0.01
Preterms	22,791	1,473 (2,622)	Ref.
Terms	433,191	710 (907)	< 0.01

aGA: Gestational Age - bwGA: Weeks of gestation
cSD: Standard Deviation

Table IV ➢ Percentages of hospital costs and non-hospital costs in the cumulative total costs (€) in each GA category during the first year of life. Comparisons between the ≤ 32 wGA category and the other preterm and term births categories, and comparisons between all preterms (< 37 wGA) and terms (≥ 37 wGA)

GAa category	Hospital costs		Non-hospital costs	
	% in total costs	P	% in total costs	P
≤ 32 wGAb	92.76 %	Ref.	7.24 %	Ref.
33 – 34 wGAb	90.02 %	< 0.01	9.98 %	< 0.01
35 – 36 wGAb	82.31 %	< 0.01	17.69 %	< 0.01
≥ 37 wGAb	70.81 %	< 0.01	29.19 %	< 0.01
Preterms	89.11 %	Ref.	10.89 %	Ref.
Terms	70.81 %	< 0.01	29.19 %	< 0.01

aGA: Gestational Age - bwGA: Weeks of gestation

The distribution of the most frequent non-hospital services in very preterm infants was: pharmacy (37.90 %); consultations (21.80 %); physiotherapy (17.00 %); biology (3.75 %); technical procedures (3.00 %); hospital pharmacy (2.59 %); medical supplies/equipment (2.25 %); nursery care (1.78 %); respiratory support (1.64 %); imaging (1.57 %); transportation (1.12 %); vaccines (1.07 %); medical visits at home (0.85 %).

The distribution of the most frequent non-hospital services in term infants was: pharmacy (48.74 %); consultations (30.18 %); physiotherapy (8.36 %); biology (2.04 %); medical supplies/equipment (1.69 %); imaging (1.48 %); vaccines (1.40 %); medical visits at home (0.90 %).

Average cumulative total costs during the first year of life

In order to analyse the proportion of hospital costs and non-hospital costs in the total costs (hospital + non-hospital) incurred during the first year of life, according to GA categories, only newborns for which the whole care pathway was reconstructed were included. Therefore, the total costs were assessed from the same 455,982 births.

The total hospital cost incurred by the 455,982 newborns was € 1,028,391,723. Preterm births (< 37 wGA) and very preterm births (≤ 32 wGA) accounted for a significant proportion of the total cost. Preterm births accounted for € 274,731,601 (26.71%); very preterm births for € 141,726,471 (13.78%); births at 33 – 34 wGA for € 58,353,009 (5.67%); births at 35 – 36 wGA for € 74,652,121 (7.26%); and term births for € 753,660,122 (73.29%).

The total non-hospital cost incurred by the 455,982 newborns during the first year of life was € 344,263,800. Preterm births accounted for € 33,578,124 (9.75%); very preterm births for € 11,060,194 (3.21%); births at 33 – 34 wGA for

€ 6,468,452 (1.88%); births at 35 – 36 wGA for € 16,049,477 (4.66%); and term births for € 310,685,675 (90.25%).

The proportion of total hospital cost in the total cost was higher among low GA births and decreased significantly with increasing GA. Conversely, the proportion of total non-hospital cost in the total cost was smaller among low GA births and increased significantly with increasing GA *(table IV)*.

DISCUSSION

This is the first study conducted in France to measure the economic burden of prematurity within the framework of a Health Insurance system. Both hospital and non-hospital costs were assessed in the first year of life of live-born singletons (survivors and non-survivors). All the average costs per newborn increased with decreasing GA. Several possible perspectives, expenditure items and time horizons have been adopted in the literature. All the reviewed studies reported a main finding of a clear inverse relationship between costs and GA at birth and in the first year of life [16, 22, 36, 37].

The major strength of this study is that it is based on the records of a large cohort of births and on a comprehensive database, which allowed us to evaluate the amounts paid by the public health insurance agency for hospital and non-hospital care of preterm and term births. The successful linkages of a large number of births with their corresponding hospital admissions and their non-hospital care consumptions allowed us to successfully reconstruct the whole care pathway [35] and to evaluate the main costs incurred by each GA category during the first year of life. Nearly all births in France (about 800,000) are recorded in the PMSI-MCO database: only deliveries at home (4‰) are not included. From the 560,172 singleton births recorded by the PMSI-MCO database, we have successfully reconstructed the trajectory of care over a 13-month period and estimated the costs for 83.4 % of them. All births could not be included because the information required for this study (GA, costs, and whole care pathway) was missing for some. We chose to limit results to single live-born infants because many technical limitations make the analysis of multiple births uncertain.

Our study provides information for the scientific community and for public decision makers on the magnitude of the average costs of preterm and very preterm births in France compared with the cost of term births. The study also highlights the differences in support needs in preterm and term infants.

First, the initial period of hospitalization concentrates the majority of hospital admission costs in the first year of life. In this period, the average LOS was longer than that for readmissions. It is also noteworthy that the average cumulative hospital and non-hospital costs were markedly higher for low GA births and decreased with increasing GA. Compared with term births, the average cumulative hospital cost of very preterm births was up to 30 times higher in the first period, and up to 25 times higher for the entire first year of life. The average cumulative non-hospital cost was 5 times higher in the first year of life. These results also showed that all other preterm births (33 – 36 wGA) also had higher cumulative costs compared with term births, a finding that fits well with the inverse relationship between GA and both mortality and morbidity [38,39].

Second, very preterm infants, other preterm and term infants account for 14 %, 13 % and 73 % of the cumulative hospital costs, respectively, and for 3 %, 7 % and 90 % of total non-hospital costs, respectively. Overall, the proportion of hospital costs is higher among low GAs and decreases significantly with increasing GA. Conversely, the proportion of non-hospital costs is smaller among low GAs and increases significantly with increasing GA.

Third, the distribution of outpatient services for preterm infants is different from that for term infants: prematurity increases the needs for physiotherapy, biology, respiratory support and hospital pharmacy.

Previous studies also reported significant cost differences between preterm and term infants. In the United States, the average hospital cost per survivor in the first period for infants born at < 28 wGA was 30 – 50 times higher than that for term births [36,40,41] (up to 56 times higher in our study). The cost for infants born at 28 – 32 wGA was 13 – 26 times higher than for those born at term (26 times higher in our study). In the literature, the average length of stay in the first period was also longer for low GA and decreased with increasing GA. As in our study, the percentage of low GA newborns readmitted to hospital was higher that of other GA newborns [36, 40, 41].

Clinical studies have reported the long-term effects of prematurity [16]. Therefore economic studies should be developed to investigate the long-term consequences of prematurity, by including multiple points-of-view and multiple categories of costs, such as non-medical direct costs, indirect costs, or intangible costs.

The estimation of the costs of prematurity in France and its multiple components has a number of interests. In particular, it could be used to justify support for the reinforcement of perinatal care so as to:

- improve coordination and efficiency in the monitoring of pregnant women;
- improve the anticipation of high-risk cases; improve research to reduce the prematurity rate;
- diminish morbidities associated with prematurity.

Furthermore, prevention would avoid much of the physical and psychological suffering among patients and their families, the costs of which have not been evaluated. The economic benefits of these measures would be assessed, especially insofar as what these preventive measures would lead to in terms of costs avoided in the medium or long term [30]. It would also constitute a first step in the decision-making process, by orienting the allocation of resources or any budget and by providing process in the planning of care [27].

Our study presents some limits. We did not include the population of twin births for technical reasons. Further studies should be done when these technical problems will be solved. Furthermore, as stated in *appendix 2*, the evaluation of hospital costs was based on official tariffs, which can be very different between the public and the private hospital sectors, and that may change over one year. This may introduce a degree of variability in the costs we calculated for each hospitalization in the same homogeneous group of diseases. Finally, our study did not include specific services during stays, for which complementary fees usually have to be estimated. It concerns the consumption of "expensive drugs" and "implantable medical devices" during stays. These hospital services were underrepresented in our databases, but in future studies, they must be taken into account.

It would be interesting to analyse the determinants of the higher costs of preterm births. Such an analysis could be done according to the type of disease as well as the following characteristics: the GA at birth, the gender, the length of stay, the technical level of the maternity unit, the type of professional consulted, and the region of birth. More generally, it would be interesting to perform analyses on a longer time horizon in order to know the evolution of care consumption and the evolution of costs after the first year of life.

CONCLUSION

Our study is the first to measure the financial impact of prematurity in France. The results presented in this paper highlight the magnitude of the cost of preterm births and particularly very preterm births in our country. Healthcare professionals, scientists, the public authorities and society at large need to be made aware of these results to underline the imperative of developing preventive measures against this public health problem.

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APPENDICES

Appendix 1 ➢ Data sources and their configuration in the National Health Insurance Inter-Regime Information System (SNIIRAM)

Sources of hospital care data (PMSI-MCO database linked to the SNIIRAM)

The "French Medical Information System Program in Medicine, Surgery and Obstetrics" database (PMSI-MCO database) lists administrative and medical information related to all hospital admissions in the public and private sectors. This information is contained in "Anonymized Abstracts of Stays" (RSA) generated by each hospital admission. The successive RSAs of a patient with several hospitalizations are linked, thus allowing the chronological reconstruction of the hospital care pathway while respecting anonymity. This linkage is enabled via an anonymous patient-ID (a linkage number) that is previously generated for each hospital admission by replacing the patient's social security number, date of birth and sex by an irreversible chaining key. This process involves a computer function named "Nominative Information Blanking Function" using an algorithm developed by Dijon University Hospital (France) [35].

I ▪ Information provided by the RSA are: 1/the Homogeneous Group of Diseases (GHM: French Diagnosis Related Groups) in which the hospitalization is classified; 2/the level of neonatal care (monitoring, intermediate, intensive care); 3/the length of stay; 4/ the diagnosis and procedures; 5/the hospital of admission; 6/the newborn's characteristics (age at admission, gender, birth weight, term at birth, residential zip code). The RSA tables are similar for both public and private hospitals.

II ▪ Additional medical tables can be linked to the RSAs in order to improve medical information and include the medical procedures performed, diagnosis, and the status of the hospital.

III ▪ Other additional tables containing detailed administrative, consumption and economic information are also available in the SNIIRAM, and can be linked to the anonymous ID-patient. However, the structure of these additional tables can be different between the public sector and the private sector.

In the public sector, two types of additional information are available:

❶ Tables containing informative data on the patient's situation in terms of social security (needed to calculate the amounts finally paid by the health insurance agency for hospital admissions – See appendix 2).

Indeed, for each hospital admission, the amounts paid by the health insurance agency have to be calculated using this information, combined with other external information, as in the first place the official prices published for each GHM in the public sector.

❷ Billing files concerning hospital external services provided in the public sector (medical acts performed in hospital for non-hospitalized patients), for which the amounts paid by health insurance are directly available.

In the private sector, all of the hospital services (admissions and external services) are directly billed by the hospitals to the Health Insurance Agency and are therefore available in the SNIIRAM in the form of billing files.

Finally, the structured data tables are different between the public and private hospitals depending on the sources, level of information and logic of understanding and use.

Sources of non-hospital care data (DCIR database in the SNIIRAM)

The "Inter Health Insurance Institutions Consumption Data" database (DCIR database) is composed of a central table named "table of medical services", which contains individual information on the medical services, beneficiaries, providers, hospitals, insurance institutions, and reimbursements from mandatory health insurance. Other tables with additional referential coding can be linked per patient to this main table in order to provide additional detailed information on the health care services consumed: medical consultations, hospital drug prescription, non-hospital drug prescription, biology exams, transportation, and implantable medical devices. Therefore this DCIR database contains all non-hospital care services provided in the extra-hospital sector (general practitioners, specialists, physiotherapists, supplementary examinations (biology, radiology...), functional rehabilitation, medical transportation, and reimbursements of prescribed drugs) but also all hospital external services performed in the private sector (indistinguishable from other non-hospital services).

Appendix 2 ➢ Calculation of the cost of hospitalization within the framework of the health insurance system

Any hospitalization, whether in the public or private sector, is first costed on a basic amount *(a)*, from which a second specific cost is then calculated according to the patient's situation in terms of social security *(b)*. It represents the exact amount paid by the health insurance agency to the hospital where the patient was treated.

The basic amount depends on prices published in the Official Bulletin of the French Republic, per GHM. These prices differ according to the sector (public or private), to the date of hospital release, and to the length of hospital stay. Any other additional amounts have to be added in cases of admission to a neonatology unit, or a neonatal intensive care unit, or a neonatal resuscitation unit. Finally, a geographical coefficient is applicable to the GHS price and to the additional amounts in order to take into account the specificity (e.g. property prices) in relation to the geographic location. These coefficients are official and available in the Official Bulletin.

The cost of hospitalization within the framework of the health insurance system includes the previously-calculated basic cost and additional information about daily amounts paid by the patient for his stay (with a multitude of cases of exemption). Depending on the case, the cost of a stay paid by the health insurance agency corresponds to 100 % or 80 % of the previously-calculated basic cost of the stay, from which certain amounts paid by non-exempt patients may be deducted.

For the public sector, all of these steps were completed.

In the case of missing amounts in the private sector, basic hospitalization costs were recalculated and 100 % of the cost was considered paid by the health insurance agency because it concerned birth stays only. Indeed, the cost to the health insurance agency is always 100 % for birth stays, as the part paid by the patient is zero. Another difficulty with the private sector was that, unlike for the public sector, the official costs of hospital stays do not contain honorary fees. Private honorary fees are available separately in the billing files and must be taken into account. However, we did not include these honorary fees because they were not available for many stays in the private sector.