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Nicolas Todd

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Effets sanitaires à long terme des stress de la Première Guerre mondiale

Thèse soutenue le 13 novembre 2017, devant le jury composé de :

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« Aucun document n'a la vérité du registre paroissial,
ce registre de comparution qui consigne l'instant »

Pierre Chaunu, *La Civilisation de l'Europe Classique*, 1966

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Contents

Remerciements **1**

Contents **3**

List of figures (chapters 1-3) **5**

List of tables (chapters 1-3) **6**

Résumé long **7**

Summary **17**

Scientific output during the PhD **19**
I. Scientific output in relation to the PhD 19
Published articles 19
Submitted articles 19
Oral presentations 19
II. Scientific output unrelated to the PhD 20
Published articles 20
Articles in preparation 20
Oral presentations 20
Other works 21

Acronyms **23**

Introduction **25**
I. The biology of early life stress 26
The Developmental Origins of Health and Disease hypothesis 26
Animal models of early life stress 28
II. The epidemiology of early life stress 30
III. Bereavement during the Great War as a historical experiment in maternal stress 32

Chapter 1: The development of a cohort of French war orphans born 1914-1916 ..... **35**
I. The pupille de la Nation status 35
II. Call to the Database of Those died for France in the First World War 36
III. Methods of record linkage verification 39
IV. Non-orphan pupilles: a systematic study 43
V. Definition of a cohort of matched non-orphans (MNOs) 44
The rule for selecting MNOs 44
Vicinity in birth registers and places of birth 44
VI. Longevity information used 47
VII. Classification of parental occupations and imputation of missing data 49
Classification of parental occupations 49
Imputation of missing occupations 51

Chapter 2: Applying to the pupille de la Nation status 53
I. Association between socioeconomic status (SES) and propensity to request the pupille status 56
SES and year of adoption 56
SES and final adoption rate 61
II. Accessibility of the pupille status for illegitimate children 62

Chapter 3: Two demographic pitfalls 65
I. Migrations: the flee from Paris 65
II. Migrations: war refugees from invaded regions 67
III. Date of birth and the probability of father's loss 69
Observed trends in probability of fatherly loss 69
A simple model 72
Practical consequences 76

Chapter 4: The naming of orphans in France during World War One: a study of a nationwide cohort of "pupilles de la Nation" 79

Chapter 5: Impact of social inequalities at birth on the longevity of children born 1914-1916: a cohort study 103

Chapter 6: Prenatal loss of father during World War One is predictive of a reduced lifespan in adulthood 121

Conclusion and perspectives 133

Bibliography 137

Appendices 145

List of figures (chapters 1-3)

Figure 1. Examples of epigenetic regulation of gene expression
Figure 2. HPA axis
Figure 3. Birth certificate of a pupille de la Nation, with the adoption by the Nation, marriage and death notifications
Figure 4. Died for France certificate of the father of pupille whose birth certificate is shown in Figure 3
Figure 5. Main record linkage verification method
Figure 6. Birth certificate corresponding to the birth certificate (Figure 3) and Died for France certificate (Figure 4) shown as examples
Figure 7. Conscription record associated with Figures 3,4,6
Figure 8. Type of birth by registration time, 8th arrondissement of Paris
Figure 9. Type of birth by registration time, 5th arrondissement of Paris
Figure 10. Concordance between pairs of certificates according to distance
Figure 11. Types of individuals according to date of death
Figure 12. Propaganda poster at the occasion of Bastille Day 1918
Figure 13. Year of adoption by the Nation according to paternal military rank
Figure 14. Adjusted effect of district of birth on adoption year
Figure 15. Adjusted effect of maternal age at infant's birth on adoption year
Figure 16. Year of adoption by the Nation according to paternal occupation
Figure 17. Adjusted effect of paternal occupation on adoption year
Figure 18. Adjusted association between age at father's death and legitimacy
Figure 19. Monthly number of live births in Paris
Figure 20. Date of birth of orphans according to place of military service of the father
Figure 21. Monthly number of live births in Paris and monthly number of pupille orphans' births in the 15 Parisian arrondissements included
Figure 22. Cohort-specific probability of death at war, age-specific male fertility rates in 1914-1916 and age-specific fall in male fertility between 1914 and1916
Figure 23. Evolution of the n_m / N_m ratio over time
Figure 24. Evolution of the $n_{m, pre}$ / N_m and $n_{m, post}$ / N_m ratios over time
Figure 25. Dates of birth of prenatal and postnatal orphans

List of tables (chapters 1-3)

Table 1. Classification of paternal occupations on a random sample of 200 MNOs

Table 2. Agreement with external rater on maternal occupations

Table 3. Parametric terms in model [1]

Table 4. Significance of smooth terms in model [1]

Table 5. Paternal occupations in the 35 MNOs alive at 31 years identified as war orphans compared with pupilles orphans

Résumé long

L'objectif de cette thèse a été de tester l'existence d'une perte de longévité à l'âge adulte chez les enfants exposés pendant la Première Guerre mondiale à un stress maternel intense, la perte au front du mari.

Contexte

La Première Guerre mondiale fut un événement d'une violence inouïe. L'armée française, fondée sur la conscription universelle, perdit 1,4 million d'hommes – soit près de 20% de l'ensemble des incorporés. Environ 70% de ces hommes avaient entre 20 et 35 ans en 1914. Les mères enceintes lorsque la mobilisation générale fut décrétée, le 1er août 1914, vécurent à partir de ce jour une expérience de stress d'une ampleur inédite. Certaines perdirent leur mari, de manière largement aléatoire, pendant ou après la grossesse. Les conséquences de cet événement traumatique maternel extrême sur la santé de l'enfant sont restées largement inexplorées.

La biologie des stress a mis en évidence des mécanismes par lesquels le stress psychologique vécu pendant la plus petite enfance agit sur la santé tout au long de la vie. Cette connaissance a surtout été acquise sur des modèles animaux, essentiellement murins. Il a par exemple été montré qu'un stress prénatal de retenue (*prenatal restraint stress*) avait pour conséquence à l'âge adulte une dysfonction de l'axe hypothalamo-pituito-surrénal (axe HPA), avec une suractivité basale et induite par un test de stress. Ces changements phénotypiques ont été reliés au niveau moléculaire à des changements épigénétiques sur les gènes de certains effecteurs de l'axe HPA.

L'étude chez l'Homme des effets à long terme des stress de la petite enfance est beaucoup plus complexe car il y est plus difficile d'isoler la contribution individuelle de facteurs souvent très corrélés les uns aux autres. Ainsi chez les individus soumis à des stress chroniques durant l'enfance : mauvaises conditions alimentaires et de logement, faible niveau éducatif, exposition aux agents infectieux et au stress parental, forment souvent une grappe de conditions défavorables. De la même manière, perte d'un parent pendant la grossesse et longévité diminuée peuvent être les effets d'une cause partagée – en particulier une fragilité

commune (*shared frailty*) sans que l'une cause l'autre. Au surplus, il semble impossible de savoir comment se recombinent les risques maladie-spécifiques mis en évidence par les études centrées sur une seule pathologie.

La guerre de 1914-1918 présente donc, pour l'épidémiologie, un complément utile à l'étude de cohortes contemporaines. Le stress périnatal étudié – la perte du père –est précisément défini, univoque, et ne peut faire l'objet d'un quelconque biais de rappel. Les individus soumis à celui-ci ont été sélectionnés de manière largement aléatoire. Le recul dans le temps permet de suivre les individus étudiés sur longue période et de quantifier un effet total du stress d'intérêt sur la mortalité adulte.

Méthodes

Récolte des données

Les propriétés de la Grande Guerre évoquées plus haut ne suffisaient pas à en faire modèle exploitable pour les stress de la petite enfance. Fallait-il encore qu'il fût possible, grâce aux sources disponibles et à leur combinaison, de constituer un système d'observation idoine. Nous nous sommes appuyés sur un statut juridique original, celui de pupille de la Nation, institué par la loi du 27 juillet 1917 pour les orphelins, auxquels étaient assimilés les enfants de grands invalides de guerre. Ce statut, qui rendait éligible à certaines aides, notamment financières, était attribué par les tribunaux civils sur requête du représentant légal de l'enfant, en général la mère dans le cas d'un orphelin. Le statut de pupille étant à minima honorifique, aucune condition de ressources n'était exigée des familles d'orphelins, de sorte qu'il pouvait être demandé pour tous. En raison du temps nécessaire à la mise en place du dispositif, les premières « adoptions par la Nation » datent de 1918. Parce que la loi de juillet 1917 prévoyait en son article 8 l'apposition, en marge de l'acte de naissance, d'une mention d'adoption par la Nation, nous avons pu recenser l'ensemble des pupilles de la Nation nés dans 15 arrondissements parisiens, le Kremlin-Bicêtre et Neuilly-sur-Seine entre le 1er août 1914 et le 31 décembre 1916, et dans 9 autres villes (Bordeaux, Lyon, etc.) entre le 1er août 1914 et le 31 décembre 1915. Au total, l'acte de naissance de 7,250 pupilles a été à ce jour identifié et transcrit.

Pour chaque pupille né à Paris, Bicêtre, Neuilly et Bordeaux a été relevé dans le même registre de naissance (en remontant) l'acte de naissance du premier non-pupille de même sexe et même âge maternel (± 2 ans), appelé *matched non-orphan*, ou MNO (n=5,671).

Afin de déterminer, au sein des pupilles de la Nation, l'ensemble des orphelins, nous avons cherché les pères par nom et année de naissance dans la Base des Morts pour la France, disponible en ligne (http://www.memoiredeshommes.sga.defense.gouv.fr/), qui contient de manière quasiment exhaustive l'ensemble des soldats français morts entre le 3 août 1914 et le 1er juin 1919. Des méthodes de vérification du *linkage* ont été développées afin d'écarter les problèmes posés par les homonymies et sont détaillées et illustrées dans le chapitre 1. Le certificat de Mort pour la France a fourni la date de décès, le genre de mort (maladie, tué à l'ennemi, etc.) et le grade du père. Parmi les 7,250 pupilles inclus, 4,061 ont été identifiés comme orphelins de guerre par consultation de la Base des Morts pour la France.

Informations sur la longévité

Les actes de naissance transcrits à l'état-civil ont fourni, les dates de décès postérieures à mars 1945 pour tous les individus inclus, quel que soit le lieu de décès. Etant donnée la période d'inclusion et la période à laquelle nous avons recueilli les données, 31-99 ans est la tranche d'âge sur laquelle les décès de l'ensemble des individus inclus ont été observés. Les individus dont la date de décès n'est pas connue peuvent être morts avant mars 1945 ou être encore vivants au recueil des données. Un individu sans mention (mariage, divorce, etc.) après 1945 a été considéré comme mort avant mars 1945.

Parce que les pupilles sont suivis conditionnellement au fait d'avoir survécu jusqu'à l'adoption par la Nation (à l'âge de ~ 5 ans), les orphelins morts dans la période infanto-juvénile ne sont pas présents dans l'échantillon, au contraire des MNOs morts dans la même période. En conséquence, la proportion observée d'individus vivant à 31 ans est chez les MNOs très inférieure à celle observée chez les orphelins inclus. Or, environ 45% des MNOs ont été appariés à des pupilles qui ont été identifiés comme non-orphelins et donc non-inclus dans les analyses : ils formaient donc un « stock » de MNO non-utilisés (auquel s'ajoutent les MNOs vivants à 31 ans mais dont l'orphelin est mort avant 31 ans, ou dont l'orphelin est d'un père mort de maladie – et a été exclu des analyses afin d'éviter les problème de fragilité partagée et des effets à long-terme d'une infection précoce). Afin d'inclure dans l'analyse la fraction des orphelins vivant à 31 ans dont le MNO était mort avant 31 ans ou se trouvait être

de père inconnu, il a donc été procédé à un ré-appariement entre orphelins vivants à 31 ans dont le MNO était mort avant 31 ans et MNOs disponibles vivant à 31 ans.

Classification des professions et imputation

Les professions paternelles étaient disponibles sur l'acte de naissance, sauf dans le cas des enfants illégitimes ou des orphelins prénataux officiellement déclarés comme posthumes. Les professions maternelles et paternelles ont été classées à l'aveugle en respectivement 8 et 6 catégories. Les données ont été complétées grâce à une imputation multiple par équations chaînées (MICE). Les analyses impliquant la profession paternelle ont été conduites sur 10 jeux de données imputées puis recombinées.

Méthodes statistiques

L'analyse des prénoms (cf. infra) s'est faite en modélisant la probabilité de transmission du prénom paternel dans un modèle additif généralisé ayant la fonction de lien et la distribution d'erreurs de la régression logistique. Le même outil a été utilisé pour modéliser la probabilité de survie jusqu'à 31 ans chez les MNOs, ainsi que la proportion d'enfants illégitimes chez les pupilles orphelins. Un modèle de Cox à effets mixtes a été utilisé pour étudier le risque après 31 ans chez les MNOs. L'étude du caractère significativement différent des écarts de longévité chez les paires prénatales et postnatales (et au sein des paires prénatales, masculines et féminines) s'est faite par des tests de permutation.

Quelques considérations sur la démographie des orphelins de 14-18

Le chapitre 2 étudie les conditions d'accès au statut de pupille de la Nation. La loi ne prévoyait aucune condition de ressources pour les orphelins. Le chapitre montre que la propension des familles à demander pour leur enfant le statut de pupille n'a varié en fonction du statut social que dans la mesure où l'*upper class* retardait l'adoption de ses enfants et atteignait un taux final d'adoption inférieur. Plus important, il montre que les enfants illégitimes (c'est-à-dire nés d'une mère non mariée) nés dans la période d'inclusion ont été largement exclus du statut de pupille, et ce d'une manière âge au décès du père spécifique : les enfants illégitimes dont le père est mort très tôt dans le vie ont été le plus massivement

exclus. En pratique, cela commande soit de restreindre l'étude aux paires d'orphelins et MNOs légitimes, soit de conduire une analyse de sensibilité sur ces seules ces paires.

Ainsi que montré au chapitre 3, les dates de naissance des orphelins ont une distribution différente de celle de l'ensemble des naissances. Plus important encore, les dates de naissance d'orphelins pré- et postnataux (ayant perdu leur père avant ou après la grossesse) diffèrent, pour des raisons purement mécaniques. Un modèle simple permet de comprendre les principales raisons de ces dates de naissance spécifiques. Pour l'analyse de la longévité des orphelins, cette spécificité des dates de naissance est particulièrement importante du fait de certaines caractéristiques de la guerre. En premier lieu, les contextes épidémique et nutritionnel ont varié au cours de la période d'inclusion. Or l'un et l'autre de ces contextes ont été relevés par des études précédentes comme pouvant faire varier l'espérance de vie à l'âge adulte de plusieurs mois. Ensuite, la guerre a généré des migrations dont deux types sont à considérer dans notre étude. D'abord une fraction significative des populations des départements envahis par l'armée allemande ou proches des zones de combat a migré vers les régions non-envahies à l'abri du front – en particulier la région parisienne. Ces migrations se sont étalées dans le temps et ont changé progressivement, et de manière implicite, le support des services d'état-civil inclus. Ensuite, dans le seul cas de Paris, une fraction de la population a fui devant le siège de la ville qui s'annonçait début septembre 1914. Dans les deux cas, on ne peut faire l'hypothèse d'un risque homogène de migration. Notre choix de méthode d'appariement, qui inclue comme facteurs le lieu et la date de naissance, assure qu'un orphelin et son MNO appartiennent bien à la même population sous-jacente et contrôle donc à la fois pour le problème des migrations et celui de la fluctuation du 'macro environnement' nutritionnel et infectieux.

Résultats

Un comportement maternel altéré : le choix du prénom (chapitre 4)

Le seul comportement maternel potentiellement altéré par la perte prénatale du père et directement accessible par la source dont on dispose, les actes de naissance, est le choix du prénom de l'enfant. Le prénom a attiré notre attention pour une raison simple : si la date de décès du père est connue grâce au certificat de mort pour la France, le stress maternel

commence *stricto sensu* à l'annonce dudit décès. En d'autres termes, un conflit dans lequel les décès de militaires ne seraient annoncés qu'avec des mois de retard à la famille ne pourrait servir de modèle à l'étude des stress prénataux. L'analyse des prénoms a révélé qu'une perte du père avant la naissance multipliait par ~ 2.7 la probabilité de recevoir son prénom. Ce résultat élémentaire permet de conclure que le stress vécu par les orphelins prénataux a effectivement statistiquement débuté dans la période prénatale.

Du point de vue de l'histoire des comportements pendant la Grande Guerre, le choix du prénom présente une caractéristique importante et assez rare : il est en effet disponible sans restriction de classe sociale. C'est la raison pour laquelle nous avons conduit une analyse plus détaillée du choix du prénom dans la cohorte d'orphelins. Nous montrons en particulier que le choix du prénom du père mort pendant la grossesse dépendait du milieu social : si une perte prénatale du père multipliait par ~ 2.5 le risque de transmission de son prénom s'il était soldat ou sous-officier, c'était par ~ 5 chez les enfants d'officiers. L'analyse a de plus montré que dans tous les groupes considérés, une perte en tout début de grossesse maximisait la transmission du prénom. Le chapitre 4 évoque des pistes d'explication de ce changement de comportement.

Inégalités socio-économiques face à la mort (chapitre 5)

L'analyse de la mortalité des MNOs a montré un fort écart de survie jusqu'à 31 ans selon la profession du père. Le taux de survie le plus bas était observé chez les enfants d'ouvriers, qui représentaient environ 1/3 des MNOs. Le statut légitime ou illégitime de la naissance était aussi très fortement associé à la survie jusqu'à 31 ans. Pour ce qui concerne la survie à l'âge adulte (après 31 ans), une association entre profession du père et mortalité a été retrouvée chez les femmes uniquement.

Association entre perte du père et longévité à l'âge adulte (chapitre 6)

Une différence moyenne de longévité restant à 31 ans de 2.4 années est trouvées entre orphelins prénataux et leurs MNOs. Par contraste, la différence observée entre les orphelins postnataux et leurs MNOs est de 0.3 années. L'écart orphelin-MNO est significativement différent entre paires prénatales et postnatales. Le résultat est légèrement amplifié lorsqu'il est restreint aux paires orphelins-MNOs où les deux membres sont légitimes (2.6 années pour les paires prénatales ; 0.4 années pour paires postnatales). Il est retrouvé en étudiant les

médianes ; en excluant les paires réappariées ainsi qu'en restreignant l'analyse aux paires nées avant mai 1915 (conçues avant août 1914). Une tendance est trouvée pour un effet accru avec une perte au 3e trimestre de grossesse. Aucune différence n'est mise en évidence entre orphelins et MNOs lorsque l'orphelin a perdu son père avant 1 an ou avant 6 mois.

Afin d'identifier les âges auxquels ces écarts de longévité ont été réalisés, l'analyse de l'espérance de vie à chaque âge après 31 a montré que la surmortalité des orphelins était due à une surmortalité avant 65 ans.

Discussion

La conjonction entre l'absence de mise en évidence d'association entre perte postnatale du père et la mise en évidence d'une association entre perte prénatale du père suggère un effet de programmation *in utero* spécifique. Des mécanismes biologiques par lesquels un stress prénatal peut conduire à une santé altérée à l'âge adulte ont été décrits dans la littérature. Le transfert accru de glucocorticoïdes maternels vers le fétus, résultant de leur surexpression et de la baisse de l'activité de la 11β-HSD2, enzyme normalement très exprimée dans le placenta et catalysant l'inactivation du cortisol, semble jouer un rôle-clef dans la programmation par le stress maternel. La surexposition du fétus au cortisol a des effets systémiques, en particulier sur l'axe HPA fétal en cours de maturation.

Le résultat négatif chez les orphelins postnataux mérite aussi de l'attention. On eut en effet pu supposer l'existence d'une baisse significative de la longévité associée à la perte postnatale et à ses conséquences socioéconomiques – notamment la perte de revenu – ainsi qu'à ses conséquences sur le comportement maternel et le soin apporté à l'enfant. La longévité n'est peut-être pas un indicateur de santé assez sensible pour mesurer les effets d'une perte postnatale. Peut-être aussi certaines caractéristiques de la réponse à une perte du mari pendant la Grande Guerre (solidarités familiales, charité privée, secours de l'Etat) ont pu constituer des protections contre l'événement. Dans cette perspective, ce serait à la fois l'*early life adversity* et le contexte dans lequel elle survient qui relèveraient de la santé publique.

Se pose la question de la sélection des orphelins dans l'enfance. Les populations étant hétérogènes (génétiquement, socialement, etc.), une *early life adversity* peut, en augmentant la mortalité des plus fragiles, enrichir la proportion d'individus robustes parmi ceux atteignant

l'âge adulte. Schématiquement, sont alors comparés à l'âge adulte une population exposée à l'*early life adversity* et une population d'individus non-exposés 'normale' : ainsi, sélection et débilitation agissent en sens contraire sur la mortalité observée à l'âge adulte, la première pouvant en conséquence brouiller les effets de la seconde. Alors qu'une première étude n'avait pas trouvé de différences de mortalité à l'âge adulte entre générations exposés in utero à la Famine finlandaise des années 1860 et générations non exposées, il a été récemment montré que la sélection qui s'était opérée avait été assez forte pour masquer une différence d'environ 1 an d'espérance de vie à 40 ans.

Il semble que le problème de la sélection soit beaucoup moins crucial dans le cas d'une perte du père en 14-18. Notons d'abord que, s'il s'avérait que la perte du père avait sélectionné les plus robustes parmi les orphelins, l'effet de la perte du père sur la longévité après 31 ans – mesuré à ~ 2.5 ans – devrait être révisé à la hausse : nous aurions sous-estimé la taille de l'effet, et non rapporté un faux positif. Ensuite, l'*early life adversity* étudiée se distingue nettement des famines pour ce qui concerne ses effets immédiats. Si une famine est par définition une crise de mortalité dans l'instant, rien n'indique que la mortalité des orphelins ait augmenté dans les premières années de vie – la question reste largement ouverte. Si augmentation de la mortalité immédiate il y eut, il semble extrêmement improbable que son ordre de grandeur ait été comparable à une mortalité de famine. De sorte que la sélection, qui suppose une mortalité importante et répartie de manière inhomogène sur les individus, n'a pu être que modeste. Un indice direct de l'absence de sélection est l'équilibre des professions des pères de MNOs et des orphelins analysés (vivants à 31 ans) : une sélection aurait laissé pour signature, chez les orphelins, un déséquilibre en faveur des groupes sociaux les plus favorisés – ce qui a par exemple été observé dans le cas de la Famine finlandaise.

Perspectives

L'étude des causes de décès, disponibles après 1968, offre une fenêtre raccourcie mais fondamentale sur la vie adulte des orphelins de notre cohorte, qui avaient déjà 53 ans environ. Elle pourra cependant éclairer les mécanismes sous-jacents à l'accroissement de la mortalité adulte des orphelins prénataux.

La question de la mortalité des orphelins avant 31 ans ne pourra être attaquée en s'appuyant sur le statut de pupille, puisque celui-ci est donné conditionnellement au fait d'avoir survécu jusqu'à 1918, date de début des adoptions par la Nation. En revanche, une étude cas-témoin pourrait permettre de tester l'existence d'une association entre perte du père et décès avant 31 ans. Les cas seraient l'ensemble des individus sans mention postérieure à 1945 (aux quelques erreurs de classification près, ce sont les individus morts avant 31 ans) ; les témoins des individus choisis dans les mêmes registres mais dont la date de décès est connue, et qui ont donc survécu jusqu'à 31 ans. Le père de chaque sujet inclus serait ensuite cherché dans la Base des Morts pour la France.

Enfin, des études récentes suggèrent l'existence d'une transmission aux générations suivantes de marques épigénétiques acquises au cours de la vie, au gré de l'expérience, notamment de stress. Des soldats rentrés traumatisés du front ont conçu des enfants après guerre. On ne peut pour l'instant que spéculer sur l'existence de telles transmissions dans leur cas, et peut-être essayer de renseigner la question.

Mots-clefs : Hypothèse d'Origine Développementale des Maladies ; stress maternel ; *early life adversity* ; décès du conjoint ; Première Guerre mondiale ; cohorte historique ; cohorte éteinte ; pupilles de la Nation ; orphelins ; *natural experiment* ; mortalité ; inégalités socio-économiques ; mortalité infantile ; sociologie des prénoms

Summary

The thesis proposes and explores the First World War as a historical model in early life psychological stress. The Developmental Origins of Health and Disease (DOHaD) hypothesis predicts increased susceptibility to chronic diseases in adulthood for those exposed to an extreme psychological trauma in very early life. Programming by *in utero* exposure to maternal glucocorticoids or by a disturbed early postnatal environment, according to the DOHaD hypothesis, is indeed expected to be associated with impaired long-term health and therefore result in increased mortality and reduced lifespan in adulthood.

Motivated by the DOHaD hypothesis, we therefore collected vital information on French orphans born 1914-1916 thanks to the "pupille de la Nation" distinction, a legal status created in 1917 and granted upon request to all orphans, irrespective of their wealth or income. Notification of "adoption by the Nation" was by law inscribed on the birth certificate of a newly adopted child. Birth registers thus provided a census of all pupilles born in the included cities during the inclusion period as well as long-term mortality follow-up. To this day, ~ three quarters of Paris as well as nine other cities have been included, and the birth certificates of 7,250 pupilles have been digitized. Call to the Died for France Database enabled us to identify war orphans among pupilles and retrieve the paternal date of death. Positive methods of linkage verification were devised to avoid the problems posed by homonyms. Matched non-orphans (MNOs) were drawn from the same birth registers. For each orphan, his MNO was therefore chosen born in the same district at the same time, to avoid potential problems posed by migrations and changes in nutritional and infectious environments during the war. The outcome of interest was longevity of those who survived to 31 y.

Since maternal psychic stress began at announcement of the partner's death, not his date of death, we checked that orphans who lost their father before birth (prenatal orphans) were indeed prenatally exposed to maternal stress. Systematic evidence for prenatal altered maternal behaviour was found by the study of first names given to orphans: in our cohort of orphans, a prenatal loss of father was associated with a 2.7-fold increase in father's name transmission.

The main result of the study is that an orphan-MNO difference in adult longevity of ~2.5 years was found for prenatal orphans, but that no difference in adult longevity could be measured between orphans who had lost their father after birth (postnatal orphans) and their MNOs. These two results are uneasily explained by long-running socioeconomic consequences of the early loss of father, which must have been experienced by both types of orphans. They rather suggest early trauma in utero has programming effects on biological susceptibility in adulthood strong enough to significantly alter longevity. The fact that no loss of lifespan was found in the case of a postnatal loss of father further suggests efficient buffers to early postnatal stress existed in French society.

Scientific output during the PhD

I. Scientific output in relation to the PhD

Published articles

Todd N., Valleron A.-J., Bougnères P. (2017). Prenatal loss of father during World War One is predictive of a reduced lifespan in adulthood. *Proc Natl Acad Sci USA*, 114(16), 4201.

Todd N., Le Fur S., Bougnères P., Valleron A.-J. (2017). Impact of social inequalities at birth on the longevity of children born 1914-1916: a cohort study. *PLOS ONE*, 12(10).

Submitted articles

Todd N., Valleron A.-J., Bougnères P., The naming of orphans in France during World War One: a study of a nationwide cohort of "pupilles de la Nation" (submitted to *Hist Methods*).

Oral presentations

"Réponses juridiques et symboliques aux problèmes de filiation pendant la Première Guerre mondiale", invitation to the conference *Filiations*, Université Paul Valéry, Montpellier, Octobre 13, 2017.

"A study of the very long-term health consequences of World War I in a French cohort born 1914-1916", *War hecatomb Conference*, Universidade NOVA, Lisbon, June 20, 2017.

"Des travaux de l'Académie de Médecine à l'Hypothèse d'Origine Développementale des Maladies: les enfants de 14-18 cent ans après", invitation to the conference *Les Académies en guerre*, co-organized by the Nationale Akademie der Wissenschaften Leopoldina, the Académie des sciences and the Royal Society at the Université de Lorraine, Metz, June 9, 2017.

"World War One as a model for very long-term consequences of early life stress", invitation to the Max Planck Institute for Demographic Research, Rostock, June 7, 2017.

"In utero and postnatal psychological maternal stresses have different effects on longevity: studies in World War 1 orphans", *Annual Meeting of the European Society for Paediatric Endocrinology (ESPE)*, Paris, September 12, 2016.

"Les orphelins de la Première Guerre mondiale. Biologie d'un événement", invitation to the *Séminaire d'histoire de la famille et de la démographie*, Université Paris-Sorbonne, December 18, 2015.

II. Scientific output unrelated to the PhD

Published articles

Mercereau L.*, Todd N.*, Rey G., Valleron A.-J. (2017). Comparison of the temperature-mortality relationship in foreign-born and native-born died in France between 2000 and 2009. *Int J Biometeorol*. *: equally contributed.

Todd N., Valleron A.-J. (2015). Space-Time Covariation of Mortality with Temperature: A Systematic Study of Deaths in France, 1968-2009. *Environ Health Perspect*, 123(7), 659.

Articles in preparation

Le Stunff C., Castell A.-L., Todd N. *et al.*, Fetal growth is associated with the CG methylation of the P2 promoter of the IGF1 gene (submitted to *Clin Epigenetics*).

Oral presentations

"Mise en parallèle des augmentations de la température moyenne et de la température de mortalité minimum en France, 1968-2009", *Congrès de la Société Française de Santé et Environnement*, Paris, November 24, 2015.

"The impact of climate on mortality in developed countries : History and analysis of the French death certificates, 1968-2009", invitation to the *Alliance Summer School in Science and Policy*, Columbia University, Paris, July 4, 2014.

Other works

Todd N. (2016), book-review of *Gender-Specific Life Expectancy in Europe 1850–2010*, edited by M. Dinges and A. Weigl, *Annales de démographie historique*, 132, 278.

Todd N. (2015), La taille au secours des historiens : un exemple d'Histoire biologique, *Médecine Clinique, Endocrinologie et Diabète*, 79, 7 (didactic article).

Acronyms

11β-HSD2 : 11β- hydroxysteroid dehydrogenase type-2

AVP: vasopressin

BMF: Base des Morts pour la France (Died for France database)

DOHaD: Developmental Origins of Health and Disease

GAM: Generalized Additive Model

HPA: hypothalamic-pituitary-adrenal axis

Mice: multivariate imputation by chained equations

MNO: matched non-orphan

NCO: non-commissioned officer

NR3C1: glucocorticoid receptor

SES: socioeconomic status

s.e.: standard error

Introduction

The First World War was an unexpected event of formidable violence. For more than four years, European populations experienced total war. The war-induced demographic problem is most often posed in terms of military mortality: to limit to France alone - about 40 million inhabitants in 1914 – approximately 1,4 million soldiers died during the conflict [1]. The same demographic situation can also be approached from a more special viewpoint, that of orphans: tens of thousands of children lost their father at a very early age during the conflict, an event that radically changed their mothers' behavior. The consequences of this extreme trauma on their health have so far remained unexplored.

Modern biology has yet revealed mechanisms linking stress experienced at early stages of development (due to events grouped under the generic expression of "early life adversities") and increased susceptibility to chronic diseases in adulthood. Strong evidence has come from animal models. The study in humans is in general much more complex because it is difficult to isolate the individual contribution of factors that are often very correlated with each other. Thus, in individuals undergoing chronic stress during childhood, poor nutrition and housing conditions, low educational level, exposure to infectious diseases and parental stress, often form a cluster of adverse conditions. Common causes can lead to depression of the mother and that of the child, without the former actually causing the latter. Early death of a parent and shortened lifespan may only reflect the genetic component of longevity, whose heritability is about 0.25 in contemporary societies [2], or more generally may only be due to shared frailty. The use of exceptional historical situations such as the First World War makes it possible to overcome these problems because of the precise definition of the perinatal stress considered and the largely random selection of individuals exposed to it. Furthermore, in a context of unprecedented increase in life expectancy [3,4], the First World War offers an opportunity for follow-up of the studied individuals over a very long age-span, thus enabling the detection of all potential differences in mortality.

The aim of this PhD thesis was therefore to propose and explore the First World War as a quasi-experimental situation for the study of early life stress in humans. To achieve this epidemiological goal, we had no choice but to delve into the specific social context brought

about by the War. This way, we gathered results that I hope will make this work of some interest also to historians of the Great War.

I. The biology of early life stress

The Developmental Origins of Health and Disease hypothesis

In the late 1980s, David Barker and colleagues made an unexpected observation: the existence of a relationship between birth weight on the one hand (taken as a proxy for fetal nutrition) and mortality from ischemic heart disease throughout life on the other [5]. This correlation, resistant to control by classical risk factors (socioeconomic status, smoking, etc.) and supplemented by other studies (in particular on the Dutch Famine of 1944-45 [6-8] and on animal models), lead to the formulation of the Barker hypothesis, today known in its extended formulation as the Developmental Origins of Health and Disease (DOHaD) hypothesis [9,10]. In short, this hypothesis states that the conditions under which an individual's perinatal life takes place play a crucial role in life-long susceptibility to disease.

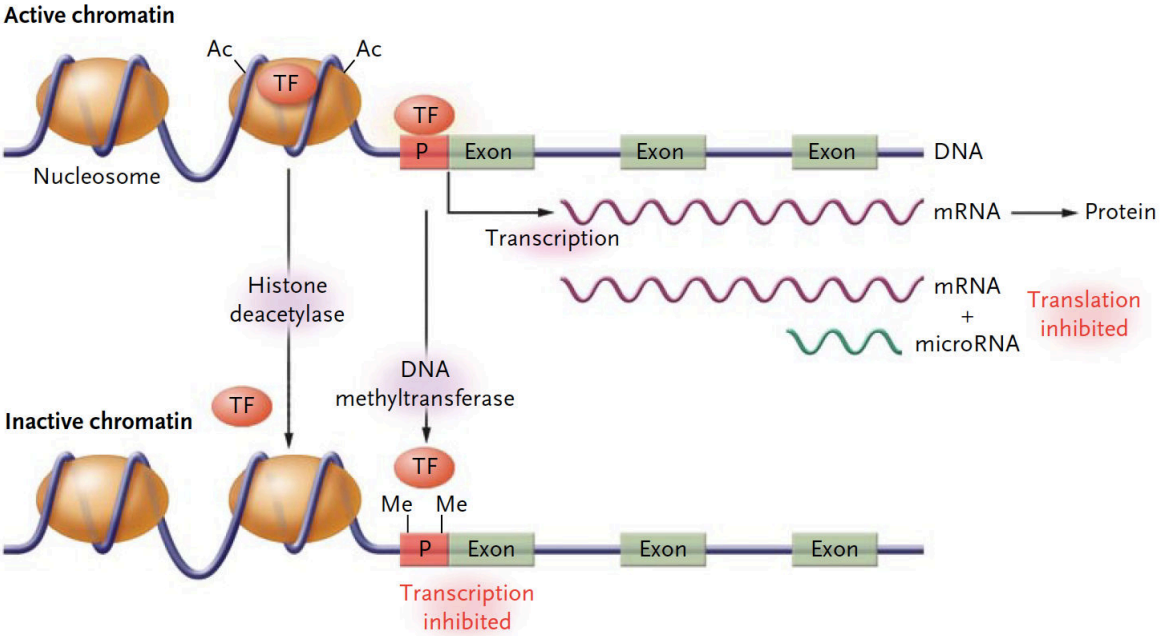
A link has been made between the DOHaD hypothesis and epigenetic mechanisms. These are, according to the most common definition, all mechanisms regulating gene expression that 1) do not involve changes in DNA sequence and 2) are stably transmitted from mother cell to daughter cells during mitosis. For the most studied, epigenetic marks are (Figure 1):

- DNA methylation: covalent addition of a methyl group to a cytosine base immediately followed by a guanine (CpG dinucleotide). DNA methylation is the most proximal epigenetic mark and most extensively studied. It usually silences gene expression by interfering with the binding of transcription factors to their binding sites in DNA;

- Histone post-translational modifications: covalent modifications of core histones such as methylation, acetylation or phosphorylation of specific residues of histone tails. Histone modifications persistently change the state of chromatin and make it more or less accessible to the transcription machinery, thereby altering gene expression;

- Post-transcriptional regulation by miRNAs (small non-coding RNAs that are ~ 20 nucleotides in length): miRNAs hybridized to mRNA reduce the level of protein synthesis.

Figure 1. Examples of epigenetic regulation of gene expression.



DNA or Histone modifications control access of transcription factors (TFs) to the DNA, thereby modifying the transcription rate in messenger RNA (mRNA). Top: the presence of acetyl groups (Ac) on specific lysine residues of histones generally results in a more open chromatin. MicroRNAs that hybridize to mRNA reduce the level of protein synthesis. Bottom: Methylation at CpG sites of the promoter (P) regions generally results in reduced transcription. Source: Gluckman *et al.*, *N Eng J Med*, 2008.

These three epigenetic mechanisms are usually highly inter-related (e.g. changes in histone acetylation can alter DNA methylation). They may differ from one tissue to another and thereby contribute to cellular differentiation (under the effect of innate signals). They can also be modulated by environmental conditions (under the effect of external signals), randomly or deterministically, especially at early developmental stages [11]. This sensitivity of epigenetic marks to perinatal cues allows developmental plasticity – the ability of an organism to develop according to its specific environment – and would be adaptive, enhancing the organism's Darwinian fitness (both in terms of survival and reproductive success): according to the DOHaD hypothesis, the perinatal environment is to be interpreted as the best prediction of future environmental conditions [12,13]. Adaptation to the perinatal environment would therefore allow adaptation to the predicted adult environment, notably taking the risk, if the environment changes, to generate a mismatch resulting in disease and impaired survival [14].

In practice, three types of early life environmental cues have been extensively investigated in the context of the DOHaD hypothesis: nutrition, infections, and psychological stress. It can already be noted that natural experiments, in particular famines [7,8,15-17] and epidemics [18-21], have been extensively studied to investigate long-term effects of early life nutrition and infections. We focused on psychological stress.

Animal models of early life stress

Several animal models, mainly murine, have been developed to study the effects of early life stress on adult health [22]. Naturally, stress experienced during (prenatal stress) and after pregnancy (postnatal stress) are distinguished, for the corresponding biological pathways are so very different.

The most commonly used paradigm for prenatal stress is prenatal restraint stress, in which a pregnant rat is restrained several times a day in a plastic transparent cylinder under bright light. Pregnant rats exposed to prenatal restraint stress give birth to an offspring whose hypothalamic-pituitary-adrenal axis (HPA axis; Figure 2) is altered, with increased basal and stress-induced corticosterone levels [23]. This hyperactive HPA axis is associated with more frequent depression [24] and anxiety-like [25] behaviors in adulthood. Prenatal restraint stress also entails impaired spatial learning and memory, associated with reduced synaptic plasticity [26] and lifespan neurogenesis [27] in the hippocampus. Prenatal restraint stress is associated in adulthood with lower methylation of the *CRH* (corticotropin-releasing hormone gene) promoter in the hypothalamus [28] as well as other epigenetic changes in other brain regions [29,30].

The ‘programming’ mechanisms linking prenatal stress and an altered phenotype in adulthood are not yet fully elucidated [22]. Maternal stress-induced excess glucocorticoid secretion has been proposed as a candidate mechanism for fetal programming [31]. Maternal adrenalectomy (that removes the source of maternal glucocorticoids) abolishes the exaggerated stress-induced corticosterone secretion observed in adulthood in prenatally stressed offspring, suggesting prenatal maternal stress-induced increase in glucocorticoid secretion plays a programming role on the fetus [32]. The role of 11β-hydroxysteroid dehydrogenase type-2 (11β-HSD2) has been studied more recently. This enzym, heavily

expressed in the placenta, is a "barrier" that inactivates corticosterone and ensures low foetal corticosterone levels until late gestation. Chronic restraint stress has been shown to reduce placental expression and activity of 11β-HSD2 [33] (this down-regulation being mediated at least in part by increased tissue-specific methylation of the gene promoter [34]), leading to an increased transfer of maternal corticosterone to the fetus. Because maternal cortisol levels are much higher than fetal levels, even moderate decrease in placental 11β-HSD2 can entail strong overexposure of the fetus to maternal glucocorticoids, which in turn can lead to persistent changes in gene regulation and fetal development of many organs, notably the HPA axis [35,36].

Regarding postnatal stress, a seminal study by Michael Meaney, Moshe Szyf and coworkers showed that low maternal care (poor licking and grooming) in the first week of postnatal life increases offspring's hippocampal methylation of a promoter of *NR3C1*, the glucocorticoid receptor gene [37]. This increased methylation is associated with altered acetylation of the lysine 9 residue of histone H3. The hippocampus regulate hypothalamic CRH expression through negative feedback (Figure 2), so that increased hippocampal *NR3C1* methylation, associated with decreased gene expression, leads to decreased feedback in the HPA axis and increased HPA activity [38] : increased corticosterone secretion is thus observed under acute stress in poorly licked rats. Periodic infant-mother separation during early postnatal life is also frequently used to model postnatal stress. This model has notably shown a persistent increase in vasopressin (AVP) expression in the paraventricular nucleus (PVN) of hypothalamus associated with reduced methylation in a regulatory region of the *Avp* gene [39], as well as an overexpression of POMC in the pituitary, again associated with hypomethylation in a regulatory region of the *Pomc* gene [40]. Maternal separation experiments in rhesus monkeys (*Macaca mulatta*) have also been shown to deregulate glucocorticoid secretion [41] as well as the immune system, with enhanced expression of genes involved in inflammation [42].

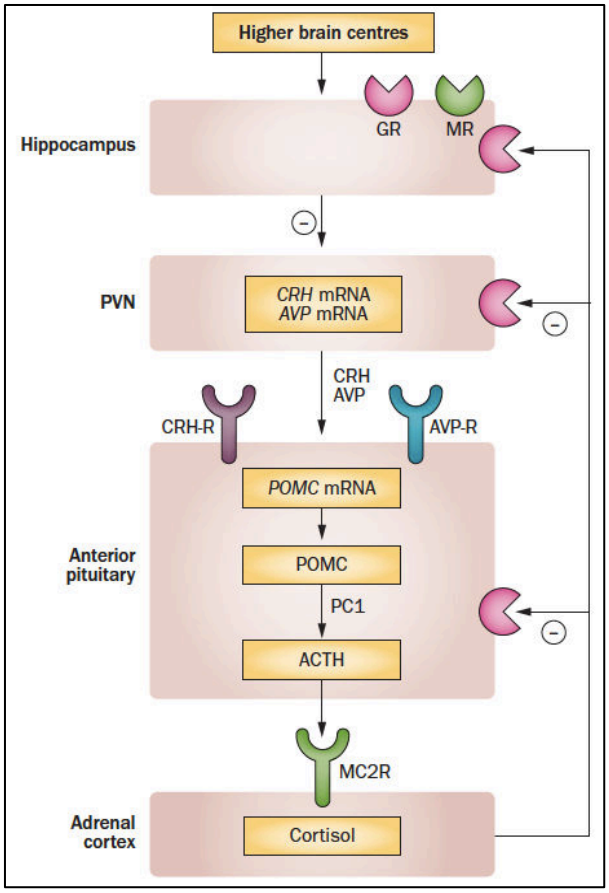


Figure 2. HPA axis

The paraventricular nucleus (PVN) of hypothalamus secretes CRH and vasopressin (AVP). These factors bind to their receptors, CRH-R and AVP-R, in corticotropic cells of the anterior pituitary, thereby increasing POMC synthesis and ACTH secretion. POMC is cleaved by prohormone convertase 1 (PC1) to synthesize ACTH. ACTH, after binding with its receptor MC2R, stimulates production and secretion of corticosteroids (cortisol in humans) in the adrenal cortex.

Abbreviations:
ACTH: adrenocorticotropic hormone;
AVP: vasopressin;
AVP-R: vasopressin receptor;
CRH: corticotropin-releasing hormone;
CRH-R: CRH receptor;
GR: glucocorticoid receptor (=NR3C1);
MC2R: ACTH receptor;
MR: mineralocorticoid receptor;
PC1: prohormone convertase 1;
POMC: pro-opiomelanocortin;
PVN: paraventricular nucleus.

Source: Moisiadis et al., *Nat Rev Endocrinol*, 2014

II. The epidemiology of early life stress

Studies in humans have found associations between psychological stress in early life and increased susceptibility to specific diseases in adulthood. Based on the Danish Civil Registration System, it has been found that children prenatally exposed to maternal bereavement (due to the loss of the husband, of a child or of a relative during pregnancy) were at higher risk of type 1 diabetes (adjusted incidence rate ratio: 2.03) [43] and type 2 diabetes (adjusted incidence rate ratio: 1.31) [44]. Higher risk of schizophrenia was also found for those prenatally exposed to the May 1940 invasion of the Netherlands (relative risk: 1.15) [45]. World War 2 (WW2) has been used as a model for early postnatal stress. Sixty years after the event, members of the Helsinki Birth Cohort (born 1934-1944) separated from their parents during the War reported 20% more severe depressive symptoms in the Beck Depression Inventory [46] and showed increased blood pressure [47] and cardiovascular morbidity [48,49]. In the 1958 British Birth Cohort (National Child Development Study), presence in early life of adverse conditions (non-exhaustive list: maltreatment, undernutrition,

dirtiness, family member in prison or on probation, family member with a mental illness, parental separation – e.g. due to death of one of the parents or divorce) was associated in adulthood with increased allostatic load, a measure of overall physiological wear-and-tear [50].

Some human studies have investigated the molecular basis of these associations. High salivary cortisol levels have been found in offspring exposed prenatally to maternal depression [51,52] and anxiety [53] or postnatally to maternal depression [54]. HPA axis deregulation is a risk factor for cardiovascular [55] and neuropsychiatric diseases [56-58]. The methylation of the *NR3C1* promoter in peripheral blood leukocytes was higher in Tutsi mothers exposed to the Rwanda genocide during pregnancy and in their children than in a group of unexposed same-ethnicity mothers (living abroad at the time of the genocide) and their children [59]. Similarly, in a study of 25 mother-newborn dyads from the Democratic Republic of Congo, higher *NR3C1* promoter methylation in newborns' cord blood was predicted by maternal exposure to war [60]. *NR3C1* has also been found hypermethylated at age 2 months in infants whose mother experienced depression during the second or third trimester of pregnancy [61]. *Post mortem* analysis in suicide victims revealed higher methylation of the *NR3C1* promoter for suicide victims with a history of childhood abuse compared to suicide victims with no history of childhood abuse, who showed levels of *NR3C1* methylation similar to that of controls [62]. *NR3C1* has been extensively studied, but epigenetic changes induced by early life stress likely exceed this sole locus. A genome-wide study for instance found that a maternal history of depression was associated with methylation differences in genes involved in immune system functions in newborn cord blood T lymphocytes and adult offspring *post mortem* hippocampi [63].

In short, strong evidence exists for a link between early life psychological stress and biological vulnerability in adulthood. This evidence has been acquired in the exploration of both animal models and epidemiological studies. It is yet unknown to what extent this increased biological vulnerability translates into reduced lifespan. Indeed, it seems very hard to know how all the reported disease-specific risks combine within the population of those exposed to early life stress. Furthermore, given that a large portion of the human evidence comes from situations with a strong endogenous component (for instance, the association between maternal depression and offspring's depression may in part be the result of a shared risk), it is hard to quantify the causal component in the associations measured between early

stress and impaired health later in life. Lower survival in childhood (between birth and age 15 y) has been shown to be associated with loss of a parent, especially the mother, for children born 1850-1922 in the Netherlands [64] and for Spanish children born 1870-1950 [65]. Studies that have tackled the very long-term mortality consequences of an early loss of a parent, or more generally of an early life stress, are still few. No excess mortality has been found between 27 and 69 y for the 1,726 members of the Helsinki birth cohort (followed 1971-2003) who experienced parental separation during WW2 [49]. In the 1958 British Birth Cohort, increased all-cause mortality before age 50 y was found for the 4,543 individuals who experienced the events studied by [50] (see above) [66].

For these reasons, we turned to the study of the First World War and tried to identify the potential loss of lifespan associated with an early death of father, whether in the pre or postnatal period. We hypothesized that programming by *in utero* exposure to maternal glucocorticoids or by a disturbed early postnatal environment, under the DOHaD hypothesis, would lead to impaired long-term health and therefore result in increased mortality and reduced lifespan in adulthood.

III. Bereavement during the Great War as a historical experiment in maternal stress

Bereavement in France during WW1 has several characteristics that make it a unique historical experiment in early life stress:

- universal conscription ensured an equality in exposure to risk that was admittedly incomplete but by any historical standard exceptional;
- loss of the partner is a maternal stress of extreme intensity, that is unequivocal and not submitted to recall bias;
- mothers were individually exposed to stress (not by clusters, as in an invasion or any other macrolevel stressor), yielding the opportunity to select unexposed individuals born at exactly the same time and place;
- public authorities functioned properly in non-occupied regions of France, where populations experienced no major social disruption (e.g. famine);

- an exact starting date exists for each individual exposed, therefore giving the possibility to distinguish the effects of prenatal and postnatal stress[1];
- the analysis can be restricted to those conceived before the beginning of the war, for whom no fertility selection could be at play;
- the cohort born 1914-1918 is quasi-extinct, so that whole-life mortality is available;
- the intensity of the conflict enables the study of a large sample born in a short timespan, thus minimizing period effects e.g. due to medical improvements.

The first chapter summarizes the methods that enabled the development of a cohort of orphans born 1914-1916 in non-occupied regions of France. The creation of this cohort relied on an original legal status devised in 1917 and called the "pupille de la Nation" status. The chapter shows that combining information available on birth registers with that of an online database of soldiers died during the war yields a simple and high-quality observation system with very long term follow-up of orphans. Chapter 1 also describes the rule for selecting non-pupilles individuals used as comparators of orphans' adult mortality (called matched non-orphans, abbreviated MNOs).

The second chapter discusses the conditions under which, in practice, the pupille de la Nation status was granted. It shows that, as already noted by contemporary observers, the propensity to request this status was lower in the upper class than in the rest of the population. It also shows that illegitimate children (i.e. born to an unmarried woman) who lost their father in very early life were indeed largely excluded from the pupille status, a phenomenon that had so far remained unnoticed and must be taken into account in the analysis of orphans' adult mortality.

Chapter three describes two demographic pitfalls that need and be avoided to properly analyze the adult mortality of orphans. In particular, migrations leading to changes through time in the population of pregnant women as well as season of birth effects on longevity are potentially of crucial importance and do need to be addressed, given that prenatal and

[1] All mothers experienced shared stressors other than the husband's death during the War. For instance, most were aware of the high risks that their husbands, brothers or friends were running. Similarly, most were confronted to new challenges and responsibilities in their daily lives. Only for the stressor under investigation, which was arguably of extreme intensity, an exact starting date can be established.

postnatal orphans have – for purely mechanical reasons – specific distributions of dates of birth.

The fourth chapter (submitted manuscript) analyzes a simple maternal behavior, name giving. It is a venture in the field of cultural history, and hopefully a contribution to the description of mourning practices during WW1. It finds a strong change in the probability of transmission of the father's name for prenatal orphans. This change was of equal magnitude for male and female orphans, was found more pronounced in officers' offspring and finely controlled by age at father's loss, with a loss in very early pregnancy being associated with the highest probability of name transmission.

Chapter five (published article) explores one of the possibilities given by the birth registers used: the fact that they provide both parental socioeconomic status (SES) at the time of the birth and whole-life mortality enables the analysis of whole-life mortality according to SES at birth in the cohort of MNOs. We found very strong differences in median ages at death according to paternal occupation and legitimacy of the birth. This was mainly due to marked differences in infant and child mortality. Surprisingly, we found an association between paternal SES and mortality in adulthood in women only.

The final chapter (published article) compares the adult lifespan of orphans to that of their MNOs. It finds a strong decrease in lifespan for prenatal orphans, with a trend for an increased effect for a third trimester loss. By contrast to what was observed in prenatal orphans, no loss of lifespan was measured for postnatal orphans. Taken together, these two results strongly suggest a specific *in utero* programming effect.

Chapter 1: The development of a cohort of French war orphans born 1914-1916

I. The pupille de la Nation status

The pupille status was created by the law of July 27, 1917. Article 1 of this law stated: "France adopts orphans whose father, mother or breadwinner died during the war of 1914 as a military or civilian victim of the enemy. Assimilated to orphans are the children born or conceived before the end of war, whose father, mother or breadwinner are unable to earn a living through work, as a result of injuries or diseases due to or made worse by the war. The children thus adopted shall have the right to protection, material and moral support of the State for their education under the conditions and limits defined by this Law, until they have reached the age of majority" (then age 21 y) [2] [67]. Without taking the orphan to his family, "the nation bears the burden, partially or totally, of the material maintenance and education necessary for the normal development of the pupille in the case of insufficient family resources"[3] (article 4), thanks to an *ad hoc* administration, the *Office National des Pupilles de la Nation*, established notably to examine applications for financial support and allocate it on a case-by-case basis[4]. The pupille de la Nation status thus had very practical consequences (grants, allowances, etc.) but was also, whatever the income level, honorific. As stated by a widely distributed leaflet intended for families:

> "The Nation grants its pupilles their highest title of honor for she wanted to bestow upon them a form of moral nobleness. Rich and poor will have it at heart to claim it." [5] [68]

[2] "La France adopte les orphelins dont le père, la mère ou le soutien de famille a péri, au cours de la guerre de 1914, victime militaire ou civile de l'ennemi. Sont assimilés aux orphelins les enfants, nés ou conçus avant la fin des hostilités, dont le père, la mère ou le soutien de famille sont dans l'incapacité de gagner leur vie par le travail, à raison de blessures reçues ou de maladies contractées ou aggravées par suite de la guerre. Les enfants ainsi adoptés ont droit à la protection, au soutien matériel et moral de l'Etat pour leur éducation dans les conditions et limites prévues par la présente loi, et ce jusqu'à l'accomplissement de leur majorité".

[3] "La Nation assume la charge, partielle ou totale, de l'entretien matériel et de l'éducation nécessaires au développement normal du pupille dans le cas d'insuffisance de ressources de la famille".

[4] This was one the reasons why the *Office* was organized in local branches, named the *Offices départementaux des Pupilles de la Nation*.

[5] "La Nation a voulu conférer à ses Pupilles une sorte de noblesse morale. Elle leur donne le plus beau des titres de gloire. Riches et pauvres auront à cœur de le revendiquer".

The pupille de la Nation status was granted by the local civil tribunal, at the request of the legal representative of the child, usually the mother for war orphans. At total, around 1,100,000 children were adopted by the Nation [69].

The decisive element that made possible the development of a cohort of pupilles is article 8 of the law of July 1917: "notification of the adoption, if it has been decided, shall be made at the request of the public ministry in the margin of the birth certificate of the child"[6]. This notification allows for the rapid identification of all pupilles de la Nation born in a given place in a given period of time (see Figure 3 for an example).

All pupilles born August 1, 1914 – December 31, 1916 in selected districts of Paris and born August 1, 1914 – December 31, 1915 in selected cities (see Appendix 1) were included[7]. Each project (Chapter 4: transmission of paternal first name to orphans; Chapter 5: study of the mortality of MNOs; Chapter 6: comparison of the adult longevity of orphans and MNOs) was carried out at a different stage of data collection and therefore used a different database. At total, 7,250 pupilles de la Nation have been identified to date. Due to a time constraint, matched non-orphans were recruited only for Paris districts and Bordeaux (see below and Appendix 1). Unless otherwise specified, analyses given in Chapters 1-3 were performed on orphans of the full dataset (7,250 pupilles).

II. Call to the Database of Those died for France in the First World War

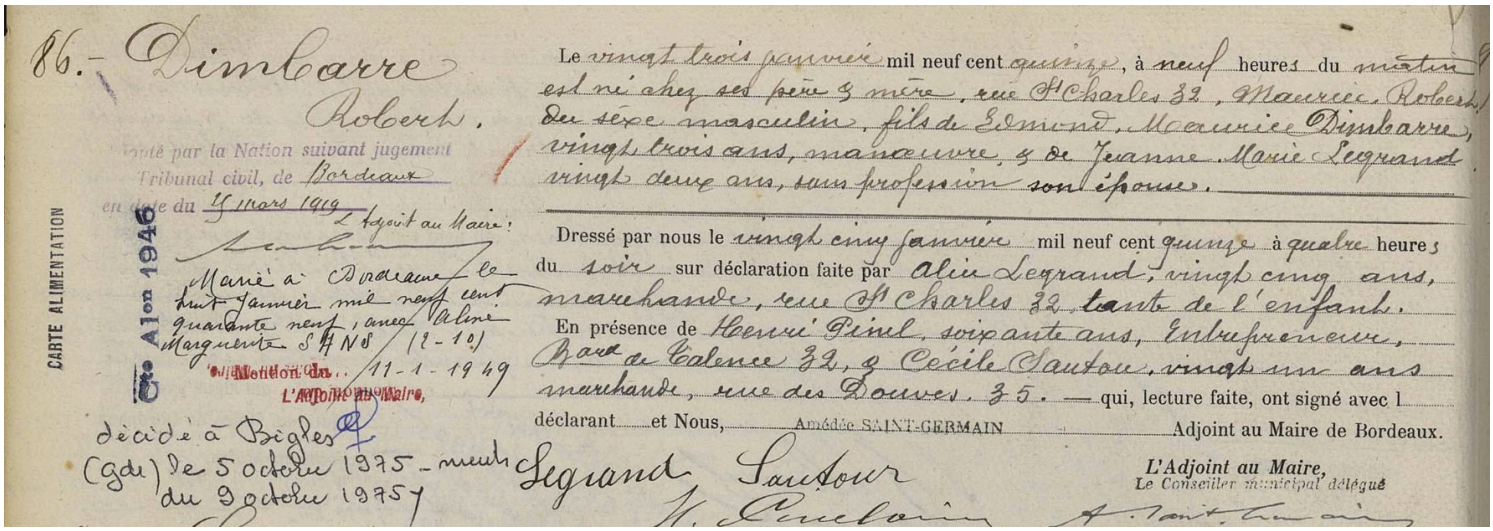
Exceptions left aside, pupilles de la Nation are of two types: orphans on the one hand, children of severely disabled soldiers (wounded or ill) on the other. If the law of July 1917 in theory authorized adoption of a child who had not been recognized by his father provided that the father had acted as the breadwinner ("soutien de famille"), the father is in fact almost always known in our cohort (only 37 of the 7,250 pupilles were never recognized by their father; see Chapter 2). In order to identify orphans among pupilles, the father of each pupille (whose name and age are available on the birth certificate of the latter) was searched for in the

[6] "Mention de l'adoption, si elle a été prononcée, est faite, à la requête du ministère public, en marge de l'acte de naissance de l'enfant".

[7] This choice of a short timespan in practice makes the inclusion of siblings a rare event, which is made even more unlikely by the fact that births of orphans are concentrated before May 1915 (see Chapter 3). Thus, even though all siblings obviously became orphans simultaneously, thus forming clusters, our study needs not take into account this phenomenon.

General file of militaries of the French army died during the First World War, available online[8]. Better known as the *Died For France Database* (*Base des Morts pour la France*, abbreviated BMF), this database was created after the War by the French administration and includes about 1.4 million soldiers who died between August 3, 1914 and June 1, 1919, whether or not they received the Died for France distinction ("mention Mort pour la France")[9]. It is therefore virtually complete. The record associated with each search result provides the military rank, date and type of death (killed in action, missing in action, etc.; see Figure 4 for an example).

Figure 3. Birth certificate of a pupille de la Nation, with the adoption by the Nation, marriage and death notifications.

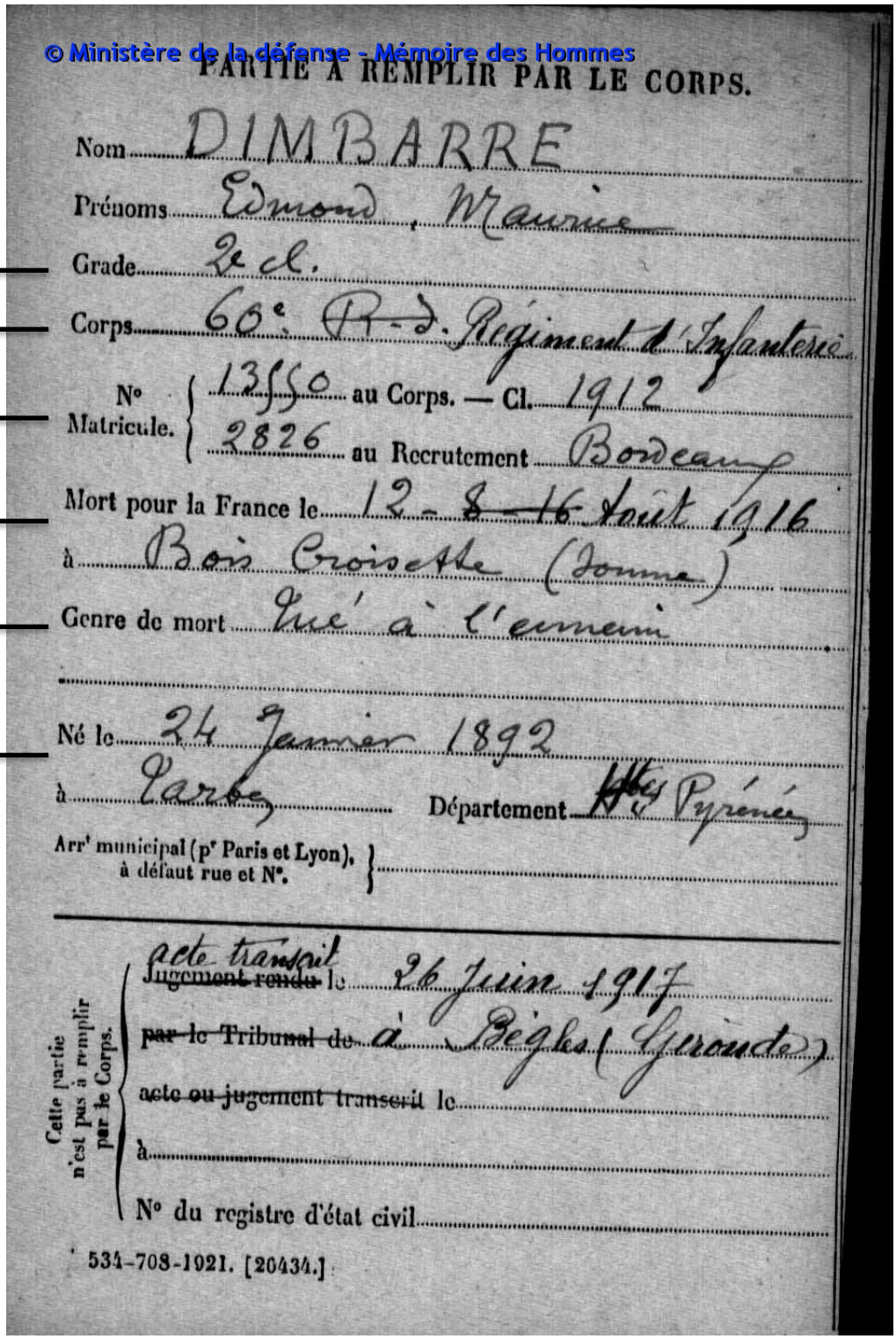

86.- Dimbarre
Robert.
Adopté par la Nation suivant jugement
Tribunal civil, de Bordeaux
en date du 15 mars 1919
Le Maire:
Marié à Bordeaux le
huit janvier mil neuf cent
quarante neuf, avec Aline
Marguerite SAINS (2-10)
Mention de
11-1-1949
L'Adjoint au Maire,
décédé à Bigles
(Gde) le 5 octobre 1975 - mention
du 9 octobre 1975
CARTE ALIMENTATION
Cte A 1er 1946
Le vingt trois janvier mil neuf cent quinze, à neuf heures du matin
est né chez ses père & mère, rue St Charles 32, Maurice Robert,
Du sexe masculin, fils de Edmond, Maurice Dimbarre,
vingt trois ans, manœuvre, & de Jeanne Marie Segrand
vingt deux ans, sans profession son épouse.
Dressé par nous le vingt cinq janvier mil neuf cent quinze à quatre heures
du soir sur déclaration faite par Alin Segrand, vingt cinq ans,
marchande, rue St Charles 32, tante de l'enfant.
En présence de Henri Peiel, soixante ans, Entrepreneur,
Quai de Talence 32, & Cécile Santour, vingt un ans
marchande, rue des Douves, 35. — qui, lecture faite, ont signé avec l
déclarant et Nous, Amédée SAINT-GERMAIN Adjoint au Maire de Bordeaux.
L'Adjoint au Maire,
Le Conseiller municipal délégué
Segrand Santour

[8] *Fichier général des militaires de l'armée française décédés au cours de la Première Guerre mondiale*, Available at http://www.memoiredeshommes.sga.defense.gouv.fr/. For more detailed descriptions of the database, see the description online as well as 70. Lemarchand C (2008) Le fichier général des militaires de l'armée française décédés au cours de la Première Guerre mondiale. Revue historique des armées: 132-133. 71. Prost A (2008) Compter les vivants et les morts : l'évaluation des pertes françaises de 1914-1918. Le Mouvement Social 222: 60.

[9] The database originally made available online contained the ~ 1.3 million soldiers who did receive the "mention Mort pour la France", a distinction created by the law of July 2, 1915. In November 2014, the files of the ~ 95,000 soldiers who did not receive the "mention Mort pour la France" were added online.

Also, it must be noted that because the BMF stops in June 1919, pupilles of our cohort (born 1914-1916) with a father died after June 1, 1919, while classified as non-orphans, actually became orphans, at some point after age 2.4 years. The systematic study of non-orphans described in section IV of this chapter (see below) revealed that most deaths after June 1, 1919 were deaths by disease. Among the 171 fathers of pupilles born in Nîmes and Tarbes, the conscription register of 147 was found, and yielded the date of death for 99/147 (the 48/147 with unknown date of death likely died at least a few years after 1919). Only 13/99 died after June 1, 1919. On these 13 died after June 1, 1919, 11 died of disease and 2 died of injuries. Because those whose father died of disease were anyway excluded (see p. 41), the censoring of the BMF on June 1, 1919 therefore seems of very minor consequences on the final dataset analyzed.

Figure 4. Died for France certificate of the father of pupille whose birth certificate is shown in Figure 3.



Military rank

Regiment

Conscription record information

Date and place of death

Type of death

Date and place of birth

III. Methods of record linkage verification

The search for pupilles' fathers in the BMF frequently gave several results, those being homonyms having the same age at the time of the birth of the considered pupille. Another problematic case is that of a pupille's father who was severely disabled – therefore absent from the BMF – who is the namesake of a soldier who died during the war, himself in the BMF.

In case of doubt about the identity of the father, the birth certificate of each soldier returned by the search in the BMF was checked until positive identification of the father was achieved. Indeed, the BMF certificate indicates the place and date of birth of each soldier (see Figure 4). As the vast majority of XIXth century French civil registers have been digitized and made available online, the verifications were carried out on the websites of the various *archives départementales*. The comparison of the name of the wife of the soldier (available in the marriage notification inscribed on his birth certificate) and that of the mother of the pupille (available on his birth certificate) yields an elementary and exact method of verification of the linkage between birth registers and the BMF. This method, summarized below (Figure 5; see Figure 6 for the continuation of the example used in Figures 3 and 4), works provided the pupille's parents married at some point, regardless of the date of marriage.

Figure 5. Main record linkage verification method.

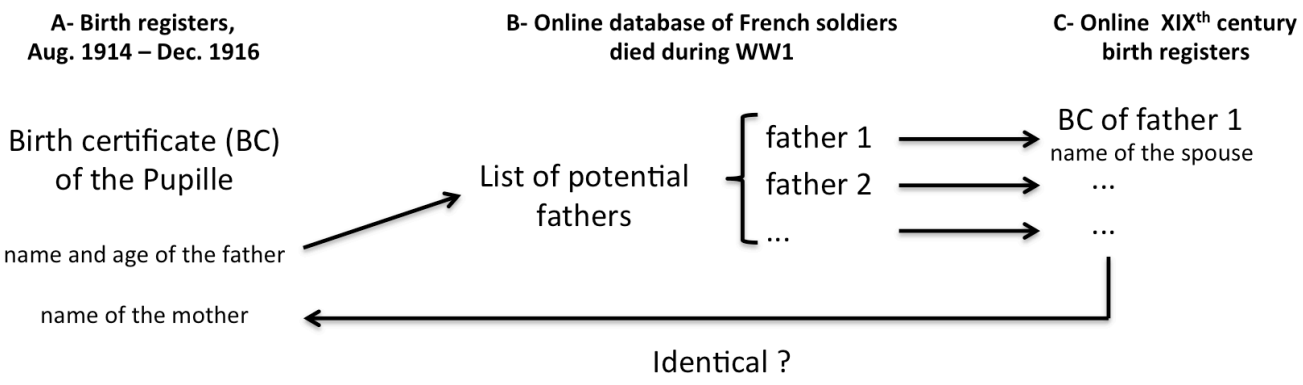
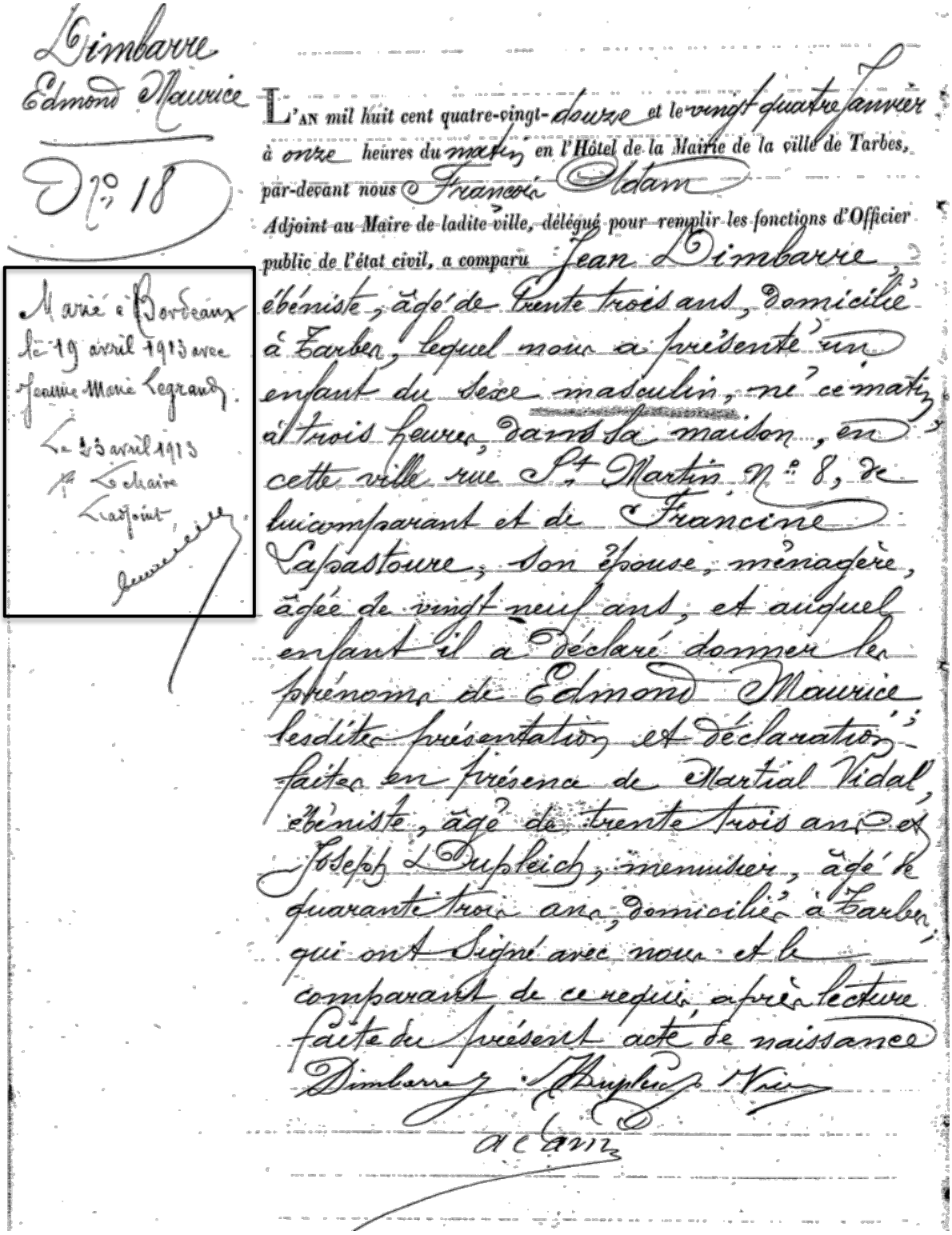


Figure 6. Birth certificate corresponding to birth certificate (Figure 3) and the Died for France certificate (Figure 4) shown as examples.



Dimbarre
Edmond Maurice
N° 18

L'an mil huit cent quatre-vingt-douze et le vingt quatre janvier à onze heures du matin en l'Hôtel de la Mairie de la ville de Tarbes, par-devant nous François Adam Adjoint au Maire de ladite ville, délégué pour remplir les fonctions d'Officier public de l'état civil, a comparu Jean Dimbarre, ébéniste, âgé de trente trois ans, domicilié à Tarbes, lequel nous a présenté un enfant du sexe masculin, né ce matin à trois heures, dans sa maison, en cette ville rue St Martin, N° 8, de lui comparant et de Francine Lapastoure, son épouse, ménagère, âgée de vingt neuf ans, et auquel enfant il a déclaré donner les prénoms de Edmond Maurice lesdites présentation et déclaration faites en présence de Martial Vidal, ébéniste, âgé de trente trois ans et Joseph Dupleich, menuisier, âgé de quarante trois ans, domiciliés à Tarbes qui ont signé avec nous et le comparant de ce requis après lecture faite du présent acte de naissance

Dimbarre J. Dupleich Vidal

A Lavaur

Marié à Bordeaux le 19 avril 1913 avec Jeanne Marie Legrand.
Le 23 avril 1913
Le Maire
L'adjoint

The wife's name, found in the marriage notification (circled area), matches the mother's name on Figure 3, therefore yielding positive identification of the pupille's father.

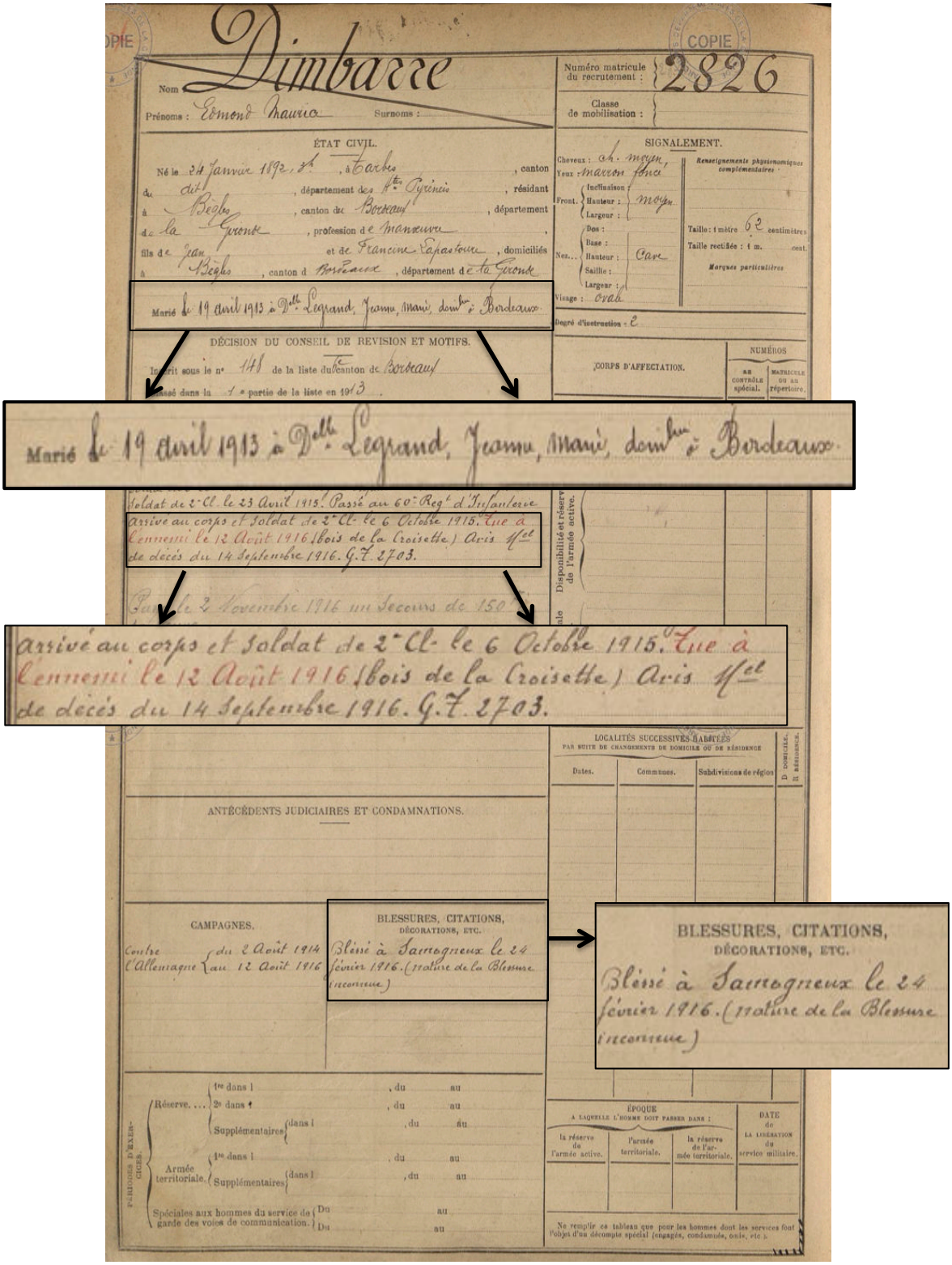
In the case of a pupille whose parents never married, the act of recognition by the father was checked (this act giving the place and date of birth of the father, it removes all possible doubts) if the civil registration service where recognition took place (known thanks to the recognition notification inscribed on the birth certificate of the pupille and which mentions both the place and date of recognition) was one of the services included in the study. Thus, for a child born in the 14th *arrondissement* of Paris but recognized by his father in the 3rd arrondissement, we checked the act of recognition in the 3rd arrondissement. For children recognized or legitimized by judicial process (see Chapter 2), we examined the judgments, which were by law transcribed on the district of birth's registers, and thus readily accessible.

Finally, in the unresolved cases that remained, e.g. a XIXth century birth register not yet digitized, we checked, if available, the conscription registers[10]. Created at the time of conscription and continuously updated from then on, these registers enabled the army to keep track of each man until his being discharged of his military obligations. They have been digitized by most *départements* for the cohorts that fought during WW1. They give, if established and updated with care, the successive addresses and occupations of the conscript or even sometimes the spouse's name, which are all elements enabling identification (see Figure 7).

Among the 7,250 included pupilles, 4,061 were identified as war orphans. In the comparison of adult longevity of orphans with that of MNOs, the low proportion (~ 15%) of orphans born to a father died of disease were excluded in order to avoid the issue of shared frailty or the potential confounding by early-life tuberculosis infection, that can remain latent for decades before reactivation [72,73].

[10] *Registres matricules du recensement militaire*. Current completion of digitization may be seen at https://francearchives.fr/Map/223684. The specific *bureau de recrutement* where the conscript's military record was created is notified on the BMF certificate.

Figure 7. Conscription record associated with Figures 3,4, 6.



Had the birth certificate (Figure 6) not been available, the conscription record, containing the spouse's name (top extended section), would have also enabled positive identification of the father. Also recorded are diseases, wounds (bottom extended section) and circumstances of the death (middle extended section).

IV. Non-orphan pupilles: a systematic study

The 3,189 / 7,250 pupilles classified as non-orphans are those whose father was not found in the BMF. Their being classified as such may therefore be due to the incompleteness of the BMF, an error on age, a misspelling, a reversal of first and middle names or even imperfect methods of verification of the record linkage. To ensure that these phenomena did not lead to a high classification error rate, that is that the pupilles declared non-orphans were indeed in their vast majority non-orphans, we systematically searched for the fathers of non-orphan pupilles born in two cities, Nîmes and Tarbes, in the local conscription registers (*Registres matricules du recensement militaire*). These conscription registers provide information on wounds received, diseases suffered from, and circumstances of the death (see Figure 7 for an example): they thus shed light on the military experience of all fathers. Nîmes and Tarbes were chosen because the départements they belong to, respectively Gard and Hautes-Pyrénées, not only digitized their conscription registers, but indexed them, making it possible to readily carry out a search by name that, if unsuccessful, we extended to all the départements that similarly have indexed their conscription registers and made them available in the *Grand Mémorial*[11]. Individuals who migrated between military service and the birth of their child are therefore largely excluded from this investigation, which despite this limitation makes it possible to get an idea, rough as it may be, of the proportion of pupilles mistakenly classified as non-orphans, and more importantly of the consequences of such misclassifications on the final dataset analyzed (about which it must be stressed that orphans whose father died of disease were excluded from).

Between August 1, 1914 and December 31, 1915, 171 pupilles were born in Nîmes and Tarbes. On the 90 pupilles classified as non-orphans by the search in the BMF, the conscription record of 68 fathers was retrieved (62 in the local archives, 6 in the *Grand Mémorial*). Among these 68 fathers, 11 died before June 1919: 3 at the front, 8 at the rear (4 of disease, 4 of unknown cause). It is most likely that the 4 fathers who died at home of causes unknown to the army died of disease. Extrapolating the relevant proportion of 3/68, we would therefore have missed 141 orphan pupilles whose fathers did not died of disease among the 3,189 pupilles who were classified as non-orphans by the search in the BMF. On the other hand, among the 4,061 pupilles classified as war orphans by the search in the BMF (see p. 41), examination of BMF certificates revealed that 3,445 of them were born to a father not

[11] Available at http://www.culture.fr/Genealogie/Grand-Memorial.

died of disease. In other words, less that 5% of orphan pupilles useful for the analysis (i.e. whose father did not die of disease) would be 'missed' because we relied on the BMF to identify orphans among pupilles.

V. Definition of a cohort of matched non-orphans (MNOs)

The rule for selecting MNOs

We compared orphans' adult lifespan to that of matched non-orphans (MNOs; individuals not exposed to father's death during WW1) to assess orphan's potential loss of adult lifespan. Because MNOs were selected before call to the BMF, a MNO was associated to each pupille, whether orphan or non-orphan. The rule for selecting MNOs was the following: for each pupille, the MNO was the closest (going upward in the birth register) same-sex birth whose mother's age was that of the pupille's mother (± 2 years). As a consequence, a pupille and his MNO are matched on district of birth, date of birth, sex and motherly age.

Vicinity in birth registers and places of birth

The rule for choosing MNOs implies that a pupille and his MNO are physically close in the birth register. We wondered whether this implicitly paired on the type of birth (homebirth, hospital birth, midwife's house birth). Indeed, the birth certificates were written on the register on a daily basis, as those coming to declare births arrived at the civil registration service. By law, a declarant had to had attended the delivery then come to the civil registration service within three days after the delivery[12]. In peacetime, the declarant of a homebirth was usually the father, but relatives, neighbors, a midwife or a physician, could all assume this role provided they were present at delivery. Were births taking place at hospital/midwives' houses declared one by one, e.g. by relatives accompanying the pregnant women (1), or did an employee or midwife came to declare at once all births that had occurred in the preceding days (2)? In situation (1), there is no autocorrelation in the registers. In situation (2), being born at the same hospital /midwives' house entails being close in the register, so that conversely choosing MNOs physically close in the register also pairs implicitly on type of birth: homebirths will tend to be close to homebirths and births from one hospital/midwife's house close to one another.

[12] *Code Civil*, Book I, Title II, Articles 55 and 56 (1914 edition).

To tackle this question, we studied all the births that were registered from January 1st to January 31st 1915 in two arrondissements of Paris, the 5th (144 births) and 8th (162 births). The births in the 5th district were homebirths and births occurring at 5 different midwives' houses. In the 8th district, the births registered were homebirths and that at one midwife's house and at the Beaujon hospital.

We found situation (2) prevailed: for example, births at the Beaujon hospital were declared once a day by an employee coming to the civil registration service (Figure 8). They form small blocks of 5-6 births surrounded by homebirths. In the 5th, each midwife came every ~ 3 days to declare births: they also form small blocks of 4-5 consecutive births (Figure 9). But matching of MNOs with orphans is performed on sex and motherly age. Also, re-matching was performed for orphans whose MNO died before age 31 (see Chapter 6). As a consequence, an orphan and his MNO do not follow immediately in the birth register. For the 5th and 8th districts, the median distance between an orphan and his MNO is 7 birth certificates, farther than the typical size of the aforementioned blocks. As shown on Figure 10, concordance for pairs of certificates at a distance of 7 is the 'baseline concordance', obtained for a random pair, irrespective of distance between the two certificates.

In summary, the fact that series of hospital/midwife's house births were registered consecutively makes our deterministic rule for choosing MNOs theoretically better than random sampling, but probably in an extremely modest way: orphans and MNOs concord on type of birth at best very slightly more than if MNOs had been chosen at random in the birth register.

Figure 8. Type of birth by registration time, 8th arrondissement of Paris, January 1915.

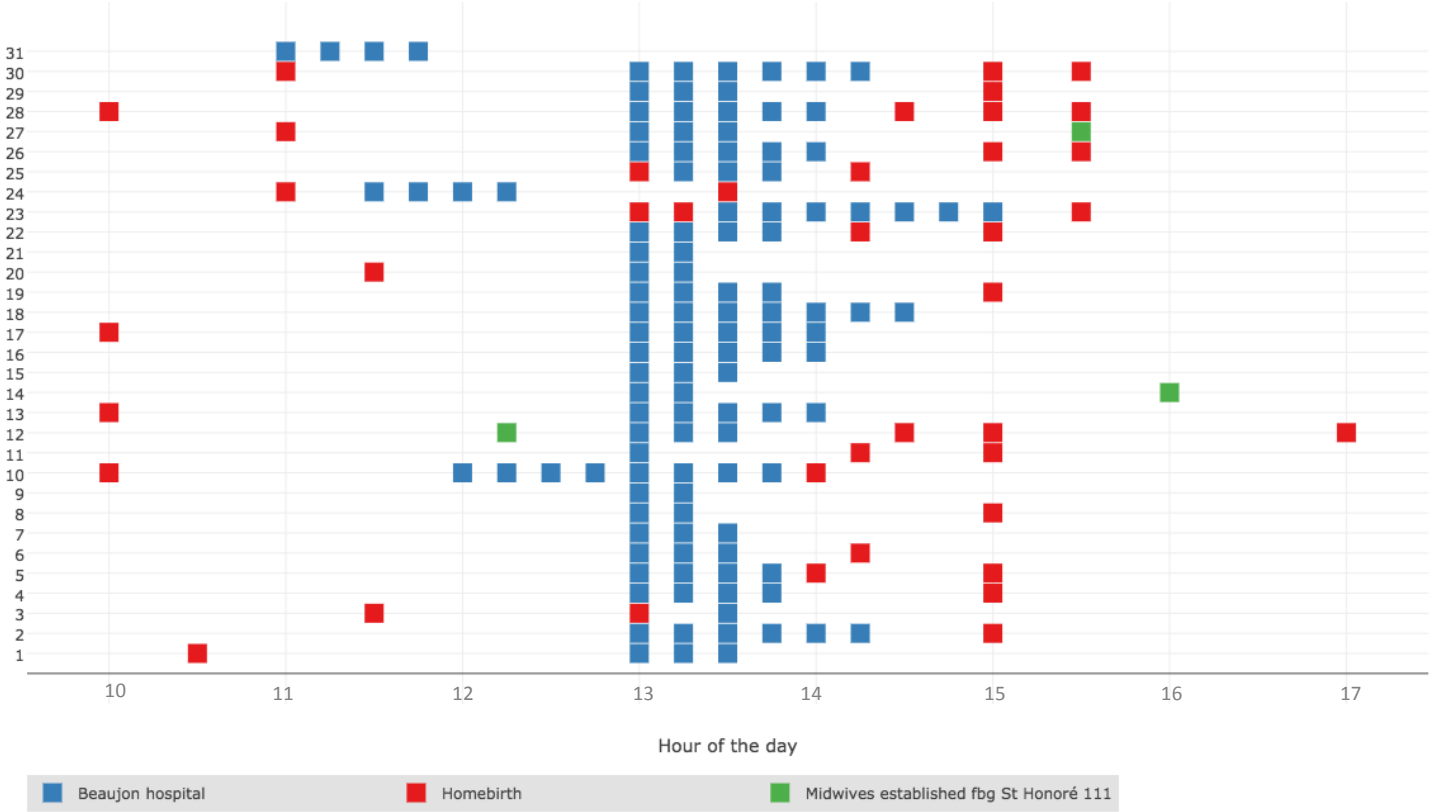


Figure 9. Type of birth by registration time, 5th arrondissement of Paris, January 1915.

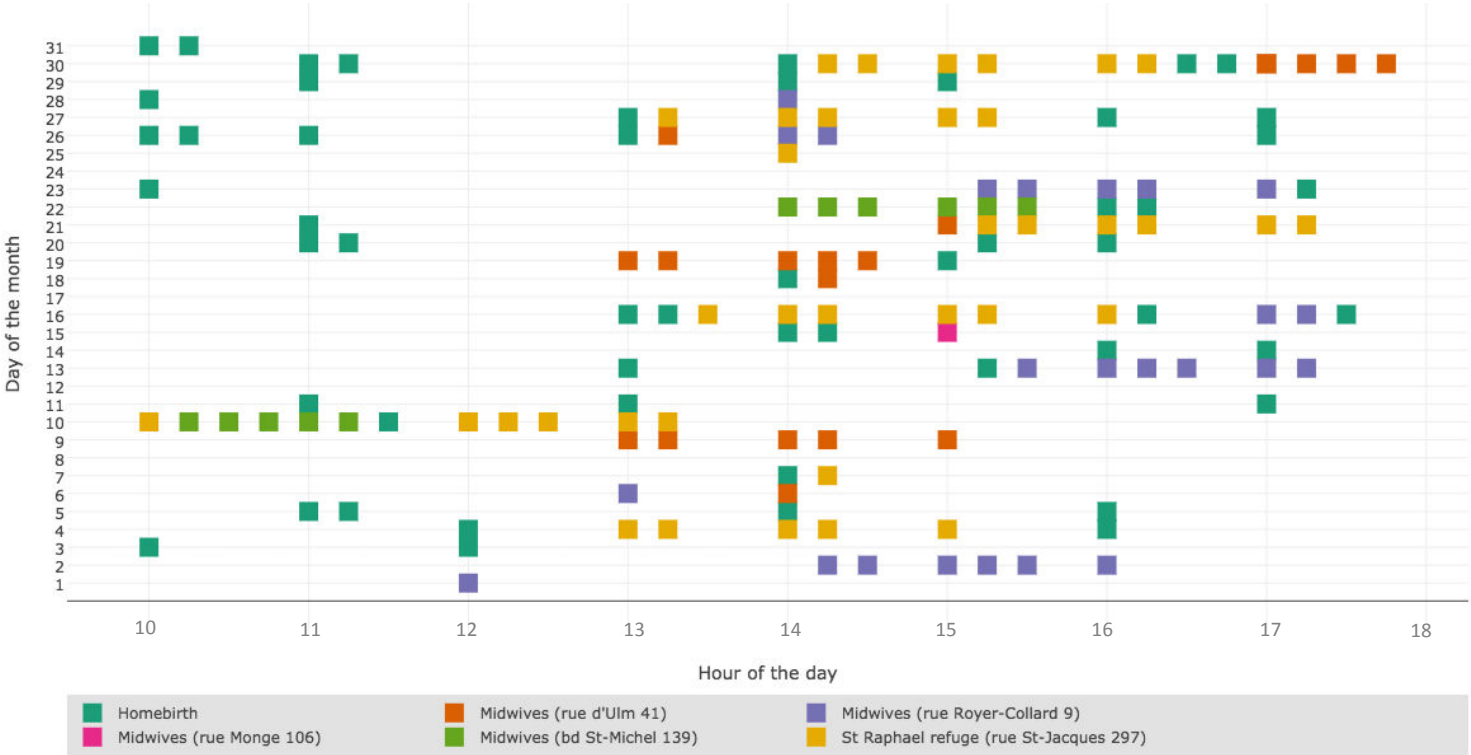
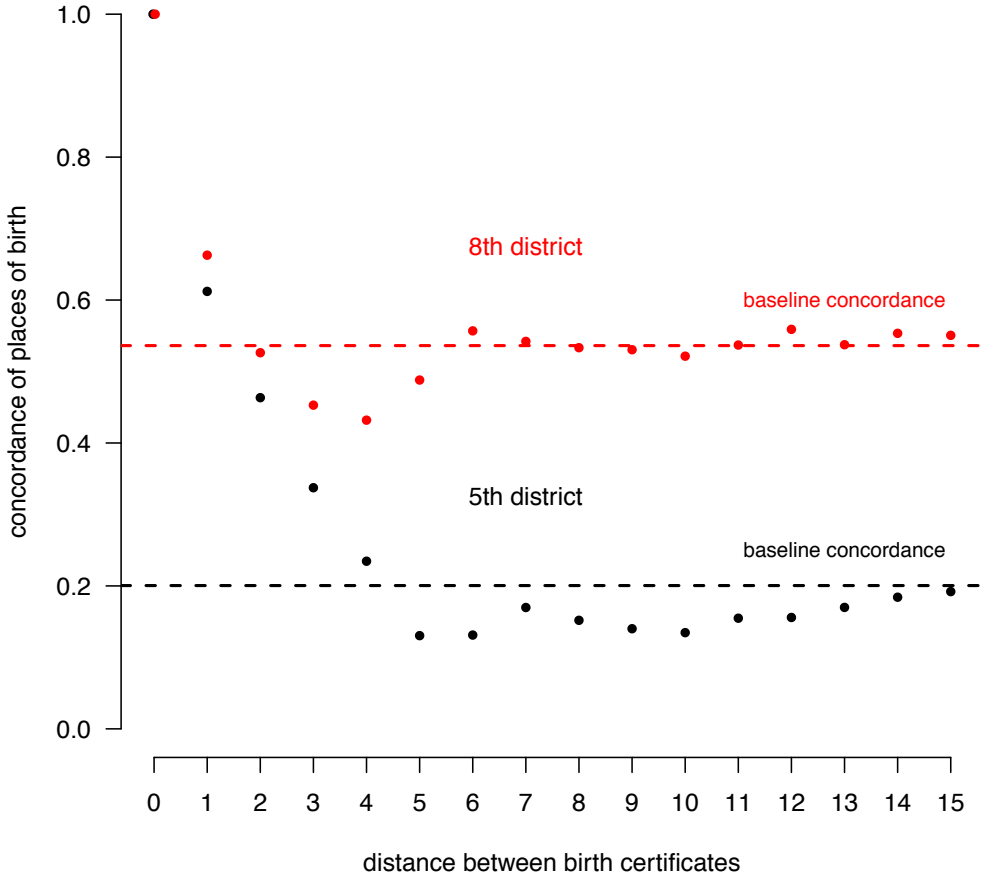


Figure 10. Concordance between pairs of certificates according to distance.

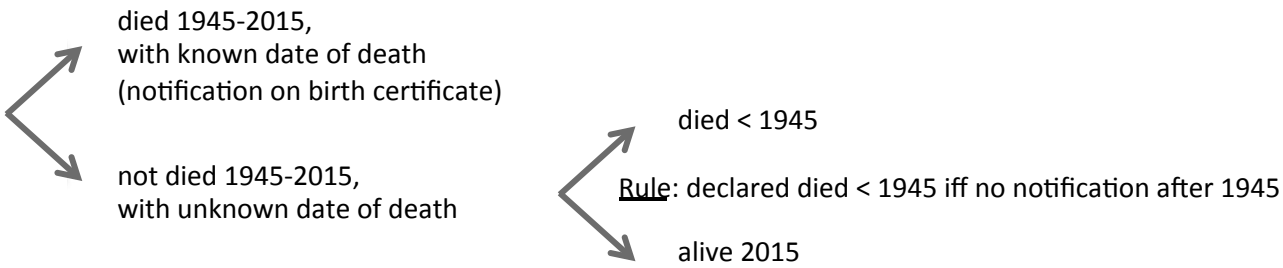


VI. Longevity information used

All included individuals were born between August 1, 1914 and December 31, 1916. Since March 29, 1945, any French city hall continuously updates its birth registers with death notifications received from the 36,000 other city halls covering France and consulates abroad (see Figure 3 for an example). As a consequence, [31; 99] years is the range on which ages at death are known for all included individuals. Death of individuals died abroad are registered and transmitted by consulates. Those fall into three categories: died at an unknown age before 31, died between 31 and 99 (with known age at death), alive at 99. An individual with no life event recorded on his birth certificate after March 29, 1945 (i.e. with no notification of marriage, divorce, guardianship or death after this date) was considered dead before 31.

Conversely, an individual without the notification of death but at least one other life event after March 29, 1945 was considered alive at 99 (Figure 11).

Figure 11. Types of individuals according to date of death.



Those died before 2015 but whose death was not registered on the birth certificate (e.g. due to an undeclared migration or due to an administrative error in transmission of the death notification) were therefore classified as died before 31 y or alive at 99 y. Comparison of the survival curve in MNOs with the nationwide survival curve strongly suggests that such classification errors are of minor importance (see Figure 2 of Chapter 5). In addition, the main analysis for comparison of orphans' and MNOs' longevities (Chapter 6) relied on the distributions of lifespans for those died between 31 and 99 y, i.e. for those whose date of death is effectively observed. Thus, except for unrealistically different non-random administrative errors or migration patterns in MNOs and in orphans, it is extremely unlikely that longevity classification errors can in any way bias the comparison of these two groups.

One caveat is that because orphans are followed conditional on being adopted by the Nation (at around age 5 y), their observed mortality before 31 is that between adoption and 31 y, $P(T < 31|T > adopt) = 1 - e^{-\int_{adopt}^{31} \lambda_{orph}(a)\, da}$, where T is the lifespan and λ_{orph} is the force of mortality. On the other hand, individuals drawn to serve as MNOs are followed from birth onwards, so that their observed probability of death before 31 is $P(T < 31) = 1 - e^{-\int_0^{31} \lambda_{MNO}(a)\, da}$. This means the observed probabilities of death cannot be compared, that in MNOs mechanically being higher than that in orphans except for an extreme difference between λ_{orph} and λ_{MNO}. It also demands care in the comparison of the orphan and MNO groups regarding characteristics that are associated with infant-child mortality, e.g.

illegitimacy or paternal occupations: for instance, given the decrease in the rate of illegitimate children between ages 0 and 5 y due to the higher mortality of illegitimate children, the crude comparison of illegitimacy rates in orphans and MNOs is potentially misleading. The only way to circumvent this problem is to compare the illegitimacy rate in orphans and MNOs alive at the same age – 31 y being the most natural candidate.

Finally, two other points must be mentioned regarding this caveat. First, it is of no consequence on our study of adult mortality: had we been able to include all orphans at birth, not adoption by the Nation, orphans analyzed would have been strictly identical to those analyzed here: in mathematical terms, $E\,(T \mid T > 31, T > adopt) = E(T|T > 31)$ since $(T > 31) \subset (T > adopt)$. The second point is that this caveat makes the cohort of pupilles useless for the study of early life mortality in orphans. While the infant-child mortality of MNOs may be studied using probability of survival to 31 as the outcome variable (see Chapter 5), other data must be collected to test whether orphans experienced a higher infant-child mortality.

VII. Classification of parental occupations and imputation of missing data

Classification of parental occupations

Birth certificates provided us with parental occupations of both pupilles and MNOs. We defined six categories of paternal occupations: i) worker; ii) craftsman; iii) employee; iv) shopkeeper; v) middle class, and vi) upper class. Similarly, we defined eight categories of maternal occupations: i) servant; ii) worker; iii), craftswoman; iv) employee; v) housekeeper; vi) shopkeeper; vii) housewife, and viii) middle and upper class. Housewife ("sans profession") and housekeeper ("ménagère") were occupations so frequently found on birth certificates that we made them independent categories. The classification of occupations was performed with all other information made unavailable.

In order to assess the objectivity of our classification (NT), we drew a random sample of 200 MNOs and asked an external investigator, Prof. François-Joseph Ruggiu (FJR), to classify parental occupations present in this sample. Cross-classifications for paternal and maternal occupations are given in Tables 1 and 2. Cohen's kappa κ was 0.62 for paternal

occupations and 0.80 for motherly occupations[13]. In both classifications, a significant part of the disagreement came from the distinction between workers and craftsmen (see e.g. Table 1): concordance was consequently significantly increased when the workers and craftsmen categories were joined (paternal occupations: κ = 0.72; maternal occupations: κ = 0.90). Given that workers and craftsmen are arguably categories anyway very close, this analysis suggests little inter-rater variability in the classification of occupations.

Table 1. Classification of paternal occupations on a random sample of 200 MNOs.

FJR / NT	Worker	Craftsman	Employee	Shopkeeper	Middle class	Upper class	Unclassified	N
Worker	17	23	7	1	2	-	4	54
Craftsman	-	41	-	1	1	-	-	43
Employee	-	-	36	1	8	-	-	45
Shopkeeper	-	3	-	20	1	-	-	24
Middle class	-	5	1	-	5	1	-	12
Upper class	-	-	-	-	2	19	1	22
Unclassified	-	-	-	-	-	-	-	0
N	17	72	44	23	19	20	5	200

NT: classification used; FJR: external rater.

[13] Cohen'kappa κ varies between -1 and 1 and measures agreement between two raters. Chance agreement between the two yields κ = 0; agreement greater than chance agreement leads to κ > 0. Full agreement corresponds to κ =1. A frequent scale used to label κ values is that proposed in 1977 by Landis and Koch: agreement is slight for κ in 0-0.20, fair for κ in 0.21–0.40, moderate for κ in 0.41–0.60, substantial for κ in 0.61–0.80, almost perfect when κ > 0.81. See 74. Cohen J (1960) A coefficient of agreement for nominal scales. Educational and psychological measurement 20: 37-46, 75. Landis JR, Koch GG (1977) The Measurement of Observer Agreement for Categorical Data. Biometrics 33: 159-174.

Table 2. Agreement with external rater on maternal occupations.

FJR / NT	Servant	Worker	Crafts.	Employee	Housek.	Shop.	Housew.	M&U class	Unclass.	N
Servant	20	-	1	4	-	-	-	-	-	25
Worker	-	16	18	-	-	-	-	-	-	34
Craftswoman	-	-	35	-	-	-	-	-	-	35
Employee	3	-	-	9	-	-	-	3	1	16
Housekeeper	-	-	-	-	31	-	-	-	-	31
Shopkeeper	-	-	1	-	-	10	-	-	1	12
Housewife	-	-	-	-	-	-	45	-	-	45
Middle and upper class	-	-	-	-	-	-	-	1	-	1
Unclassified	-	-	1	-	-	-	-	-	-	1
N	23	16	56	13	31	10	45	4	2	200

Imputation of missing occupations

Maternal occupations were virtually always available on birth certificates. Paternal occupations were missing for illegitimate children and for those officially declared as posthumous children of dead soldiers. To impute the unavailable parental occupations and those we could not classify, we performed multivariate imputation by chained equations (MICE) [76] using district and date of birth, sex, status (alive/dead) at age 31 y (see below), parental occupations, legitimacy, and maternal age. Any analysis using paternal occupations (e.g. that of year of adoption by the Nation according to paternal occupation) was conducted on 10 datasets completed using MICE, then recombined. Because imputations were needed for use of paternal occupations, we also took paternal military rank as a proxy for socioeconomic status (SES) in analyses performed on orphans alone, for whom paternal rank, though less accurate, was virtually always available.

Chapter 2: Applying to the pupille de la Nation status

Passed in July 1917, the law creating the pupille status had been fiercely debated and negotiated by opponents to State intervention in family life [69]. It was widely publicized by local authorities, e.g. by means of posters (Figure 12). No income or wealth condition was set for orphans to become pupille. All widows were thereby incited to request the status for their children. The social reception of this new legal framework for war orphans has not yet been investigated at the individual level. It has been noted, based on contemporary accounts by members of the *Office national des Pupilles de la Nation*, that the higher in the social hierarchy, the lower the willingness to request the pupille status. These accounts additionally suggest that aversion for the pupille status was finally defeated by propaganda, so that high status did not result in lower final adoption rate [69].

Furthermore, it remains unclear how illegitimate children (children born to an unmarried woman) managed to access the pupille status. Once recognized by one's father or legitimized by one's parents (at the occasion of the parents' marriage), request of the pupille status was not any longer more problematic than for a legitimate child. Based on the laws of November 16, 1912 (recognition) and April 7, 1917 (legitimation), recognition and legitimation could also be decided by a tribunal. For an illegitimate child his father had neither recognized nor legitimated by the time of his death – especially a prenatal orphan, judicial action was the only way to establish filiation. In fact, judicial recognition was generally speaking restricted to strictly defined cases (e.g. "unequivocal cohabitation" of the parents or "unequivocal written admission of paternity" by the father), as evidenced by the significant proportion of MNOs whose father remained unknown (see below). Similarly, in judicial legitimation (a special procedure opened in 1917 for war orphans), proof of the unambiguous intention of parents to marry *and* legitimize the child at the time of the father's death was demanded: as a consequence, this option was not opened for an orphan whose father died too early to be privy to his partner's pregnancy[14]. For those whose father remained

[14] Application of the law of April 7, 1917 in this specific situation was the very question raised by a lawsuit, the Ravalec – Flégeau case, ultimately judged in November 1919 by the *Cour de Cassation* (the French court of last resort for civil and criminal matters) and then studied by law reviews and legal treatises.

Flégeau, a soldier engaged to a woman called Ms. Ravalec, was killed in action in June 1916. A month before, during a leave, Flégeau and Ravalec had conceived a child, who was born February 1917. Though nobody

legally unknown, the notion of "soutien de famille" of article 1 of the law of 1917 (see Chapter 1) could instead be advanced and therefore theoretically still made the request possible. Whether these difficulties in practice excluded a significant fraction of illegitimate children from the pupille status is unknown.

Here we quantitatively document these questions. The main variable available is the year of adoption by the Nation (available in the adoption notification on the birth certificate), which we study in relation to individual characteristics of orphans, e.g. paternal military rank retrieved from the Died for France certificate. The SES of orphans not adopted by the Nation found among MNOs as well as the proportion of illegitimate children in orphans and MNOs are also of interest. We find both delayed adoptions and lower final adoption rates at the very top of society (the upper class), but no difference between the other social groups. We also show that i) illegitimate orphans who became pupilles were adopted later than legitimate orphans, ii) virtually no pupille is of unknown father, iii) the orphan pupilles group exhibits a low proportion of illegitimate children (illegitimacy rate), iv) within this group, the illegitimacy rate varied remarkably with age at father's death: it was lowest in orphan pupilles who lost their father in very early prenatal life, then increased continuously. Taken together, these results strongly suggest that, regarding orphans born 1914-1916 to an unmarried woman, those who would not have been recognized or legitimized by their father in peacetime were as could be expected excluded from the pupille status but also that, similarly, an important fraction of those who would have been recognized or legitimized by their father had he not died at war actually did not benefit from the pupille status.

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denied Flégeau was the father of this little girl and intended to marry Ravalec, because Flégeau was not aware of his fiancée's pregnancy, no proof could be given he was also willing to legitimize the child. As a consequence, Ravalec's request was rejected by the *Cour de Cassation*. This account is in short what can be found in legal works – see e.g. 77. Lévy E (1926) Traité pratique de la légitimation des enfants naturels, simples, incestueux ou adultérins. Paris: L. Tenin.

Given the question raised in the current chapter, it was interesting, and indeed crucial, to check whether Ravalec initiated the second available procedure (judicial recognition) and if the child was eventually granted the pupille status. I therefore looked up the judgment rendered by the Court of Appeal of Rennes in 1918 in order to retrieve the child's *commune* of birth and her birth certificate, the examination of which proved flabbergasting: not only paternity of Flégeau was never judicially established, but his daughter was legitimated by another man, who married Ravalec in 1920. Accordingly, Flégeau's daughter, who is known to have reached adulthood (marriage and death notifications are found on her birth certificate), never became a pupille. I thank the *Archives départementales d'Ille-et-Vilaine* for transmission of the Court of Appeal's judgment, as well as the civil registration service that transmitted the relevant birth certificate.

Figure 12. Propaganda poster at the occasion of Bastille Day 1918.

OFFICE NATIONAL DES PUPILLES DE LA NATION

RÉPUBLIQUE FRANÇAISE

14 Juillet 1918

LOI DU 27 Juillet 1917

FRANÇAISES, FRANÇAIS,

La loi du 27 Juillet 1917, sur les Pupilles de la Nation, votée à l'unanimité par la Chambre des Députés et par le Sénat, est une loi de liberté, de fraternité, de respect mutuel, de concorde et de solidarité sociales. - **Elle sera appliquée dans cet esprit.**

C'est une Loi de Liberté

La Nation, en adoptant les Orphelins de la Guerre, ne veut prendre ni la place de leurs mères, ni celle de leurs tuteurs naturels ; elle ne retire aux parents aucun droit, elle ajoute seulement sa protection à la leur. De plus, l'Etat autorise toutes les Œuvres existantes et offrant les garanties suffisantes à exercer leur patronage sur ces orphelins.

C'est une Loi de Fraternité

et non pas d'assistance. Elle est faite pour le riche comme pour le pauvre. L'Etat a contracté une dette sainte envers les Pupilles de la Nation. La loi assure à ces enfants inégaux par la fortune le même titre d'honneur. Elle les rapproche les uns des autres par un brevet de noblesse qui leur est conféré et qui rappelle le sacrifice de leurs pères tombés pour le salut commun.

C'est une Loi de Respect Mutuel

La volonté du père défunt ou, à son défaut, la volonté de la mère, sera rigoureusement observée. Leurs traditions, leurs croyances, leurs sentiments seront scrupuleusement respectés, notamment en ce qui concerne le genre d'éducation à donner à l'enfant. La loi s'efforcera avant tout de maintenir les traditions de la famille française dont les droits seront sauvegardés et dont elle favorisera la renaissance.

C'est une Loi de Concorde et de Solidarité

Elle a pour but essentiel de pratiquer l'union sacrée en accomplissant la plus noble des missions : la protection et la formation de l'enfant. La meilleure manière d'honorer ceux qui ne sont plus, n'est-ce pas de continuer cette union, partie intégrante de la force morale de la Nation, née d'un amour profond de la Patrie et scellée dans le sang des batailles ?

FRANÇAISES, FRANÇAIS,

Le 14 Juillet 1790, dans la grande fête de la Fédération la France entière, par les Représentants de toutes ses provinces, jurait au Champ-de-Mars, sur l'autel de la Patrie, de rester unie et indivisible dans la Défense de la Liberté reconquise.

Le 14 Juillet de l'an dernier, par l'émouvante revue des drapeaux, on a voulu glorifier ceux qui luttent avec tant d'héroïsme sous les plis du symbole prestigieux de la Patrie.

Pour le 14 Juillet de cette année, peut-on trouver un symbole plus touchant qu'une manifestation solennelle en l'honneur de ceux qui sont morts pour la France, et dont les enfants adoptés par la Nation vont devenir des frères et des sœurs ?

Voilà le sens et la portée exacts de la Loi du 27 Juillet 1917 sur les Pupilles de la Nation.

Elle peut et doit réunir tous les Français dans une communauté étroite des esprits et des cœurs.

LE CONSEIL SUPÉRIEUR DE L'OFFICE NATIONAL :

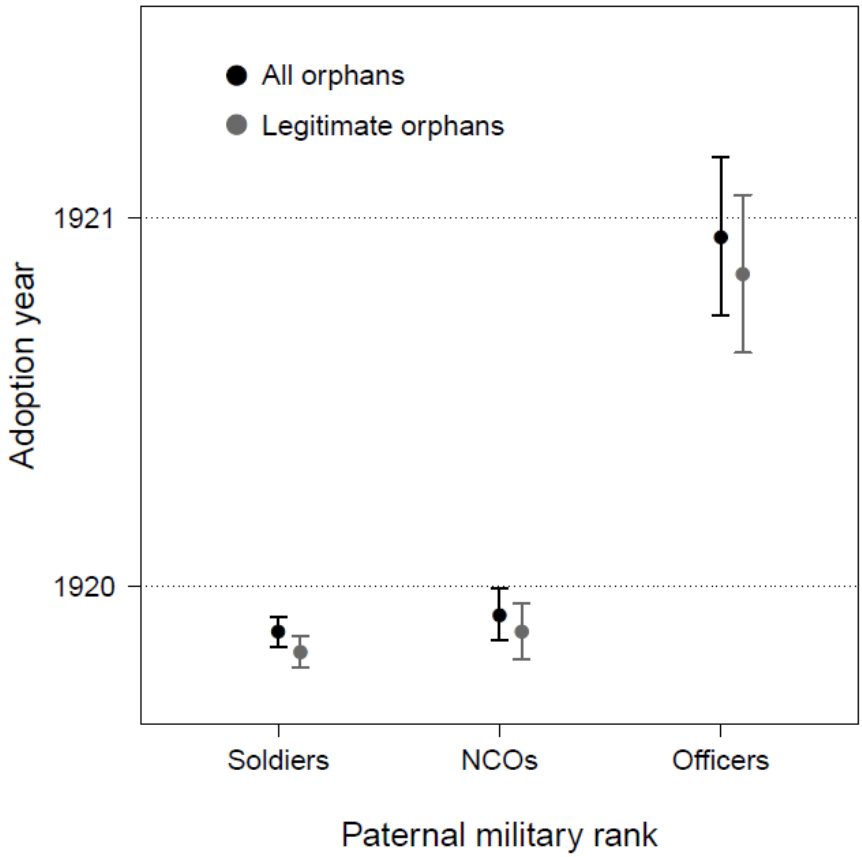
Downloaded from 14-18.crdp-limousin.fr/.

I. Association between socioeconomic status (SES) and propensity to request the pupille status

SES and year of adoption

Orphans born to an officer were adopted ~ 1 year later than those born to a soldier or non-commissioned officer (NCO) (analysis of variance: p-value = 5.1 x 10^{-13}). Adoption years for soldiers' and NCOs' offspring were indistinguishable (p=0.56). These results held when the analysis was restricted to legitimate children (Figure 13)[15].

Figure 13. Year of adoption by the Nation according to paternal military rank.



Results are given as mean adoption year ± standard error (s.e.)

[15] The paternal military rank was missing or could not be classified for n=11 orphans. This analysis of variance is thus based on the 4,050 / 4,061 orphans with known paternal rank.

To give adjusted effects of paternal military rank on adoption year, we fitted a generalized additive model (GAM) with Gaussian errors:

$$\mathrm{AY} = \alpha + Rank + Leg + Sex + Td + f_1(MA) + f_2(PA) + f_3(db) + f_4(dd) + Pla + \varepsilon \quad [1]$$

AY is the adoption year, α the intercept, *Rank* the military rank of the father, *Leg* the legitimacy of the birth, *Sex* the infant's sex, *Td* the paternal type of death (killed in action, lost in action, died of disease, other), *MA* and *PA* the maternal and paternal ages at the infant's birth, *db* the infant's date of birth, *dd* the father's date of death, *Pla* is a normal random intercept controlling for district/city of birth and ε the error term. Smooth terms are penalized cubic regression splines with respectively 8 (f_1, f_2) and 15 degrees of freedom (f_3, f_4). Model [1] was adjusted on the 3,978 / 4,061 orphans of the full dataset (7,250 pupilles) with no missing data on parental ages, father's rank and type of death (see Chapter 4, Table 1 for their baseline characteristics).

Parametric terms of model [1] are given in Table 3. The same ~ 1-year difference in adoption year was retrieved between officers' offspring on the one hand and that of NCOs and soldiers on the other hand. Additionally, we found that illegitimate children were adopted 6 months after legitimate children. Adjusted district/city of births effects are shown on Figure 14: regional differences are visible (e.g. early adoptions in Bordeaux), likely due to varying celerity of local tribunals, as well as delayed adoptions in the wealthiest districts of Paris (7th and 16th districts). Paternal date of death and infant's date of birth were found to have moderate linear effect on adoption year (1-month decrease in adoption date for each 1-year delay in father's death and 8-month delay for those born December 1916 compared to those born August 1914). Interestingly, young maternal age was found to delay adoption by the Nation (Figure 15), suggesting older mothers were better informed or swifter to take action.

Table 3. Parametric terms in model [1].

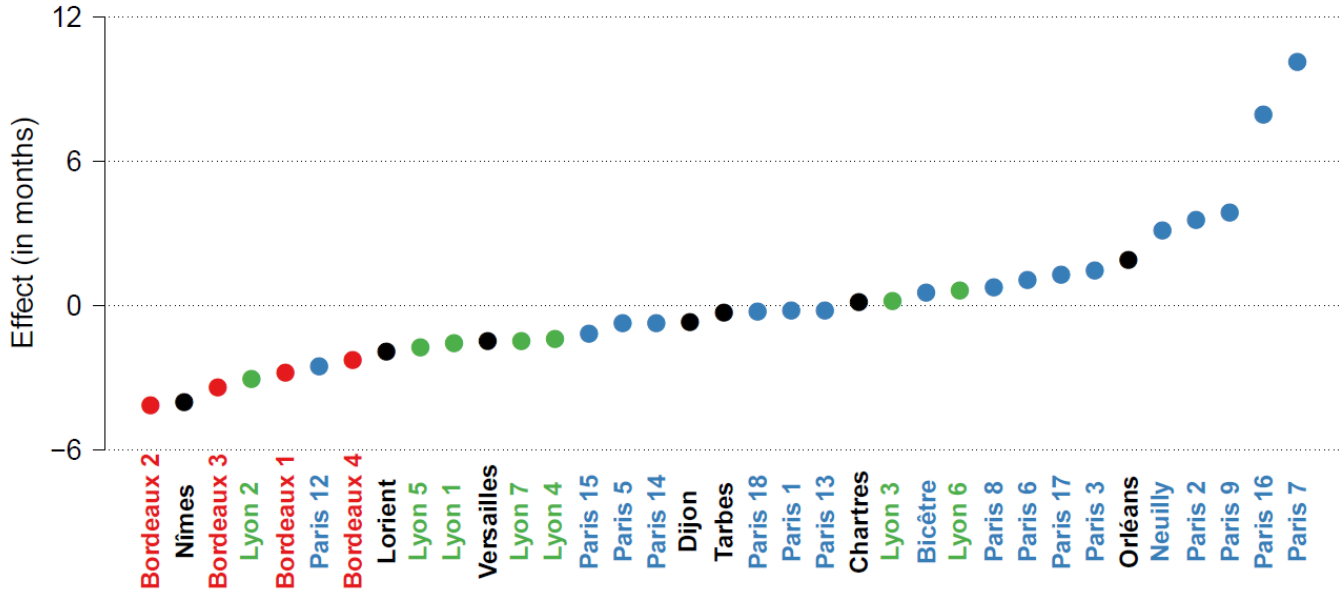
	Adjusted effect (in months) on adoption year	p-value
Sex		
F	0 (ref)	0.48
M	-1 ± 1	
Legitimacy		
Legitimate	0 (ref)	1.8×10^{-4}
Illegitimate	6 ± 2	
Paternal Military rank		
Soldier	0 (ref)	2.9×10^{-13}
NCO	1 ± 1	
Officer	13 ± 2	
Paternal Type of death		
Killed in action	0 (ref)	
Lost in action	5 ± 2	4.7×10^{-13}
Died of disease	9 ± 1	
Other	16 ± 4	

Effects are given ± standard error

Table 4. Significance of smooth terms in model [1].

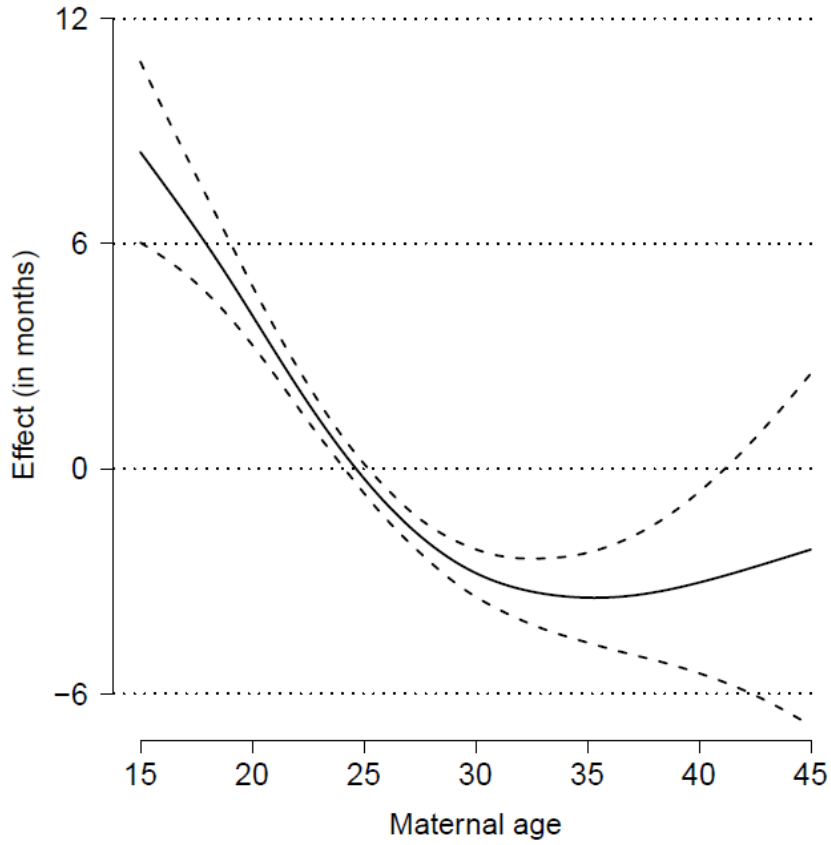
	Maternal age (MA)	*Paternal age (PA)*	*Date of birth (db)*	*Paternal date of death (dd)*
p-value	5.8×10^{-6}	0.49	8.5×10^{-4}	0.02

Figure 14. Adjusted effect of district of birth on adoption year.



Paris districts are in blue, Lyon districts in green and Bordeaux sections in red.

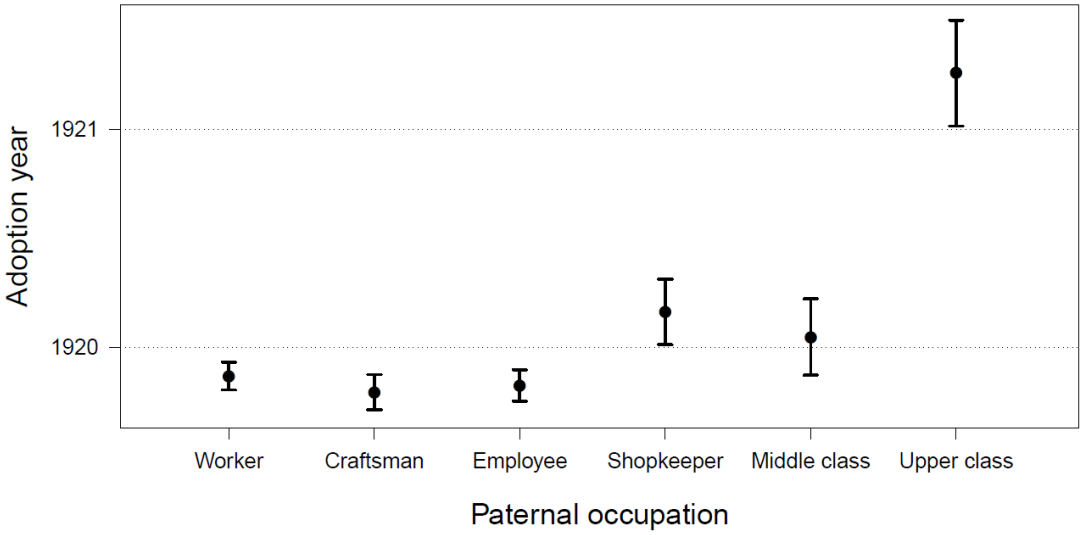
Figure 15. Adjusted effect of maternal age at infant's birth on adoption year.



Function f_1 of model [1] is plotted ± s.e.

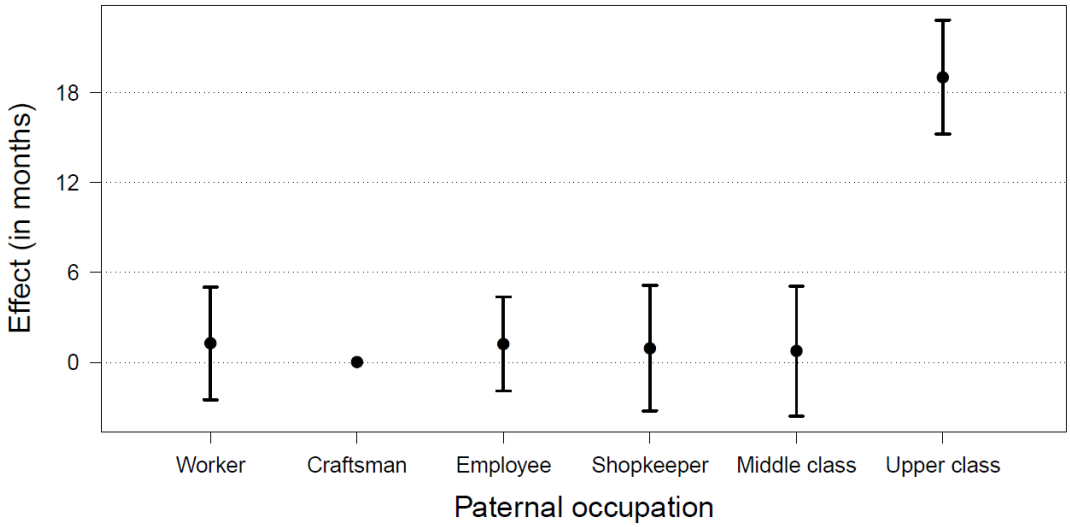
In order to refine the result obtained with military rank as a proxy for SES, we repeated the analysis with paternal occupations. Again, adoption was found postponed for those high in the social hierarchy: those born to an upper class father were adopted ~ 1.5 years after the rest of orphan pupilles (analysis of variance combined over the 10 completed datasets: $p = 4.1 \times 10^{-5}$; Figure 16). Variation between the other groups was very low (Figure 14). This was retrieved in a GAM with the same predictor as model [1] except for paternal military rank, replaced by paternal occupation (Figure 17).

Figure 16. Year of adoption by the Nation according to paternal occupation.



Mean ± s.e.

Figure 17. Adjusted effect of paternal occupation on adoption year.



Effect ± s.e. Reference group: craftsmen.

SES and final adoption rate

Assessing whether differences in final rate of adoption existed evidently cannot be achieved by the study of pupilles, who by definition were all those eventually adopted by the Nation. By contrast, the study of individuals drawn as MNOs in Paris and Bordeaux here proves useful. MNOs' fathers were searched for in the BMF to ensure that no war orphans were used as comparators of pupille orphans' longevity. By comparing the distribution of paternal occupations in MNOs identified as war orphans (those being a sample of non-pupille orphans) and in pupille orphans, one can assess the association between SES and final rate of adoption. As stressed in the previous chapter (*Longevity information*), comparison is only valid if the paternal occupations are compared in groups of pupilles and MNOs that attained a common age – 31 y being the most natural candidate.

5,671 non-pupilles births were initially drawn from birth registers to serve as MNOs. Among the 3,365 MNOs with known father and alive at 31 y, 35 (1%) were identified as war orphans (MNO orphans). Paternal occupations of these 35 MNO orphans were different from that of pupille orphans of the same cities alive at 31 y (median p-value of Fisher's exact test over the 10 completed datasets: 2.5×10^{-4}). In particular, 30% of MNO orphans were born to upper class fathers, versus 7% of pupille orphans (Table 5). No difference was found between MNO orphans and pupille orphans after removal of those born of an upper class father (median $p = 0.25$). The conclusion is straightforward: not only did upper class families delayed their offspring being adopted by the Nation, but they also achieved lower final adoption rate.

Table 5. Paternal occupations in the 35 MNOs alive at 31 years identified as war orphans compared with pupilles orphans.

	Worker	Craftsman	Employee	Shopkeeper	Middle class	Upper class
MNO orphans (n=35)	6 (17%)	3 (8%)	12 (34%)	2 (5%)	2 (6%)	11 (30%)
Pupille orphans (n= 2791)	828 (30%)	521 (19%)	879 (32%)	244 (9%)	130 (5%)	190 (7%)

II. Accessibility of the pupille status for illegitimate children

Illegitimate orphans who became pupilles were adopted later than legitimate orphans, with an adjusted difference of 6 months (Table 3).

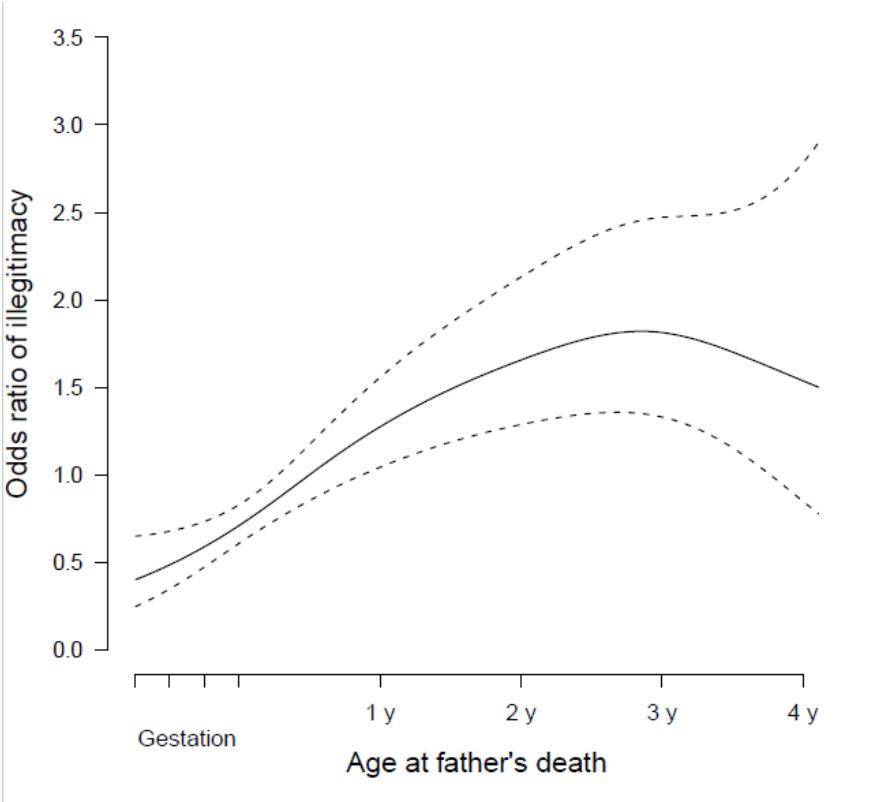
Regarding illegitimacy rate, pupilles and, among them, pupille orphans can be compared with MNOs. The remainder of this section therefore focuses on the pupilles born in Paris and Bordeaux, for whom MNOs are available. As previously mentioned, a valid comparison of legitimacy rates can only be achieved on pupilles and MNOs that have attained the same age – 31 being a natural choice. Among the 3,694 MNOs alive at 31, 8.9% (n=329) were of unknown father (illegitimate children never recognized or legitimized by their father). Among the 3,365 MNOs alive at 31 with known father, 541 were illegitimate children recognized or legitimized by their father at some point in time. By strong contrast to what was observed in MNOs, virtually no children with unknown father (i.e. never recognized or legitimized) were found in pupilles born in the same cities and alive at 31 (23 / 4,934= 0.47%). This result indicates that in our cohort born 1914-1916, proof of filiation was in practice needed before the pupille status was granted.

The question is therefore simple: to what extent filiation with the dead father could be established for illegitimate orphans? Where only those 'predestined' to remain of unknown father excluded from the pupille status? Among the 2,365 orphan/MNO pairs of the final dataset analyzed in Chapter 6, the illegitimacy rate was 9.6% in orphans and 16.9% in MNOs ($p=1.1 \times 10^{-13}$). MNOs with unknown father were removed from the analysis, so that this marked difference between pupille orphans and MNOs in the final dataset analyzed does indicate that illegitimate children whose filiation would have been established had the father not died were indeed left aside of the pupille status. Furthermore, the illegitimacy rate was 4.0% percent in prenatal orphans and 11.7% percent in postnatal orphans, but 15.8% and 17.3% in their respective MNOs. To further investigate the variation of illegitimacy with age at father's death, we adjusted a GAM with the error distribution and link function of the logistic regression:

$$\log\left(\frac{\pi}{1-\pi}\right) = \alpha + f_1(ad) + f_2(db) + f_3(MA) + f_4(PA) + Rank + Sex + Td + Pla \qquad [2]$$

where π is the probability of being illegitimate, *ad* the infant's age at father's death, the other notations being that used in model [1][16]. Functions f_1- f_4 are penalized cubic regression splines with 15 (f_1, f_2) and 8 (f_3, f_4) degrees of freedom. We found the odds-ratio of illegitimacy varied continuously with age at father's death ($p = 1.8 \times 10^{-5}$): the lowest illegitimacy rate was obtained for an early loss of father during pregnancy, while the association of the illegitimacy rate with age at father's death was found roughly flat after ~ age 2 y (Figure 18). Interestingly, the observed illegitimacy rate for those > age 2 y at father's loss was 16.5%, remarkably close to that in MNOs (16.9%), an observation that indicates explaining the low illegitimacy rate in pupilles orphans fully comes down to explaining the variation of the illegitimacy rate with age at father's death. This variation seems hard to explain by a phenomenon other that the mounting difficulties created by a precocious loss of father.

Figure 18. Adjusted association between age at father's death and legitimacy.



Dotted lines: 95% CI.

[16] Age at father's death and paternal date of death are highly correlated (Pearson correlation coefficient= 0.89) so that keeping the latter in model [2] would have resulted in an unstable estimate of the effect of age at father's death.

Chapter 3: Two demographic pitfalls

Two mechanisms relate longevity with date of birth in the context of 1914 France:

- season of birth has been shown to be associated with adult longevity [78-80]: for instance, the life expectancy at age 50 of those born in autumn was ~ 7 months higher than that of those born in the spring for Austrians died 1988-1996 [79]. This association has been interpreted as long-reaching consequences of early life nutritional and disease environments – that both usually vary throughout the year. Seasonal effects on health are already visible at birth on pregnancy outcomes (gestation length and birth weight) [81];
- the population of the included cities have varied during the period considered (August 1st 1914- December 31st 1916). The most important types of population changes for the period are to our knowledge: 1- emigration from Paris at the beginning of the war; 2- for all cities in non-invaded regions, and especially Paris, an influx of war refugees from northeastern regions. Both types of population changes are documented in the first two sections of the chapter.

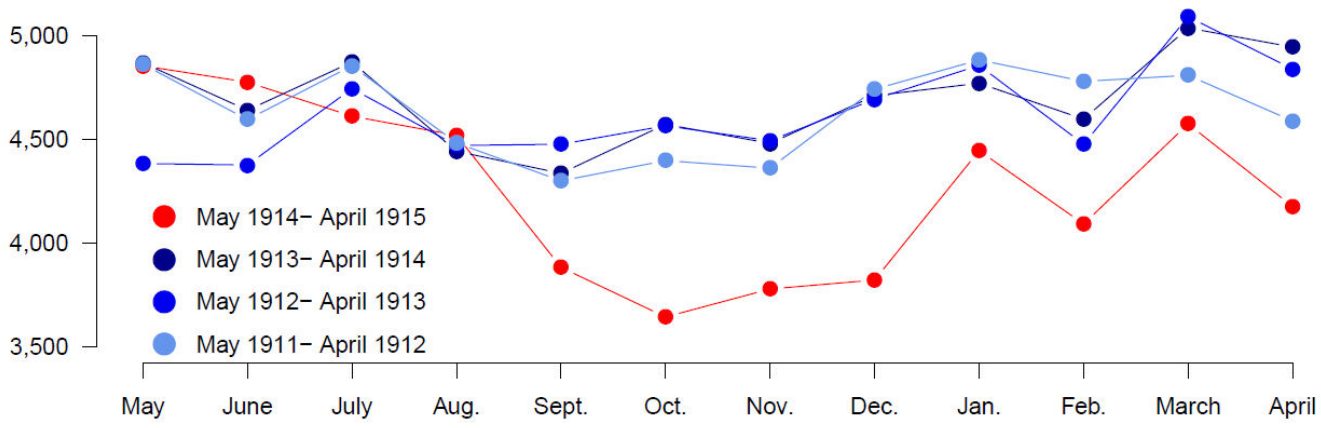
As detailed in the third section of this chapter, the distribution of dates of births indeed differs in orphans and the general population of birth, as well as between prenatal and postnatal orphans. As a consequence of the mechanisms mentioned above linking longevity with date of birth, those systematic differences in dates of birth may result in estimates of losses adult lifespan biased of several months if comparators are not chosen with care. Our choice of MNOs, born at the same time in the same district/city, ensures that their distribution of dates of birth follows closely that of their matched orphans and that the pitfalls of changing environmental conditions and changing underlying populations are avoided.

I. Migrations: the flee from Paris

After having invaded Belgium, the German armies advanced rapidly across North-Eastern France and arrived at the outskirts of Paris by late August 1914. This led the civilian and military authorities, but also the Parisian population, to believe that Paris would be

besieged, as had been the case during the Franco-Prussian War of 1870. As a consequence, the Government left to Bordeaux on the night of September 2 to 3. More crucially for population studies, parts of the Parisian population similarly sought to escape the repetition of the ghastly siege of 1870-71. Professor Adolphe Pinard, a member of the *Académie de Médecine*, for example noted that: "fear of invasion spurred the well-known exodus of a million inhabitants of Paris, among whom were few wretches"[17] [82]. Whether there were many pregnant women among those fleeing can be assessed in a simple way, by the study of the monthly number of live births in Paris in the first months of the war. Births until May 1915 are pre-war conceptions, whose number is therefore expected to be comparable with same-month values of the previous years in the absence of migrations of women delivering. As shown on Figure 19, the number of birth indeed decreased sharply as early as September 1914: the time series remained at ~ 85% of its expected value until December 1914, before a partial recovery in January 1915. This strongly suggests that a significant proportion of pregnant women left Paris in the first months of the war.

Figure 19. Monthly number of live births in Paris.



Source: *Annuaire statistique de la ville de Paris*, years 1911, 1912, 1913, 1914, 1915-1918; available at: bibliotheques-specialisees.paris.fr

[17] « la crainte de l'investissement détermina le fameux exode d'un million d'habitants de Paris, parmi lesquels se trouvaient peu de misérables. »

II. Migrations: war refugees from invaded regions

Another migratory consequence of the German breakthrough, and later of the establishment of trench warfare on French soil, was that it set in motion masses of inhabitants of the invaded regions. These refugees, fleeing combats as well as atrocities committed against civilians, real and alleged, moved by successive waves throughout the war [83]. While a portion of refugees remained in the Northern part of France, all French regions witnessed arrivals, and Paris in particular played an important role: in October 1915, about 110,000 French refugees were numbered in the Seine département[18]. Again, the question we must confront is more specific than this large-scale phenomenon: were pregnant women among those fleeing the invasion numerous enough to significantly be detected in our cohorts of orphans and MNOs?

Birth certificates provide the address of the parents, but counting those who registered as inhabitants of invaded regions will grossly underestimate the true size of the migration flow[19]. Once effectively settled in his host city, a refugee cannot be distinguished by his address from the long-established inhabitant. On the other hand, Died for France Certificates, available for orphans only, provide a more robust approach. These certificates indeed mention the place where the father was registered for conscription by military authorities (i.e. place of military service, see Figure 4). By classifying orphans based on paternal place of military service (local, non-invaded regions, invaded regions), one can try and indirectly detect the flow of refugees from the invaded regions.

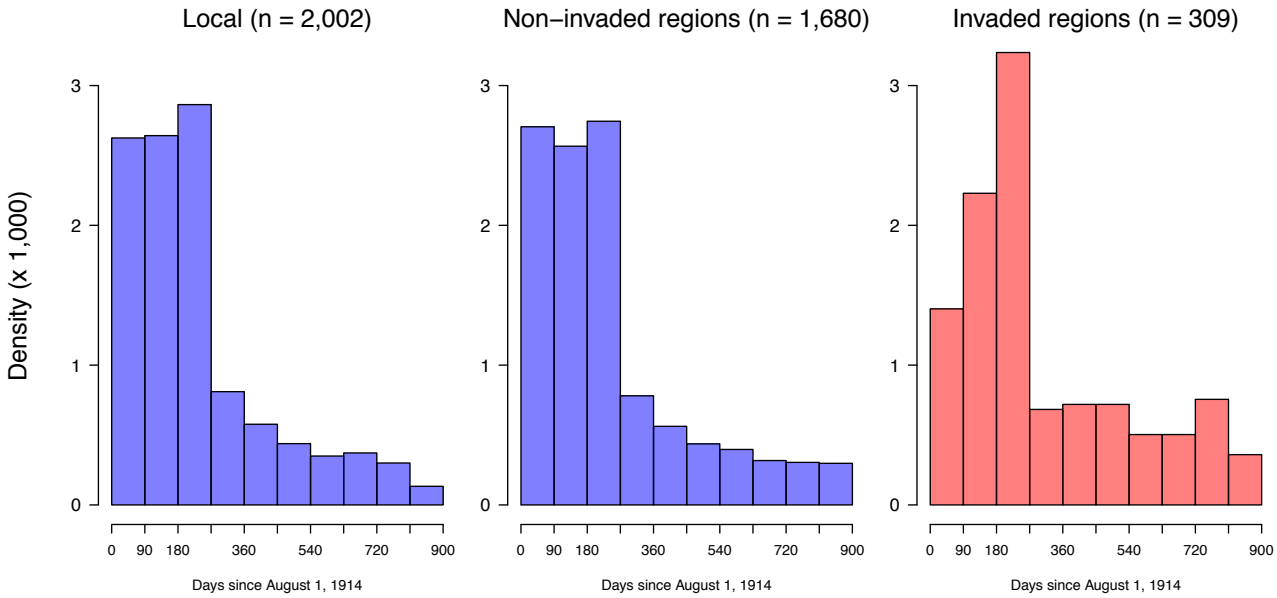
A marked difference in the distribution of dates of birth is actually visible for those whose father originated from invaded regions versus from local and non-invaded regions (Kolmogorov-Smirnov test: $p = 3.6 \times 10^{-7}$): the arrival of refugees during the first months of the conflict is visible on Figure 20 [20]. No difference was found between the local and non-invaded regions categories ($p = 0.63$).

[18] Belgians also fled to France: in October 1915, ~ 150 000 Belgian refugees were on French territory according to the Ministry of the Interior. Among them, ~ 20 000 were in the Paris region. See 84. Dupâquier J (1988) La population pendant la Première Guerre mondiale. In: Dupâquier J, editor. Histoire de la population française 4, De 1914 à nos jours. Paris: P.U.F.

[19] Maps of parental addresses as given by birth certificates, though they underestimate them, hint at those migrations. See Chapter 6, Fig. S3, panel c.

[20] A caveat is that migration may have preceded delivery by several months so that the exact timing of migrations cannot be established based on Figure 20.

Figure 20. Date of birth of orphans according to place of military service of the father.



Fathers were classified according to place of military service: local if the place of military service was the orphan's place of birth, invaded regions if the place of military service was located in an invaded département, non-invaded region otherwise[21]. The 70 orphans whose paternal place of military service was missing were removed from this analysis.

[21] The départements listed in the "invaded regions" category are: Aisne, Ardennes, Marne, Meurthe-et-Moselle; Meuse, Nord, Oise, Pas-de-Calais, Somme, Territoire de Belfort and Vosges. Those were partially or totally occupied for varying durations during the war.

III. Date of birth and the probability of father's loss

Observed trends in probability of fatherly loss

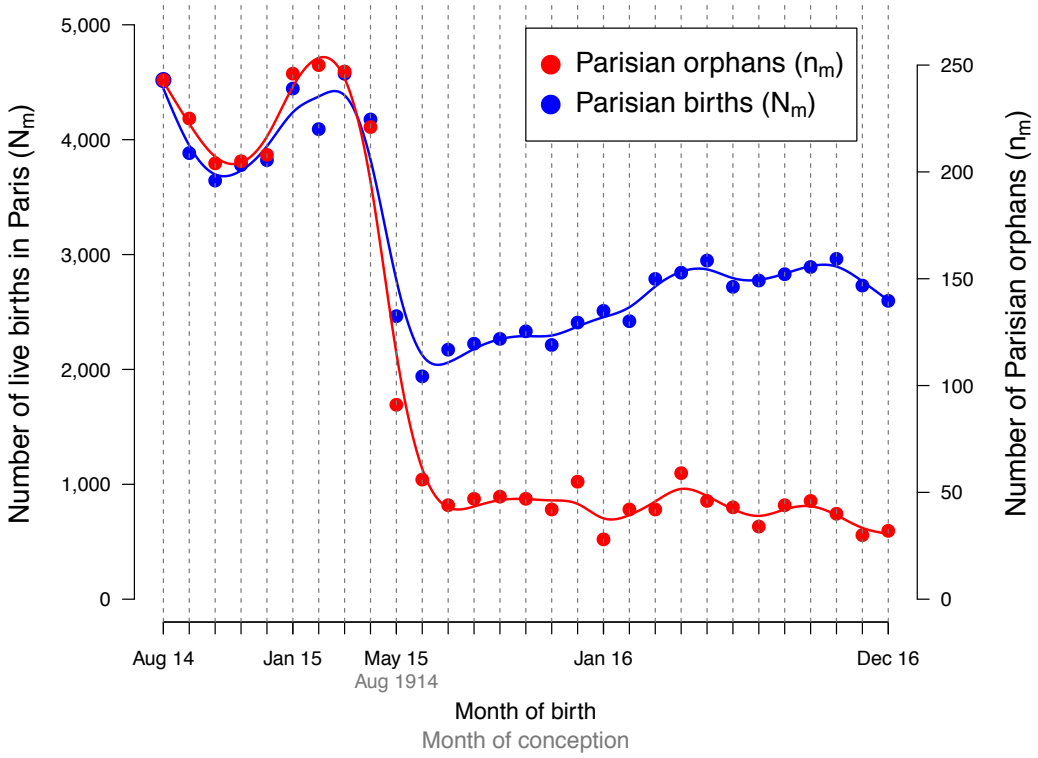
Figure 21 shows the time series of the monthly number of births in Paris (abbreviated N_m) and that of the 2,965 pupille orphans born in the 15 included arrondissements of Paris (abbreviated n_m)[22]. Two features emerge:

- a fall in fertility occurred in May1915, corresponding to a fall in conceptions nine months before, in August 1914, when soldiers were mobilized and left their families;
- the orphans' time series decline in May 1915 is stronger than that of the Parisian series. This indicates that exposure to risk and decrease in the probability to conceive were positively correlated. Indeed, those who went to the front took risks, and precisely because they went to the front, their fertility fell more abruptly. The first characteristic determining exposure to risk was age: the probability of death at war was highest for young men and the largest drop in fertility was consistently observed in young age groups (Figure 22). A noteworthy consequence is that orphan's fathers are younger than non-orphans' fathers (see Appendix 2 for a detailed analysis of paternal ages). Also, some specific occupations happened to be protective of both life and fertility because of vital importance at the rear[23].

[22] The *Annuaire Statistique de la Ville de Paris* gives the monthly number of live births by maternal arrondissement of residence, not arrondissement of birth. Thus, the 'ideal' variable, the monthly number of births in the 15 included arrondissements, could not be computed. We therefore took instead all Parisian births, a figure that incorporates the births in the 5 arrondissements not included in our study (4th, 10th, 11th, 19th, 20th). It is also critical to note that pupilles orphans are those who survived to adoption by the Nation (~ age 5), while the number of Parisian live births obviously include those to be struck by infant-child mortality. Finally, children who remained of unknown father were, as explained in the previous chapter, excluded from the pupille status. As a consequence of these facts, the number of included pupille orphans as a proportion of all Parisian births (n_m/N_m ratio), is a gross underestimation of the proportion of orphan births. Yet there is no reason to assume that the former does not inform on the time trend of the latter, that is the sole focus of this section.

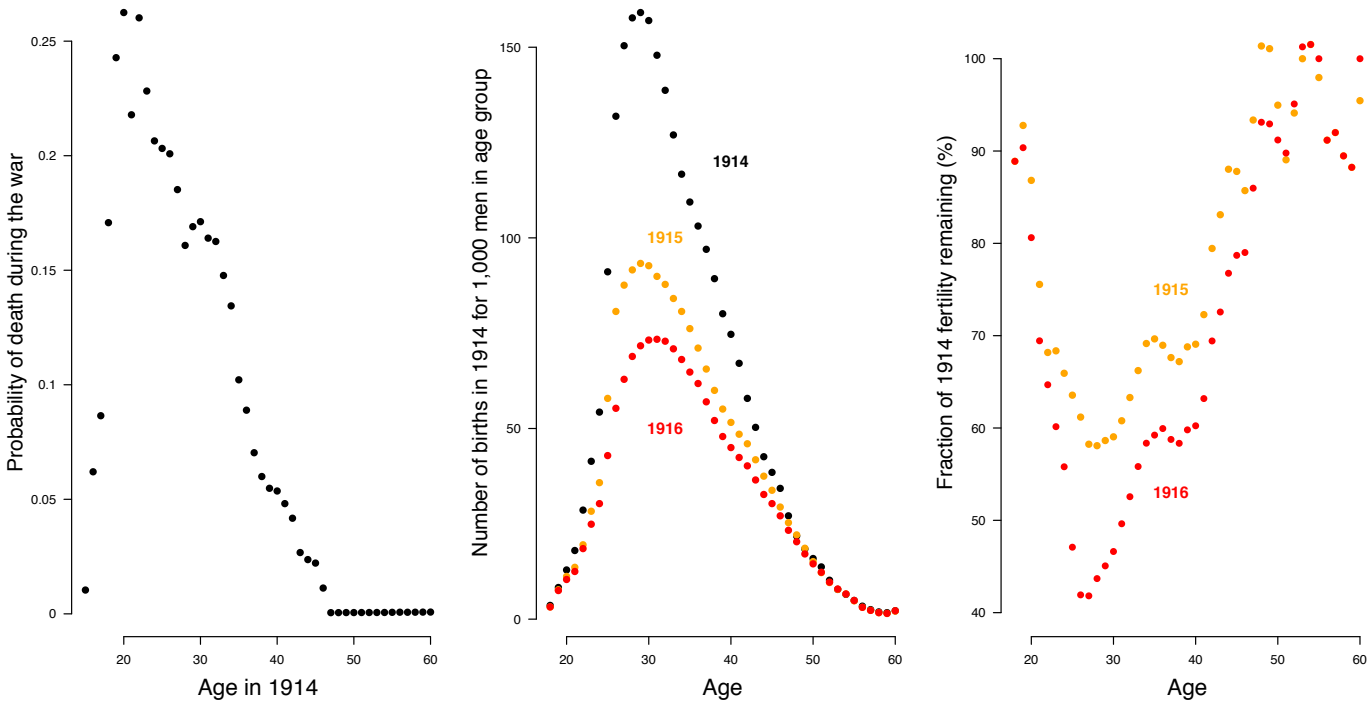
[23] This was the case of railroad workers, critical for transport of troops and supplies. We found evidence for lower risk of railroad workers by comparing the frequency of the expression 'railroad' ('chemin de fer') in paternal occupations of orphans and MNOs in the final dataset analyzed in Chapter 6: mention of railroad was found 23 times in orphans' paternal occupations versus 71 times in MNOs' paternal occupations ($p=9.8 \times 10^{-7}$). Other occupations could reduce risk without maintaining fertility: for instance, artillery officers were more protected than infantry officers, without necessarily having more frequent occasions to conceive.

Figure 21. Monthly number of live births in Paris and monthly number of pupille orphans' births in the 15 Parisian arrondissements included.



Line: cubing smoothing spline.

Figure 22. Cohort-specific probability of death at war (left), age-specific male fertility rates in 1914-1916 (middle) and age-specific fall in male fertility between 1914 and1916 (right).



Sources of data: see Appendix 2.

Figure 23. Evolution of the n_m / N_m ratio over time.

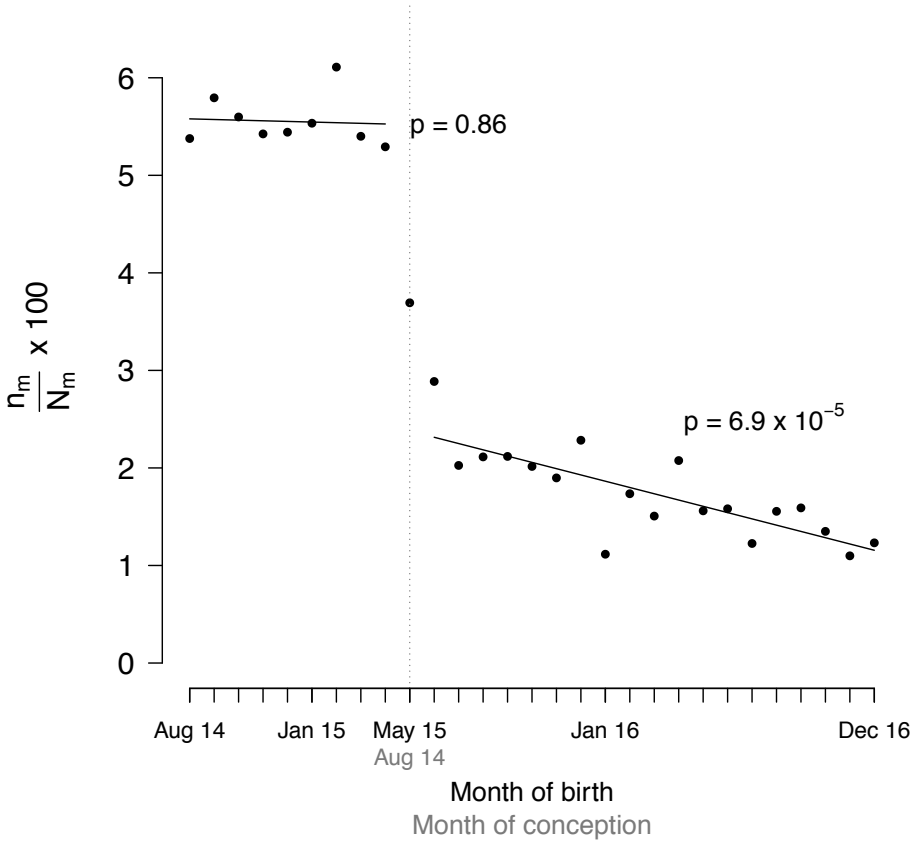
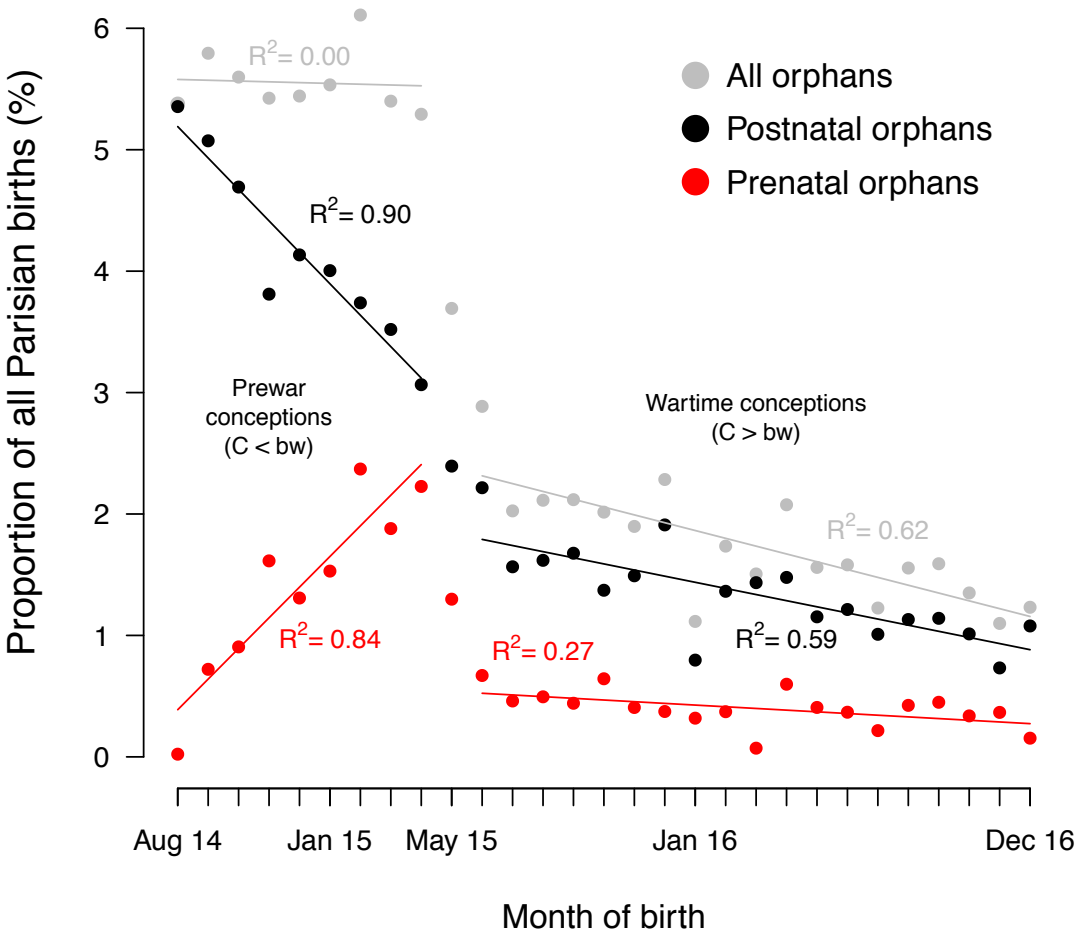


Figure 23 shows the n_m/N_m ratio: no time trend in the n_m/N_m ratio was found before May 1915 (p=0.86); after the May 1915 slump, the ratio steadily declined over time (p=6.9 x 10^{-5}). Figure 24 enables a more detailed analysis of the probability of becoming an orphan: it shows the evolutions of the ratios of prenatal (orphans who lost their father before birth) and postnatal orphans (orphans who lost their father after birth), respectively $n_{m,\ pre}/N_m$ and $n_{m,\ post}/N_m$ (with thus $n_{m,\ pre} + n_{m,\ post} = n_m$). Rates of prenatal and postnatal orphans varied in a strongly linear fashion – and in opposite directions – before May 1915 and were thereafter more noisy but both decreasing.

Figure 24. Evolution of the $n_{m,\,pre}$ / N_m and $n_{m,\,post}$ / N_m ratios over time.



R^2: coefficient of determination

A simple model

Several elements come to mind to explain Figures 23 and 24: for instance, it is intuitive that probability of a prenatal loss of father must depend on the hazard experienced by the father during the pregnancy of his wife. Similarly, the fact that conceiving a child at time *t* requires having survived until time *t* is rather indisputable. Also, the difference in the hazard lived by low-risk ('old') and high-risk ('young') fathers must contribute to the observed May 1915 discontinuity. Is a simple model that relies only on these purely mechanistic aspects capable of capturing the salient features of Figures 23 and 24? Or should more complex, cryptic, explanations be searched for? It turns out a simple model works well.

The notations are:

- *bw* and *ew* the dates the war began and ended;
- *gl* is the gestation length;
- *FD* the father's date of death;
- *C* the child's conception date (so that *C* + *gl* is the date of birth);
- *WO* the event "becoming a war orphan" (which corresponds to $FD \in [bw;\ ew]$);
- *PREWO* and *POSTWO* the events "becoming a war orphan in the prenatal period" and "becoming a war orphan in the postnatal period".

A set of simplifying hypothesis is the following:

- Let's assume infants belong to two groups, G_A ('young parents') and G_B ('old parents'). During the war, the fathers of G_A births fought and were exposed to hazard $t \rightarrow \lambda_{GA}(t)$, while fathers of G_B births remained unexposed. Risk of death in peacetime was negligible for all fathers, so that $FD \in [bw;\ ew] \cup \infty$.
- There is no reason to believe the proportion of G_A conceptions varied before the beginning of the war, so that we assume $\forall\, c < bw, P(G_A|C = c) := p_1$. The proportion of G_A conceptions afterwards is also assumed constant ($\forall\, c \geq bw, P(G_A|C = c) := p_2$). Fathers of the G_A group went to the front, so that their occasions to conceive rarefied and their contribution to total fertility declined, thus $p_2 < p_1$.

The aim is to elucidate functions f, f_{pre}, f_{post} defined for $c \in [bw - gl;\ ew]$ as:

- $f: c \rightarrow P(WO \mid C = c)$: the risk of becoming an orphan;
- $f_{pre}: c \rightarrow P(PREWO \mid C = c)$: the risk of becoming a prenatal orphan;
- $f_{post}: c \rightarrow P(POSTWO \mid C = c)$: the risk of becoming a postnatal orphan.

For $c \in [bw - gl;\ ew]$:

$$
\begin{aligned}
f(c) &= P(WO \mid C = c) \\
&= P(G_A \mid C = c) * P(WO \mid C = c, G_A) + P(G_B \mid C = c) * P(WO \mid C = c, G_B) \\
&= P(G_A \mid C = c) * P(WO \mid C = c, G_A) \\
&= P(G_A \mid C = c) * P(FD \in [bw; ew] \mid C = c, G_A) \\
&= P(G_A \mid C = c) * P(FD \in [bw; ew] \mid FD > c, G_A)
\end{aligned}
$$

For $c < bw$: The condition $FD > c$ is always met and $P(G_A|C = c) = p_1$, so that:

$$f(c) = p_1 * P(FD \in [bw; ew] \mid G_A)$$
$$= p_1 * [1 - e^{-\int_{bw}^{ew} \lambda_{GA}(t)dt}]$$

For $c \geq bw$: $P(FD \in [bw;\ ew] \mid FD > c) = P(FD \in [c;\ ew] \mid FD > c)$ and $P(G_A|C = c) = p_2$; thus:

$$f(c) = p_2 * [1 - e^{-\int_{c}^{ew} \lambda_{GA}(t)dt}]$$

Function f is therefore constant for c < bw and decreasing for c ≥ bw. Both elements are observed on Figure 23. The discontinuity at c=bw is $\frac{f(bw^+)}{f(bw^-)} = \frac{p_2}{p_1}$ (~ 0.5 based on the observed rate of orphans in April and June).

Similar computations can be worked out for f_{pre}.

For $c \in [bw - gl;\ ew]$:

$$f_{pre}(c) = P(PREWO \mid C = c)$$
$$= P(G_A \mid C = c) * P(PREWO \mid C = c, G_A)$$
$$= P(G_A \mid C = c) * P(FD \in [c; c + gl] \mid C = c, G_A)$$
$$= P(G_A \mid C = c) * P(FD \in [c; c + gl] \mid FD > c, G_A)$$

For $c < bw$: $P(FD \in [c;\ c + gl] \mid FD > c) = P(FD \in [bw;\ c + gl])$, so that:

$$f_{pre}(c) = p_1 * P(FD \in [bw;\ c + gl])$$
$$= p_1 * [1 - e^{-\int_{bw}^{c+gl} \lambda_{GA}(t)dt}]$$

For $c \geq bw$:

$$f_{pre}(c) = p_2 * [1 - e^{-\int_{c}^{c+gl} \lambda_{GA}(t)dt}]$$

Function f_{pre} depends on $\int_{\max(c,bw)}^{c+gl} \lambda_{GA}$, which is simply the cumulative hazard experienced by the father during the part of the pregnancy that took place during the war. Function f_{pre} therefore increases for $c < bw$, and reaches its maximum for those conceived just before the war began. For $c > bw$, it is noteworthy that the cumulative risk taken into account

is that during the whole pregnancy, so that the sole source of f_{pre} variation is due to heterogeneity of risk through time.

Analogous developments (or trivially noting that $f = f_{pre} + f_{post}$) yield:

For $c < bw$:

$$f_{post}(c) = p_1 * [e^{-\int_{bw}^{c+gl} \lambda_{GA}} - e^{-\int_{bw}^{ew} \lambda_{GA}}]$$

For $c \geq bw$:

$$f_{post}(c) = p_2 * e^{-\int_{c}^{c+gl} \lambda_{GA}} * [1 - e^{-\int_{c+gl}^{ew} \lambda_{GA}}]$$

It is straightforward that f_{post} decreases before bw. After bw, the evolution of f_{post} depends on the counteractions of $\int_{c}^{c+gl} \lambda_{GA}$, the cumulative hazard during pregnancy (an interval of constant width), and $\int_{c+gl}^{ew} \lambda_{GA}$, the cumulative hazard after delivery (an interval whose width ew - (c + gl) decreases).

Making further the convenient assumption that λ_{GA} is approximately constant over the war years and using $1 - e^{-x} \approx x$ [24] yields a few more insights into the specific shapes of f, f_{pre} and f_{post}. For instance, with these assumptions, for $c < bw, f_{pre}(c) \approx p_1 \lambda_{GA}(c + gl - bw)$ so that f_{pre} is approximately linear before bw, as observed on Figure 23 (R^2=0.84).

The linear fit is very close to the observed data for f_{pre} and f_{post} before bw (R^2=0.84 and 0.90, respectively). It is lower for f after bw (R^2=0.59), presumably in part because of increased intrinsic variability due to lower number of births. Making the assumption that λ_{GA} is constant would yield f_{pre} constant for $c > bw$. The first months of the conflicts were indeed

[24] Whether this approximation is valid may be assessed by considering $e^{-\int_{bw}^{ew} \lambda_{GA}}$, the probability of survival to the whole war for the group of exposed father. At total, around 8 million men were mobilized and 1.4 died. The order of magnitude of $e^{-\int_{bw}^{ew} \lambda_{GA}}$ should therefore be (8-1.4)/8 ~ 80%. The cumulative hazard $\int_{bw}^{ew} \lambda_{GA}$ is therefore ~ 0.20, small enough for the approximation to hold. All partial cumulative hazards considered ($\int_{bw}^{c} \lambda_{GA}$, $\int_{c}^{ew} \lambda_{GA}$, etc.) are below $\int_{bw}^{ew} \lambda_{GA}$ and the approximation may be used, it being more accurate for small cumulative hazards.

The real world was actually somewhat more complex because a fraction of those mobilized where at low risk (they belonged to the G_B rather than G_A group), but also because the fathers of children born 1914-1916 were on average not in the most severely hit generations (those aged ~ 20-25 in 1914; see Appendix 2): despite these sources of complexity, this rapid computation suggests $1 - e^{-x} \approx x$ can be used at least as a first approximation of $\int_{bw}^{c} \lambda_{GA}$, etc.

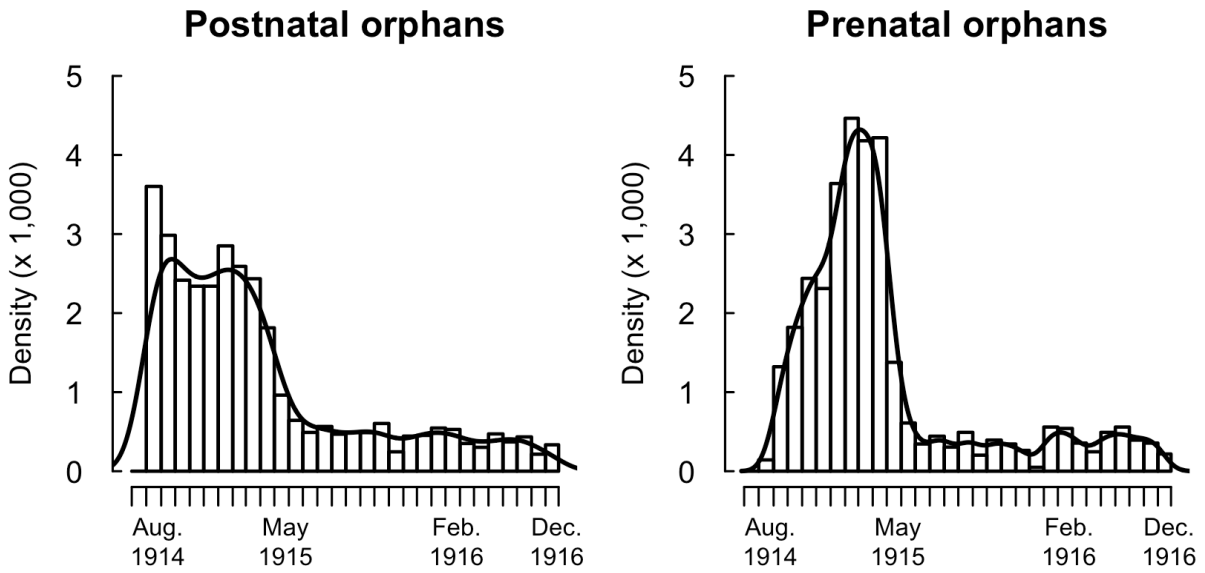
the deadliest of all, so that constancy of λ_{GA} is merely a crude approximation; accordingly, a small negative trend for f_{pre} is seen on Figure 23 (p=0.02). A constant λ_{GA} yields a decreasing evolution of f_{post} after bw.

The model is assuredly extremely simplistic in its assumptions. In reality, exposure to risk varied finely, in particular according to age: for instance, those born 1891-1893 were already serving in the army at the beginning of the war and were immediately at risk of death. Those born 1894 were enrolled in late August – early September 1914 (but arrived unprepared…), while those born 1895 were enrolled in December 1914 and escaped the hazard of the first months. Men aged > 35 served in less exposed units ('territorial regiments'). The minority of exempted soldiers was thoroughly examined during the course of the war to assess whether exemption could be cancelled, they therefore 'missed' the first months or years of the war: their risk and fertility functions hence write differently. A system of scheduled leaves was organized only in July 1915, theoretically every four months [85] so that probability of conception after the beginning of the war was likely not constant in the exposed group but rather depended on the specific hazard trajectory of each soldier. These are only a fraction of the sources of complexity that make the model here developed depart from reality. The former could therefore be refined, in particular in the joint modeling of the risk and fertility functions. Yet it seems it does capture some of the main features of Figures 22 and 23 and is especially accurate for prewar conceptions.

Practical consequences

A major practical consequence of the simple mechanisms just described is that prenatal and postnatal orphans have markedly different distributions of dates of birth (Figure 25). For example, in the final dataset analyzed in Chapter 6, while 11.1% of postnatal orphans (n=190) were born in August 1914, this was only the case of 0.2% of prenatal orphans (n=1). Conversely, in April 1915, the corresponding figures are 5.4% (n=93) and 13.3% (n=87). Another major characteristic of the variation of risk with soldier's age is that orphans' parents were younger than the average parents (see Appendix 2).

Figure 25. Dates of birth of prenatal and postnatal orphans.



The prenatal and postnatal orphans are those analyzed in Chapter 6 (n=2,365)

The fragmentary pieces of evidence gathered in the first and second sections of this chapter point to noteworthy changes in the composition of the Parisian population during the study period. It cannot be assumed that migrations occurred at random. On the contrary, SES, attitude toward risk-taking or even geographical origin and family structure, may all have contributed to the propensity to migrate. Though SES may be directly controlled for, the latters cannot.

Another important element to bear is mind is that, though no famine or large-scale epidemic struck the French civilian population of non-occupied regions before the Spanish Flu, significant variations in nutrition and infectious environments took place during the very early life of included subjects. This is in particular revealed by contemporary accounts of leading pediatricians. To give only one example, low-quality and bacterial contamination of cow milk given to Parisian infants were reported for late August 1914 [86] [25]. The previously mentioned research reporting that adult longevity may vary by several months according to prenatal diseases and nutrition is therefore yet another incentive to pay special attention to the choice of comparators. Our rule for choosing MNOs, born at the same time in the same

[25] Referring to Paris in late August - early September 1914, Adolphe Pinard wrote: " Quant à la mauvaise qualité du lait, la cause s'explique facilement, je crois, de par les circonstances de ce moment. En raison de l'encombrement des lignes de chemins de fer, les arrivages de lait subissaient, pendant cette période, des retards considérables, et le lait qui arrivait était fatalement plus ou moins altéré. "

districts (and of same maternal age), ensures they belong to the same underlying population and is designed so as to avoid the pitfalls described in the chapter.

Chapter 4: The naming of orphans in France during World War One: a study of a nationwide cohort of "pupilles de la Nation"

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[1]: INSERM U1169

Abstract: The investigation of a simple behavior, child naming, can provide insights into the varying reactions of families confronted to the extraordinary war losses of the First World War. The current study analyses names given in a large cohort of French orphans born 1914-1916, constructed thanks to the linkage of civil registers with a nationwide database of soldiers died during the War. It shows that a prenatal loss of father was associated with a strong increase in father's name transmission. The phenomenon was twice more intense in officers' offspring. Use of Generalized Additive Models (GAM) showed that the timing of the father's death finely controlled this change in naming behavior: father's name transmission was maximum when the father died at the very beginning of pregnancy.

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Introduction

Considerable attention has been paid by historians to the attitude of the families confronted to the massive losses of the First World War. In particular, recent work has focused on the formidable violence suffered by those who lost a close kin at war and has shed light on specific anthropological features of wartime mourning (Winter 1995, Audoin-Rouzeau and Becker 2000, Audoin-Rouzeau 2001, Damousi 2014). Inversion of roles between generations – with parents mourning offspring; the fact that usually relatives at first knew little of the circumstances of the death and were left speculating on the soldier's sufferings; the absence of the corpse, that in peacetime gave tangible form to the loss; the inability to perform customary funeral rituals: all have been shown to be critical components of the grief experience during WW1. These insights have notably stemmed from detailed analyses of correspondences, diaries and war novels. Evidence on individual attitudes has yet come from case studies rather than from data collected on entire populations.

The uncertainties that remain on the mourning practices of the whole population and their variations across social groups are an incentive to investigate simple behaviors on which quantitative evidence can be retrieved. In that respect, first names are of special interest. Attributing a name to a newborn being compulsory, first names are widely available. Their analysis has become a standard tool of sociology (Besnard 1979, Lieberson and Bell 1992, Berger and Le Mens 2009, Coulmont, Supervie and Breban 2016) and, more directly relevant to the current study, of social history: first names have proven valuable in varied historical investigations. Children in traditional societies were usually given the name of another family member, e.g. a grandparent (Van Poppel et al. 1999). Evolutions in the naming for kin habit have been shown to reflect at least some changes in the structure of the family, such as increased patrilinearity at the end of the Middle Ages (Klapisch-Zuber 1980, Fine 1987). The decline in family naming from the late XVIIIth century onwards has made children' names a direct measure of parents' tastes and beliefs at the time of the birth that, importantly, is not subject to recall bias. The choice of biblical names has for instance been used as a proxy for parental religiosity in XIXth century America (Hacker 1999). An index of ethnic distinctiveness of first names has recently been devised to analyze the economic success of immigrants in relation to their degree of assimilation (Goldstein and Stecklov 2016). Names

have also been shown to be reliable measures of public opinion before polls came into existence (Urbatsch 2015).

Maternal bereavement due to the father's death has recently been shown to have had very long term consequences on the adult health of French orphans born 1914-1916 (Todd, Valleron and Bougneres 2017). Specifically, a ~ 2.5 y reduction in adult lifespan was found for orphans who lost their father before birth. Relying on the same database, we searched for measurable consequences of this traumatic event outside the field of public health, and wondered whether it systematically altered child naming.

Indeed, names parents could give to their children were theoretically restricted by the law of 11 Germinal An XI (April 1, 1803): only names found in calendars or that of ancient history figures were authorized. The law was somewhat incoherent (Lévy 1913). Which calendars could be considered was unknown. Some names unquestioned by most ordinary citizens, among which feminized versions of male names, were refused by quibbling civil registration services, while Biblical calendars contained some names generally deemed preposterous. These ambiguities sometimes resulted in conflicts between parents and local authorities. Despite this purportedly rigid legal framework and the remains of the naming for kin habit, the XIXth century had seen a growth in parents' freedom of choice, as clearly reflected by the visible trends in names' popularities (Figure 1).

It has already been noted based on autobiographies or oral testimonies that transmission to newborns of the names of family members died during the War could occur (Pignot 2012, 381). This was for instance the case of historian Raoul Girardet, born October 1917, who was given the middle name of his paternal uncle, an infantry captain died September 1914 (Audoin-Rouzeau and Becker 2000, 207). Birth announcements placed in newspapers also constitute hints. For instance, on April 21st 1915, the *Society Column* of *Le Figaro* announced: "Mme Henry Brugère has just delivered a son, named Henry, after his father, captain Henry Brugère, gloriously killed near Nancy".

These isolated examples found in upper class families suggest first name choices responded to family events during WW1, but leave several important questions unanswered: the magnitude, social determinants and development through time of the phenomenon have so far remained unknown, primarily due to a lack of adequate individual-level data. To

investigate these questions, the current study analyzes the association between prenatal death of father and father's first name transmission in a large cohort of French orphans who were granted the "pupille de la Nation" status. It contributes to our understanding of the reception of the War by families without restriction to any specific social group.

Data

The pupille status was created by the law of July 27, 1917 after prolonged political debates (Faron 2001, 86-121). It made possible application to specific financial allowances and was intended as a reaction to the staggeringly high war losses and the corresponding increase in the number of orphans. War orphans and children of disabled soldiers made unable to earn an income could become pupilles and if so were then symbolically said to be adopted by the Nation. Starting in 1918, adoptions were decided by civil tribunals following a request made by the legal representative of the child, usually the mother in the case of an orphan. Once definitive, adoption was notified on the birth certificate of the pupille, as demanded by article 8 of the law of July 1917. Because financial support was attributed on a case-by-case basis by a specific *ad hoc* administration, the Office National des Pupilles de la Nation, no income condition was set for war orphans, who could all become pupilles whatever their social status.

The birth certificates of all pupilles de la Nation born August 1, 1914 – December 31, 1916 in 17 districts of Paris and August 1, 1914 – December 31, 1915 in 9 other cities were identified thanks to the "adopted by the Nation" notification, then digitized. All included cities were chosen in the non-occupied regions of France (Figure 2). At total, 7,250 pupilles were found in birth registers. In order to identify orphans among pupilles and, for them, to retrieve the father's type and date of death as well as his military rank, all fathers were searched for by name and year of birth in an online database of French soldiers died during the War, the *Database of those who died for France in the First World War*, created for administrative purposes in 1921-1922 (Lemarchand 2008)[26].

[26]The *Database of those who died for France* (abbreviated DDF) is available at: www.memoiredeshommes.sga.defense.gouv.fr/en/. The DDF includes ~ 1.4 million soldiers died between August 3rd 1914 and June 1st 1919. In case of doubt about the identity of the father, the birth certificate of each

By this means, 4,061 orphan pupilles de la Nation were identified. The small number of those whose motherly age (n=35) or father's rank (n=11), type of death (n=33) or age (n=4) was unknown was removed, yielding a final dataset analyzed of 3,978 orphans (Table 1). Among them, 978 lost their father before birth (prenatal orphans) and 3,000 lost their father after birth (postnatal orphans).

Methods

Names analyzed.

For all of the 3,978 orphans considered, the birth certificate yielded all names given at the time of civil registration. The analysis was limited to the first name. Hyphenated first names were considered as two separated names, the first of which was defined as the first name. In order to include female orphans in the analysis, comparison of father's and offspring's names was limited to the first 4 letters. For example, transmission is considered to have occurred if father's first name was Joseph and his daughter's first name was Josephine. In males, identity of the 4 first letters was almost always (98.1% of cases) the consequence of full identity, so that the un-truncated and truncated analyses are virtually identical.

Statistical analyses.

Probability π of identity between orphan's first name and father's first name was modeled in a Generalized Additive Model (GAM) (Hastie and Tibshirani 1990, Wood 2006) with the error distribution and link function of the logistic regression:

$$\log\left(\frac{\pi}{1-\pi}\right) = f_1(a_d) + f_2(d_b) + f_3(MA) + f_4(PA) + Sex + Leg + Rk + Td + Pla \qquad [1]$$

soldier returned by the search in the DDF was checked. Indeed, the DDF certificate indicates the place and date of birth of each soldier. As most XIXth century French civil registers have been digitized, the verifications were carried out on the websites of the various 'archives départementales'. The comparison of the name of the wife of the soldier (available in the marriage notification inscribed on the soldier's birth certificate) and that of the mother of the pupille (available on the pupille's birth certificate) yields a positive method of verification of the linkage between birth registers and the DDF.

Smooth functions f_1, f_2, f_3 and f_4 are represented as penalized cubic regression splines with 15 (f_1, f_2), and 8 (f_3, f_4) degrees of freedom and evenly spaced knots; a_d is the infant's age at father's death (father's date of death - orphan's date of birth), d_b the date of birth (time since August 1, 1914), *MA* the age of the mother at the infant's birth, *PA* the age of the father at the infant's birth, *Sex* the infant's sex, *Leg* the legitimacy of the birth (i.e. whether the parents were married at the time of the birth), *Rk* the military rank of the father (private, non-commissioned officer (NCO), officer), *Td* his type of death (Killed in action, Missing in action, Died of disease, Other) and *Pla* a normally distributed random effect controlling for civil registration service (i.e. place of birth ; see Figure 2). The smoothing parameters determining the effective degree of freedom of f_1–f_4 are selected to minimize the unbiased risk estimator score. The right-hand side of equation [1] will be abbreviated *X* when convenient.

Results

Age at father's death and name transmission.

Probability of transmission of father's name was strongly associated with prenatal loss: it was 43.6% in male orphans prenatal orphans versus 16.5% in postnatal orphans (p-value (p) = 1.0×10^{-35}). In females, probability of father's name transmission was 27.1% in prenatal orphans versus 9.9% in postnatal orphans ($p = 2.5 \times 10^{-20}$). Starting at different baseline values, the observed fold change (~ 2.7) was therefore extremely similar in both sexes.

The multivariate analysis showed a remarkable specificity in the association between transmission of father's name and age at father's death. Probability of name transmission was again found associated with age at father's death ($p = 6.8 \times 10^{-42}$). Reassuringly, the function f_1 linking the two variables was found flat for those already born when the father died (Figure 3a). Contrary to what was observed on the postnatal period, the probability of name transmission showed large variations within the intrauterine period. Specifically, the highest probability of transmission was attained when the father died at the very beginning of the pregnancy, with a steady decrease in probability until birth. Consistent with the multivariate

analysis, the observed transmission rate was 41.3% when the loss of father occurred in the 1st trimester of pregnancy, 37.6% in the 2nd trimester and 31.0% in the 3rd trimester (versus 14.3% in the 1st trimester of postnatal life, and 13.3% on average in postnatal life). The same pattern was found in males (Figure 3b) and females (Figure 3c).

An analysis by military rank of the father revealed a stronger increase in transmission when the father was an officer: the fold-change in transmission was 5.1 in officers' offspring, versus respectively 2.7 and 2.5 in NCOs' and in privates' offspring (Table 2). When model [1] was fitted by military rank of the father, the shape of function f_1 was retrieved at all levels of the social ladder (Figure 4). Consistent with the previous analysis that relied on the prenatal/postnatal dichotomous variable, a steeper relationship was found in the officers group.

Though military rank was a strong indication of social status in civilian life, it was by no means perfect. In order to confirm the results obtained with military rank, the analysis was performed separately on two strongly contrasted groups of orphans both based on civil registration service of birth, i.e. district/city of birth. To objectively define bourgeois and proletarian districts/cities, we selected the 7 districts/cities with respectively the highest and the lowest proportions of officers among orphans' fathers (Figure 5). The same shape for function f_1 was retrieved, as well as the steeper relationship in the bourgeois context (Figure 6).[27]

By contrast with the strong effect of age at father's death, no association of transmission with date of birth was found (function f_2 penalized to 1, $p = 0.47$). To further investigate a potential effect of date of birth, model [1] was fitted on prenatal orphans only. This yielded the same result: we found no trend for an increase or decrease in name transmission over time.

The results held when the analysis was restricted to legitimate children, when those whose father died of disease or was missing in action where removed from the dataset, and when only those whose father was killed in action were included. As a sensitivity analysis, we

[27] District of birth could differ from parental district of residence because of deliveries at maternity wards. Yet district of birth was a strong predictor of parental place of residence and social status. For a map showing recruitment areas of selected districts, see (Todd, Valleron and Bougnères 2017).

also considered whether father's first name could be transmitted at a position other than the first name. We found that 25.9% of prenatal male orphans had their father's first name as a middle name, strikingly close to 25.7%, the value for postnatal male orphans (p=0.98). Interestingly, the same analysis for females revealed a difference between postnatal and prenatal orphans: the rate of transmission as a middle name increased from 14.6% to 19.2% (p=0.02).

Name-specific effects on transmission.

Having found a strong increase in name transmission in the case of a prenatal loss of father, we wondered whether some paternal names improved or on the contrary prevented transmission to offspring. Given the conflicts reported in newspapers and in legal works between parents and civil registration services on some choices of names, the transmission to daughters might have been lower than expected when the feminized versions of the father's name created such conflicts (e.g. Henri, feminized to Henriette, sometimes refused). To search for statistical evidence of restrictions imposed by civil registration services, for each paternal name *a*, we applied (separately for male and female orphans) the following statistical procedure: for each of the *n* orphans whose father was named *a*, model [1] yielded a theoretical probability of transmission based on the orphan's characteristics (legitimacy, age at father's death, paternal military rank, etc.), $\frac{1}{1+e^{-X}}$. The sum of the Bernoulli variables Y_i equal to 1 in case of transmission, $\sum_{i=1}^{n} Y_i$, therefore follows a Poisson-binomial distribution of parameters $(\frac{1}{1+e^{-X_i}})_i$ under the assumption that there is no added effect of name *a*, therefore making possible a test of this hypothesis. For instance, the mean expected transmission rate based on model [1] was 24.9% for the 39 sons of men named Albert, and the observed transmission rate was 11/39 = 28.2% (unadjusted p = 0.58). To control the False Discovery Rate (FDR), the resulting p-values were then adjusted using the Benjamini-Hochberg procedure (Benjamini and Hochberg 1995) and considered significant at the 5% level.

For male orphans, we found no paternal first name that significantly changed the transmission rate predicted by model [1]. For female orphans, five paternal names significantly changed transmission, all increasing it (Table 3), while no paternal name was found to significantly decrease transmission.

Conclusion

This article reports that a prenatal loss of father during WW1 resulted in a ~ 2.7-fold increase in the probability of receiving the father's name. The practice, previously noticed on sparse and heterogeneous cases (father-to-son or uncle-to-nephew transmission; war or post-war birth…), was therefore found in all social groups considered. The fact that it was twice more pronounced for officers' offspring points to response differences by social background, which potentially impede generalization from case studies. Furthermore, our unique dataset combining civil registers' and military information for a large cohort of orphans enabled us to show that the timing of father's death exerted a fined-grained control over this change in behavior: those whose father died very early in pregnancy experienced the highest probability of receiving his name.

A few years after the War, sociologist Maurice Halbwachs noted that the first name given to a newborn is a fundamental instrument for the family to efficiently record in its collective memory the specific context that surrounded the birth (Halbwachs 1925, 223). It is hard to overstate the relevance of this remark for our cohort of war orphans. Such response of first names to the recent loss of a kin is reminiscent of naming behaviors observed in other mortality crisis such as the second plague pandemic (Klapisch-Zuber 1980). The will to reincarnate dead family members and more generally to symbolically ensure the family's survival, at the root of the naming for kin habit, simply seems to have taken an extreme form during WW1.

Part of the explanation for naming after the dead father may also lie in specific characteristics of the First World War. The cult of the fallen soldier, organized especially around war monuments, military cemeteries and tombs of unknown soldiers has been advanced as a major characteristic of WW1 and the immediate post-war period (Mosse 1990, 70-106). Heroization of the dead may have been a strong argument for giving his name to the orphan. In this line of thought, one can also expect that the type of death, more or less heroic, influenced name transmission. Because deaths by disease occurred mainly late in the War, orphans of fathers died of disease are overwhelmingly postnatal orphans, leaving little statistical power for this question. It can be noted however that the observed transmission was lower for prenatal orphans whose father died of disease (25.6%, vs. 36.2% for prenatal

orphans whose father was killed in action and 33.3% when the father was missing in action). Consistently, the odds ratio was 0.86 when the father died of disease versus killed in action in model [1] fitted on prenatal orphans only.

Indeed, a comparative perspective, made readily accessible by the ubiquity of first names, seems the safest way to progress in the interpretation of the observation here reported. Did naming after dead father also prevail in peacetime, a fact that would discard the heroization argument, or was WW1 indeed an exceptional period in that respect? It can also be noted that, if a peacetime phenomenon, naming after dead father would provide a general quantitative indicator of attitudes toward death, whose changes through time could then be traced in the very long run, e.g. by the replication of our study using genealogical databases that provide the first names and life events' dates for millions of individuals born in the past four centuries.

Finally, whether the choice of the dead father's name was freely made by mothers or resulted from a diffused social pressure is unknown. We did not find any time trend in the giving of father's name, suggesting diffusion did not play a substantial role in the phenomenon. Surprisingly, the change in transmission rate for female orphans was found extremely similar to that for male orphans, despite the restrictions theoretically imposed by the law of 11 Germinal an XI on the feminized versions of some male names. The arrangements needed to reach such a result suggest local authorities showed at least benevolence towards the giving of the father's name. Consistently, no specific paternal first name could be found to significantly prevent transmission, whether prenatal or postnatal. A few paternal names increased transmission, probably because their feminized versions happened to be common and fashionable choices[28]. The War indeed changed the attitude of many civil registration services regarding the strict compliance with the law of 11 Germinal an XI: in the first years of the conflict, hundreds of parents named male newborns Joffre and female newborns Joffrette, after the French Commander-in-Chief Joseph Joffre, despite the fact that these innovative first names were blatant infringements of the law. As the expression of a patriotic feeling, they were accepted by many civil registration services and were even

[28] The "Fichier Prénoms" indicates that the nine feminized versions of the five paternal names identified as over-transmitted (see Table 3) were indeed popular 1914 names (Wilcoxon test: $p = 2.2 \times 10^{-6}$): for example, Jeanne was ranked 2nd and Lucienne was 11th. The "Fichier Prénoms" records 1,180 female first names given in 1914; the mean rank of the 9 aforementioned names is 54th.

supported by some public prosecutors, in charge of controlling civil registration services (Lévy 1922, 102-108).

The shape of the age at father's death – probability of transmission curve within the intrauterine period is somewhat unexpected. One might have argued that a change in probability of transmission within the intrauterine period could have been predicted, and straightforwardly explained by delays in the announcement of father's death to the mother. Yet we found loosing one's father in the first trimester of pregnancy and in the second trimester did translate into different probabilities of name transmission. This strongly suggests that the shape of the curve in fact is not explained by delays in father's death announcement to the mother. Such delays could take place in the event where comrades of the dead spouse did not write immediately to the family. In that case, the wife had to wait for the official notification by the Ministry of War, which could take weeks to arrive if not months, or assume from the cessation of letters written by the soldier that something had gone wrong (Bette 2012, 58-84). But such delays, which were typically unlikely to go beyond a few weeks, would have translated into a flattening of the curve at early stages of pregnancy, a change not observed in our cohort (neither in the main analysis nor when those missing in action were removed).

Going beyond the quantitative evidence and investigating the naming decision process at a micro level is notoriously difficult. The correspondences exchanged between soldiers and their families show that the opinion of fathers fighting at the front regarding baby naming varied from to strong attachment to specific choices to mere advice to the mother (Vidal-Naquet 2014). In some cases relatives of the couple (grandparents, uncles, brothers and sisters) appear to have been part of the decision process: the role of these family members might have been amplified in the case of a prenatal death of father. It may be the case that the later the death of the father, the higher the probability that a mutual agreement on name had been reached between the parents by the time of the father's death. In other words, the observed pattern could be the result of an increased competition between father's name and fatherly-approved names for those whose father died late in pregnancy.[29]

[29] See for instance (Vidal-Naquet 2014) for letters exchanged by mobilized soldiers and their wives. Among these correspondences, one contains prolonged debates on the name to be given (chapter 9), while in another the father, after having given his opinion, leaves his wife fully free to decide (chapter 1). Based on a extensive study of civil registration, Edouard Levy described the varying attitude of fathers in the early XXth century, from strong preferences (e.g. for names with a political meaning), sometimes leading to conflicts with the civil registration

Even more difficult to investigate are the potential psychological consequences on the offspring. The father's name was certainly a strong reminder of the lost spouse and, together with participation in remembrance ceremonies, contributed to giving a role to the orphan in the mourning process. In some ceremonies, the orphan could receive decorations, e.g. the Military Medal, in place of his father – yet another practice that reincarnated the dead soldier into his offspring. It should however be noted that nicknames, middle names or even family names could all compete with the first name officially given at the civil registration service years or decades earlier. As a consequence, the weight of the father's name was perhaps not as persistent as anticipated.

service, to full indifference regarding this matter: some fathers were so unconcerned that the name had not been discussed by the time of delivery and had to be urgently selected at civil registration (Levy 1922, 21-33).

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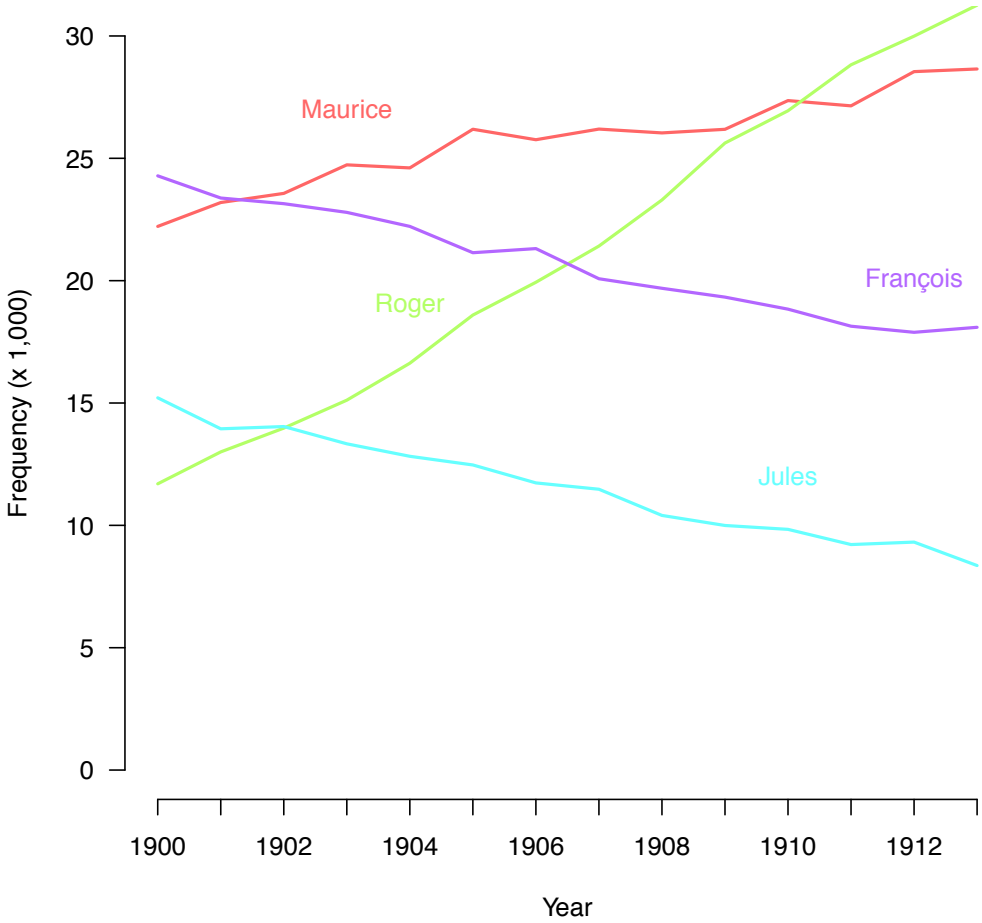
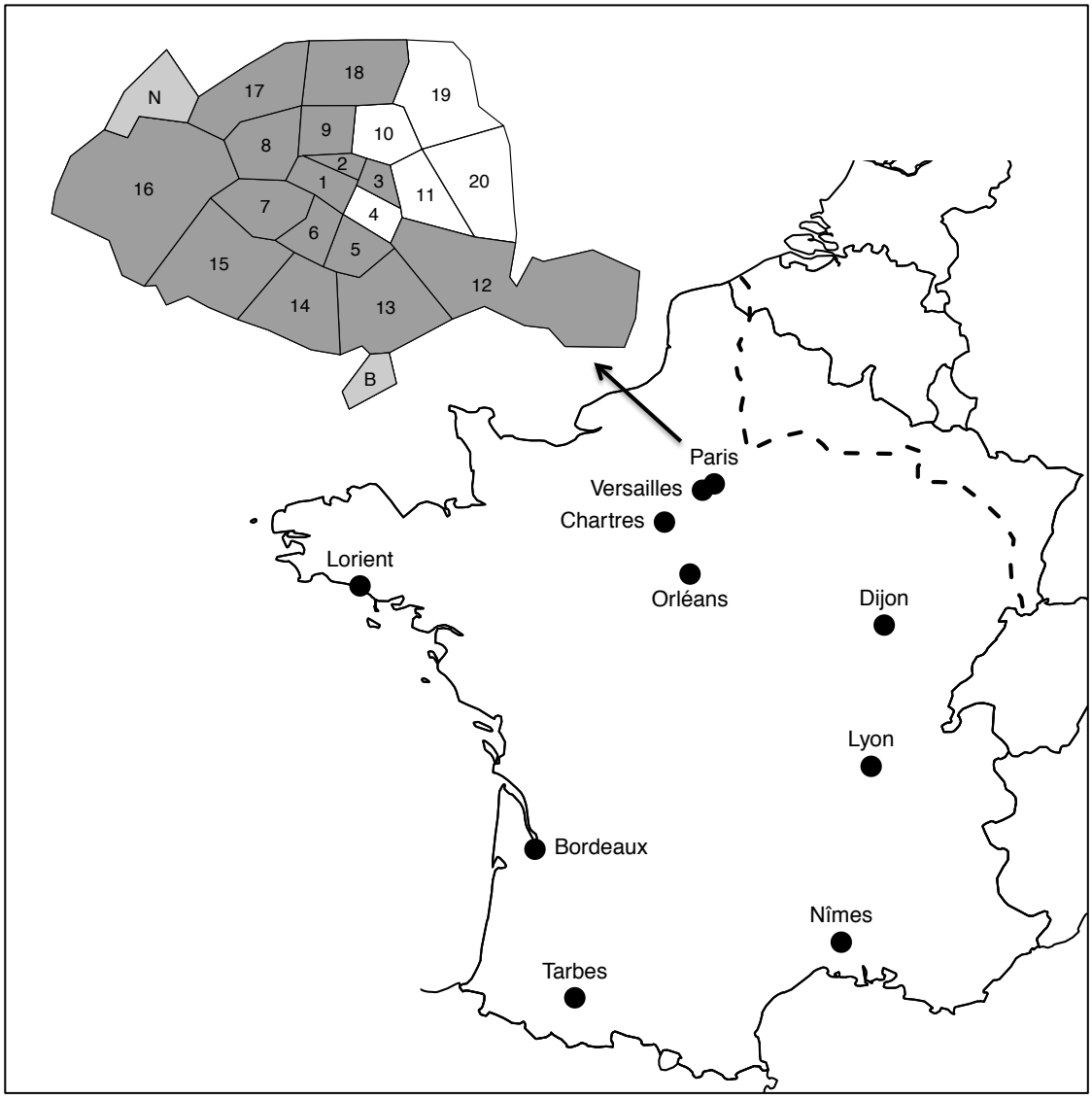
TABLES AND FIGURES

Fig. 1. Examples of early XXth century trends in names' popularities.



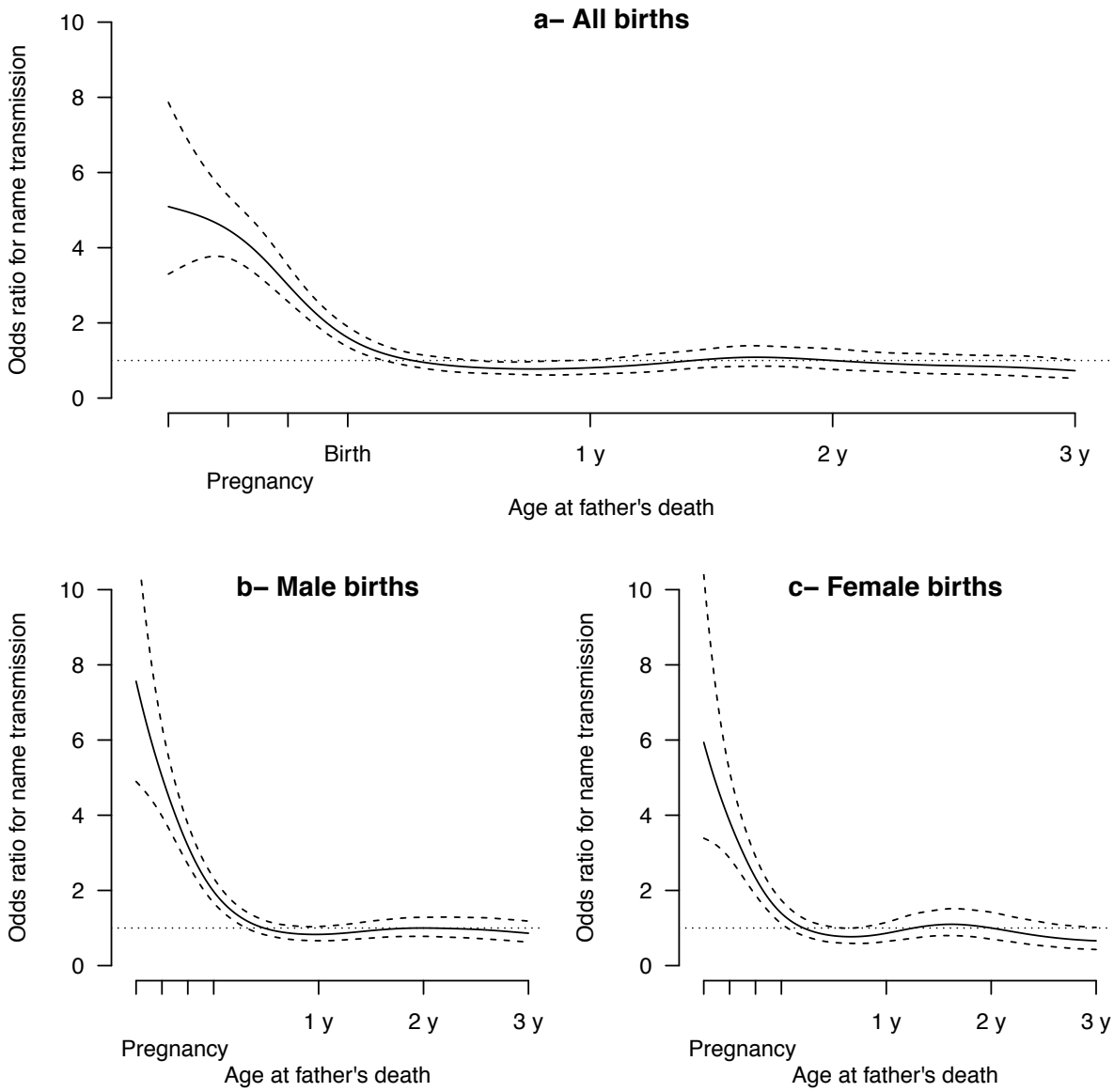
The frequencies plotted are that found in the "Fichier Prénoms", managed and curated by the French National Institute for Statistics and Economic Studies (INSEE), which gives the number of children born in France with each name each year between 1900 and 2013.

Fig. 2. Included cities (panel a) and districts of Paris (panel b).



17 Parisian districts (15 "arrondissements", and the suburban towns of Neuilly and Bicêtre) were included, each with its own civil registration service recording the births taking place on the district's territory. Lyon was divided in 7 districts (arrondissements), that similarly had independent civil registration services. Bordeaux's civil registration was organized in four independent services. At total, 35 civil registration services were therefore included in the study. B: Bicêtre; N: Neuilly. The dotted line shows the stabilized frontline from October 1914.

Fig. 3. Association between age at father's death and probability of father's first name transmission.



The transmission of father's first name to offspring was modeled with a Generalized Additive Model, first for all births (panel a), then for male (panel b) and female births (panel c) separately. All odds ratios are given with loss at age 2 y as the reference.

Dashed lines: 95% CI. Dotted line: Odds ratio = 1.

Fig. 4. Association between age at father's death and probability of father's first name transmission, by military rank of the father.

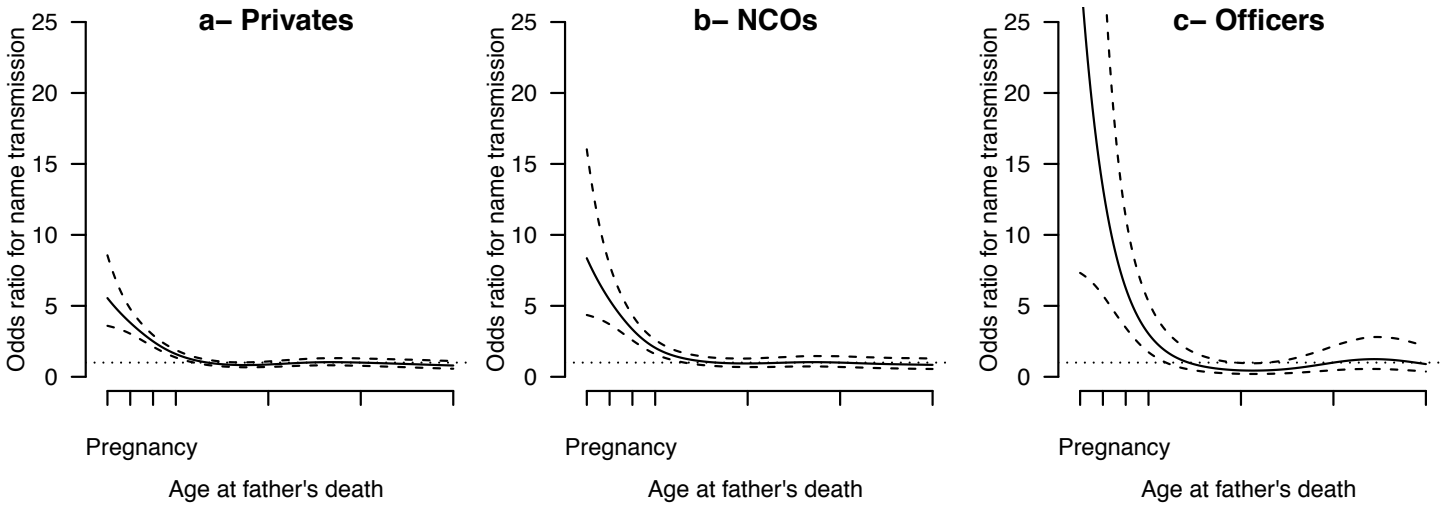
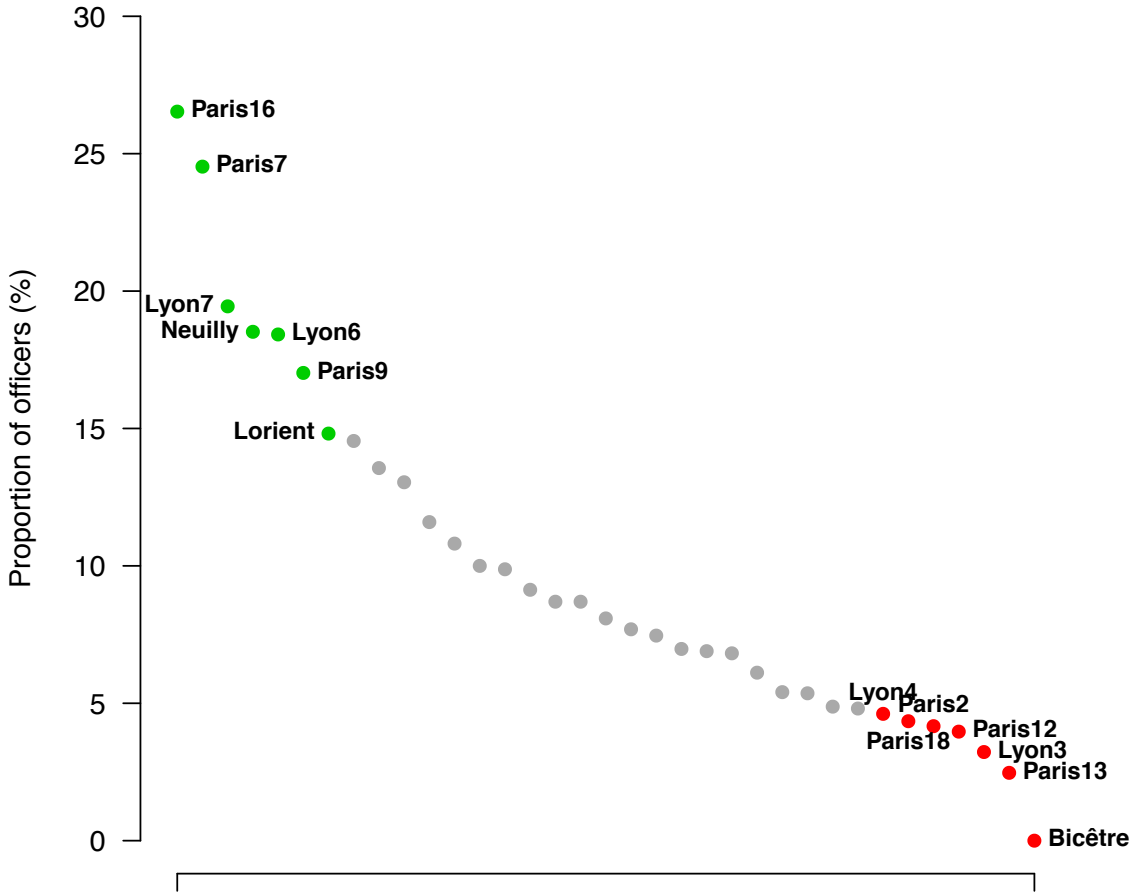


Fig. 5. Proportion of officers among orphans' fathers, by civil registration service.



Separate analyses were conducted on the orphans born in the 7 services with the highest and the lowest proportions of officers (see Figure 6).

Reading: 26.5% of orphans born in the 16th arrondissement of Paris were officers' children. All civil registration services combined, the proportion of officer's children was 6.9% in prenatal orphans and 7.3% in postnatal orphans (Table 1).

Fig. 6. Association between age at father's death and probability of father's first name transmission in the seven highest and lowest status civil registration services.

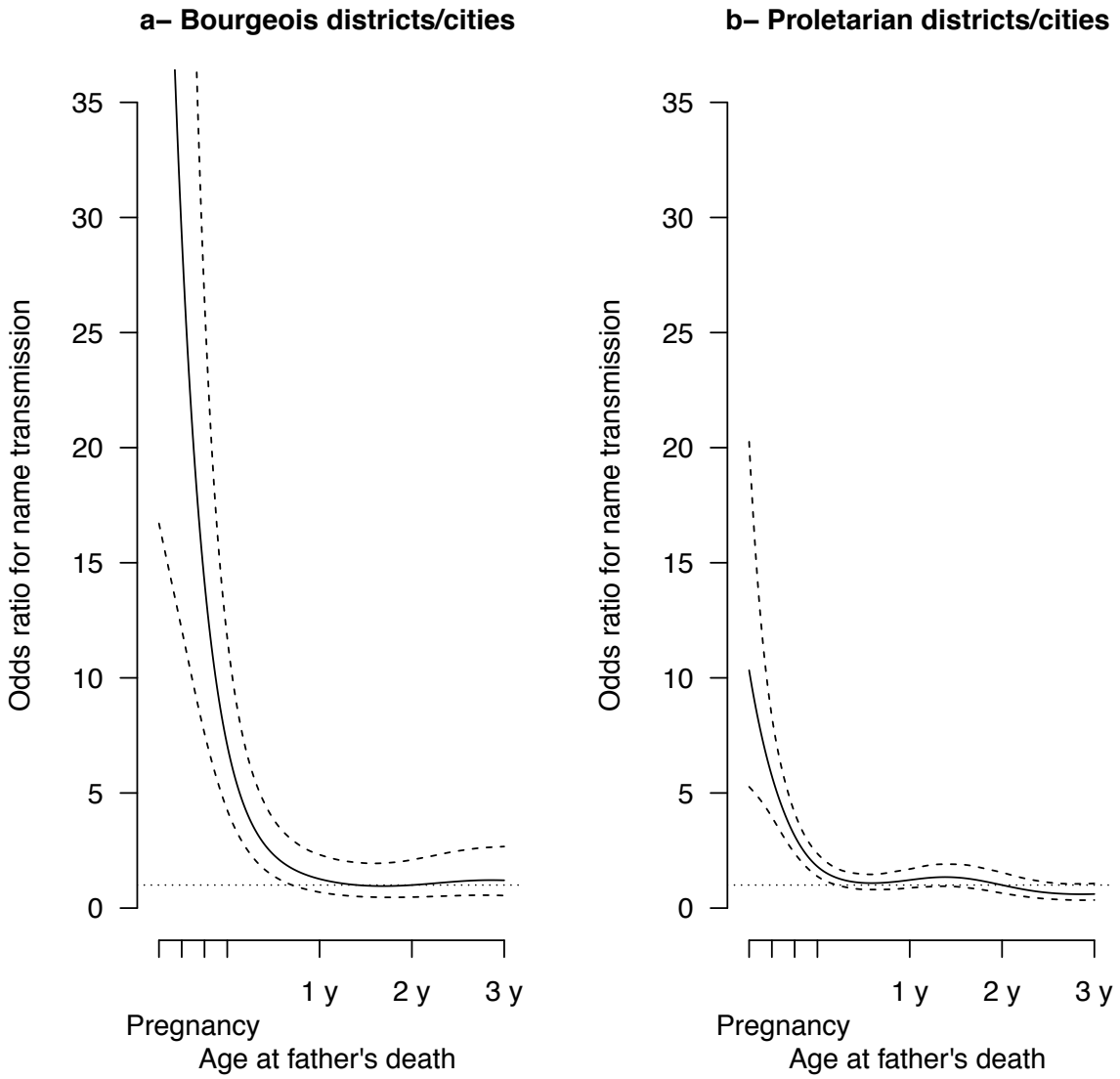


Table 1. Baseline characteristics of the 3,978 included orphans.

	Prenatal orphans (n= 978)	Postnatal orphans (n=3,000)
Date of birth, mean	23 April 1915	26 March 1915
Sex, n (%)		
Female	473 (48.4%)	1,447 (48.2%)
Male	505 (51.6%)	1,553 (51.8%)
Legitimacy, n (%)		
Illegitimate	35 (3.6%)	333 (11.1%)
Legitimate	943 (96.4%)	2,667 (88.9%)
Paternal military rank, n (%)		
Soldier	676 (69.1%)	1,949 (65.0%)
Non-commissioned officer	235 (24.0%)	833 (27.8%)
Officer	67 (6.9%)	218 (7.3%)
Paternal type of death, n (%)		
Killed in action	842 (86.1%)	2,252 (75.1%)
Missing in action	90 (9.2%)	129 (4.3%)
Died of disease	39 (4.0%)	566 (18.9%)
Other	7 (0.7%)	53 (1.8%)
Maternal age, mean (sd)	25.9 (4.4)	25.9 (5.1)
Paternal age, mean (sd)	29.5 (4.4)	29.4 (5.2)

Table 2. Transmission rate of father's first name by sex and age at father's death.

	Postnatal orphans	Prenatal orphans	Fold change in transmission	p-value
Male	16.5%	43.6%	2.6	1.0×10^{-35}
Female	9.9%	27.1%	2.7	2.5×10^{-20}

Reading: 16.5% of postnatal male orphans were given as first name that of their father.

Table 3. Transmission rate of father's first name by military rank of the father and age at father's death.

	Postnatal orphans	Prenatal orphans	Fold change in transmission	p-value
Soldier	13.7%	34.5%	2.5	4.3×10^{-32}
NCO	13.7%	37.0%	2.7	1.4×10^{-15}
Officer	8.3%	41.8%	5.1	2.4×10^{-10}

An increased effect of prenatal loss of father is visible in officers: the fold change in the transmission rate was 5.1 for officers, but only 2.7 for NCOs and 2.5 for soldiers. Adjusting for parental ages, legitimacy, sex and paternal type of death in a logistic regression, the postnatal/prenatal difference was significantly different in officers vs. soldiers + NCOs grouped (analysis of deviance: $p = 0.01$).

Table 4. Transmission rate of father's first name as a middle name, by sex and age at father's death.

	Postnatal orphans	Prenatal orphans	Fold change in transmission	p-value
Male	25.9%	25.8%	1.0	0.98
Female	14.6%	19.2%	1.32	0.02

Table 5. Paternal first names associated with a significant change in transmission to female offspring.

	Mean predicted transmission rate	Observed transmission rate	Adjusted p-value	Female versions used
André	14.7%	35.1%	0.04	Andrée
Georges	16.0%	32.5%	0.01	Georgette, Georgina
Jean	13.8%	24.6%	0.02	Jeanne, Jeannine
Lucien	15.0%	40.6%	0.02	Lucienne
Paul	16.7%	39.6%	0.005	Paulette, Paule, Pauline

Based on model [1], the predicted probability of transmission was computed for each orphan. We then tested for each of the 262 paternal names of the cohort whether the observed transmission departed from this theoretical probability. For instance, for the 32 female orphans born to fathers named Lucien, the mean theoretical probability of transmission was 15.0% (orphan 1: 13.4%; orphan 2: 8.9%, etc.). The first names being transmitted to 13/32 orphans, the observed transmission rate was 40.6%, significantly different from the theoretical rate. No paternal name was found to significant modify name transmission to male orphans. Five paternal names were found to significant modify transmission to female orphans, all increasing it.

PLOS ONE

RESEARCH ARTICLE

Impact of social inequalities at birth on the longevity of children born 1914–1916: A cohort study

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Abstract

Background

Testing whether familial socioeconomic status (SES) in childhood is a predictor of mortality has rarely been done on historical cohorts.

Methods

The birth certificates of 4,805 individuals born 1914–1916 in 16 districts of the Paris region were retrieved. The handwritten information provided the occupation of parents, the legitimacy status, life events (e.g. marriage, divorce), and the precise date of death when after 1945 (i.e. age 31 years (y) in the cohort). We used the median age at death (MAD) as a global measure of mortality, then studied separately survival to and after 31 y. Multivariate Imputation by Chained Equations (MICE), Generalized Additive Models (GAMs) and mixed effect Cox models were used.

Results

MAD showed large variations according to paternal occupation. The lowest MAD in both sexes was that of workers' children: it was 56.3 y (95% CI: [48.6–62.7]) in men and 67.4 y (95% CI: [60.8–72.7]) in women, respectively (95% CI: 13.4 y [5.7–21.3]) and 12.3 y (95% CI: [4.0–19.2]) below the highest MAD attained. MAD experienced by illegitimate children was 18.9 y (95% CI: [13.3–32.3]) shorter than of legitimate children. The multivariate analysis revealed that in both sexes survival to age 31 y was predicted independently by legitimacy and paternal occupation. Paternal occupation was found significantly associated with mortality after age 31 y in females only: accordingly difference in life expectancy at age 31 y was 4.4 y (95% CI: [1.2–7.6]) between upper class and workers' daughters.

Conclusions

Paternal occupation and legitimacy status were strong predictors of offspring longevity in this one-century historical cohort born during World War One.

Introduction

The French civil registration system is organized so that all major life events (such as marriages, divorces and deaths) are systematically notified on birth certificates, wherever these events occur. This has previously provided us with the opportunity to study the adult mortality of orphans who lost their father during World War One (WW1) [1]. The same characteristic of the French civil registration system also offers a rare opportunity for the study of whole-life mortality according to socioeconomic status (SES) at birth.

The effect of SES in early life on health across the lifespan has recently raised a growing interest among epidemiologists [2–4]. Parental SES influences nutrition, maternal stress, and exposure to infections, and can therefore act on physical parameters of a child's development during specific windows of plasticity, notably in intra-uterine life and infancy [5, 6]. Parental SES may also act on future health because it influences educational attainment and thus contributes to SES reached in adulthood, itself a strong predictor of mortality [7]. In addition, wealth is usually transmitted from parents to offspring and may affect health directly or through access to healthcare.

A global assessment of the effect of parental SES on mortality requires the study of quasi-extinct cohorts. Obviously, data on such cohorts are very difficult to obtain, so that most studies about childhood SES have examined adult mortality on short age spans, typically below 30 years. One notable exception is the recent analysis by Juárez et al. of a Swedish cohort born 1915–1929 in Uppsala, whose analysis was restricted to individuals for which at least one of the two parental occupations was known, and was stratified by age. Low SES at the time of the birth, defined by parental occupation (paternal occupation if available, maternal occupation otherwise), and marital status (i.e. legitimacy of the birth), was associated with an increase in mortality at all ages [8]. We report here an analysis of whole-life mortality according to both parental occupations at the time of birth and the legitimacy status of the birth for a cohort born 1914–1916 in Paris.

Materials and methods

Historical material used

Extraction of information from birth registers. The data that we analyzed here are those of the 4,805 "control" subjects of a project on the health consequences of WW1. They are matched for date of birth, sex and age of the mother to the "pupilles de la Nation" (orphans or children of soldiers severely disabled during WW1) born between August 1st 1914 and December 31st 1916 in 16 administrative districts of the Paris region (14 "arrondissements" (boroughs) of Paris and two suburban cities, Neuilly-sur-Seine and Le Kremlin-Bicêtre). Though they were matched to the "pupilles de la Nation", we anticipate the results obtained on this cohort may be generalized to the population of all Parisian births of the time. The following pieces of information were collected on the handwritten birth registers in each district's city hall: date of birth, sex, parental age (precision: year) and occupation (see below) at the time of the birth, legitimacy status, date of death and date of the other life events notified in the margin of birth certificates (Fig 1).

The National Commission on Information Technology and Liberties (Commission Nationale de l'Informatique et des Libertés [9]) granted us authorization to access and analyse those data (registration number 915774).

Longevity information available on birth registers. By law, since March 29th 1945, at occurrence of death, the civil registration service at the place of death systematically notifies the civil registration service at the place of birth, so that the birth certificate is updated in a few

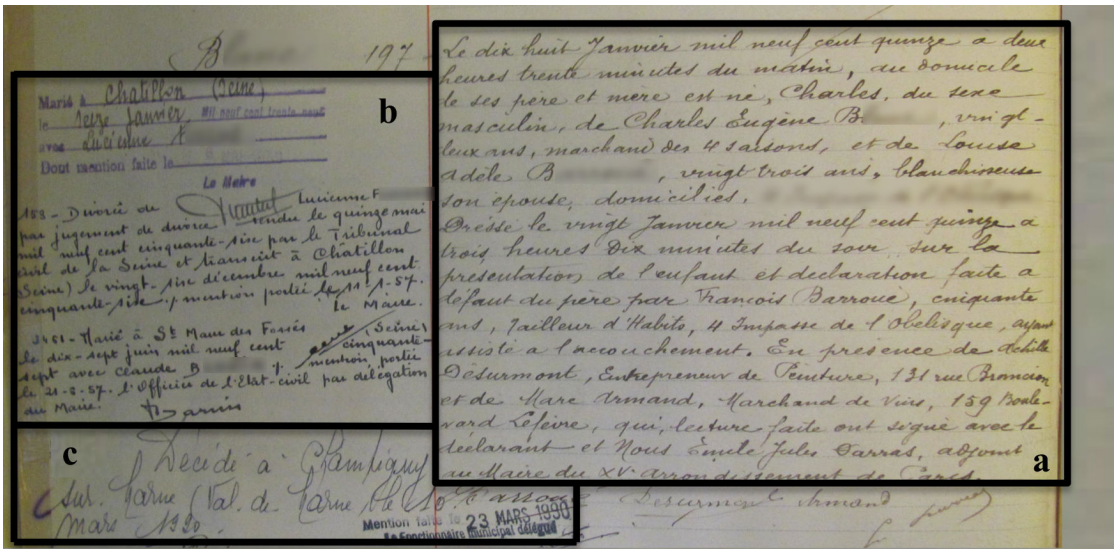

Fig 1. 1914 French birth certificate. The birth certificate gives the date of birth, sex and parental occupations at the time of the birth (zone a). The date of death, if after March 29th 1945, is available in the margin of the birth certificate (zone c). The dates of other life events (zone b) such as marriages and divorces are also notified by law in the margin (since 1897 for marriages, 1939 for divorces) and are used to classify those without a date of death. When no life event is notified after March 29th 1945, the individual is considered dead before this date. Conversely, individuals without a date of death but known to be alive on March 29th 1945 because of a life event after this date are considered alive at age 99. The birth certificate shown was registered on January 20th 1915 and is held by the city hall of the 15th arrondissement of Paris.

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weeks at most. For individuals who died abroad, information is transmitted to the place of birth by the local French consulate. Given that data collection took several months, all dates of death were checked at the end (Sept. 29 –Oct. 8 2015) to avoid differences in the time period covered between districts due to different data collection dates. Because observation of death was available from 1945 onward, there was a 29-month difference in the *age* period on which individuals born in early August 1914 and those born at the end of 1916 were observed. [31; 99] years is the age range on which all dates of death are known.

An individual without a date of death on his birth certificate may have died before March 29th 1945 or still be alive. An individual who was never observed after March 29th 1945 (i.e. for whom no notification of marriage, divorce or guardianship is present on the birth certificate after this date) was considered dead before age 31 y. In the analyses of life expectancy at 31 y (see Statistical analysis below), the longevity L_{31} of those alive at age 99 y (~ 2.5% of all individuals included) was set to 99 + e_r, where e_r is the life expectancy remaining at age 99 as given by the Human Mortality Database [10] for the French 1915 cohort (2.10 y for men and 2.52 y for women).

Classification of occupations. We defined 8 categories for maternal occupations at birth: worker, servant, craftswoman, employee, shopkeeper, housekeeper, housewife, middle & upper class. Housewife ("sans profession") and housekeeper ("ménagère") were occupations so frequently found on birth certificates that we made them categories in our classification of occupations. We defined 6 categories for paternal occupations at birth: worker, craftsman, employee, shopkeeper, middle class and upper class (Table 1). The classification of occupations was performed with all other information made unavailable, so that the investigator classifying (NT) was blind regarding the longevity associated with each occupation. The maternal occupation at the time of birth was available on 99.6% of birth certificates (n = 4,785). Except for oversights, the paternal occupation was available for legitimate children, but not for illegitimate

Table 1. Baseline characteristics of subjects.

	Legitimate births	Illegitimate births	All births
	(n = 3,424)	(n = 1,381)	(n = 4,805)
Date of birth, mean	1915-06-17	1915-06-27	1915-06-20
Sex, n (%)			
Female	1,637 (47.8%)	681 (49.3%)	2,318 (48.2%)
Male	1,787 (52.2%)	700 (50.7%)	2,487 (51.8%)
Paternal occupation, n (%)			
Worker	993 (29.0%)	299 (21.7%)	1,292 (26.9%)
Craftsman	593 (17.3%)	508 (36.8%)	1,101 (22.9%)
Employee	985 (28.8%)	277 (20.0%)	1,262 (26.3%)
Shopkeeper	312 (9.1%)	138 (10.0%)	450 (9.4%)
Middle class	198 (5.8%)	89 (6.4%)	287 (6.0%)
Upper class	342 (10.0%)	71 (5.1%)	412 (8.6%)
Maternal occupation, n (%)			
Worker	364 (10.6%)	201 (14.6%)	566 (11.8%)
Servant	241 (7.0%)	426 (30.8%)	667 (13.9%)
Craftswoman	531 (15.5%)	251 (18.2%)	782 (16.3%)
Employee	249 (7.3%)	147 (10.7%)	397 (8.3%)
Shopkeeper	194 (5.7%)	60 (4.4%)	254 (5.3%)
Housekeeper	615 (18.0%)	142 (10.3%)	757 (15.8%)
Housewife	1,174 (34.3%)	125 (9.0%)	1,299 (27.0%)
Middle/Upper class	55 (1.6%)	28 (2.0%)	84 (1.7%)
Age of the mother, mean (sd)	26.9 (4.9)	24.1 (4.7)	26.1 (5.0)
Status, n (%)			
Died before 31 y	1010 (29.5%)	633 (45.8%)	1643 (34.2%)
Died on [31; 99 y]	2324 (67.9%)	720 (52.1%)	3044 (63.4%)
Alive at 99 y	90 (2.6%)	28 (2.0%)	118 (2.5%)

¶: Paternal occupations for illegitimate births are imputed using MICE. Figures by occupation given in the Table are averaged over the ten completed datasets.

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children. We failed to classify 0.3% of all maternal occupations (n = 14) and 0.2% of all paternal occupations (n = 8). To impute the unavailable and unclassified paternal and maternal occupations, we performed multivariate imputation by chained equations (MICE) [11] using all variables in model (1) (see below) as predictors. We thereby created 10 completed datasets, on which all regression analyses were conducted. The regression coefficients obtained on the 10 datasets were then combined by Rubin's rules [12, 13].

Statistical analysis

Survival functions. The 4,805 individuals are included at birth, and fall into three categories: died before 31 y (with unknown age at death), died on [31; 99 y] (with known age at death), alive at 99 y. Any survival function S(t) is thus known at age 0 and on [31; 99 y]. This enables the computation of the median age at death in groups defined by legitimacy status, paternal occupation or maternal occupation. Bootstrap 95% confidence intervals (95% CI) were computed by first bootstrapping the data (with B = 500 bootstrap samples), and then performing multiple imputation on each bootstrap sample, as recommended by recent work [14].

Survival to 31 years. Probability of survival to age 31 y was modelled with a Generalized Additive Model (GAM) [15, 16]. A smooth function of the date of birth was included in the

predictor to capture the effect of potential unmeasured time-varying explanatory variables [17]. The model was thus:

$$\log\left(\frac{\pi_{31}}{1-\pi_{31}}\right) = PO + f_1(DB) + f_2(AM) + MO + Sex + Illeg + Arr \quad (1)$$

π_{31} is the probability to survive to age 31 y, *PO* the paternal occupation at the time of the birth, *DB* the date of birth (time since August 1st 1914), *AM* the age of the mother at birth, *MO* the maternal occupation, *Illeg* a dummy variable taking value 1 if the birth is illegitimate, and *Arr* a normally distributed random effect controlling for the district of birth. Smooth functions f_1 and f_2 are represented as penalized cubic regression splines with respectively 100 and 8 degrees of freedom and evenly spaced knots. The smoothing parameters determining the effective degree of freedom of f_1 and f_2 are both selected to minimize the unbiased risk estimator score.

Survival after 31 years. The hazard ratio (HR) on the age span [31; 99 y] was regressed on explicatory variables using a mixed effects Cox proportional hazards model:

$$h(t) = h_0(t)\exp(PO + DB + AM + MO + Sex + Illeg + Arr) \quad (2)$$

The notations are the same as above.

Differences in life expectancy at 31 years. To give adjusted estimates of life expectancy at 31 y (L_{31}) by parental occupation, we fitted GAMs with Gaussian errors, identity link and the same predictors as in model (1), with smoothing parameters selected by generalized cross validation.

Because we had to impute all paternal occupations for illegitimate children, all analyses were performed on all children, and on legitimate children alone. Analysis of deviance was used to give a global assessment of the effect of paternal and maternal occupations. In order to test for sex-specific effects, models were also fitted separately for males and females. Finally, analyses of life expectancy at 31 y were performed on all those alive at 31 y (those who died on [31; 99 y] + those classified as alive at 99 y), and those died on [31; 99 y] only. Analyses were performed in R, using the following packages: *mice* for multiple imputation [11], *mgcv* for GAM regressions [18], and *coxme* for proportional hazard models [19]. All confidence intervals given are 95% confidence intervals.

Results

Characteristics of subjects

Table 1 provides the main characteristics of the studied individuals. Among legitimate children (for which both parental occupations are noted on the birth certificate), maternal and paternal occupations were correlated (Cramer's V = 0.29; S1 Table). We found that 45.8% [43.2–48.5] of illegitimate children died before 31 y versus 29.5% [28.0–31.1] of legitimate children.

Total survival experience by parental occupations and legitimacy status

Survival varied strongly with paternal occupation (Fig 2). The highest median age at death (MAD) among women was 79.7 y [72.9–84.5], attained by those born to middle class fathers. The highest MAD among men was 69.4 y [64.9–73.8] for those born to upper class fathers. In both sexes, MAD was the lowest when the father was a worker (Men: 56.3 y [48.6–62.7]; women: 67.4 y [60.8–72.7]) (Fig 2).

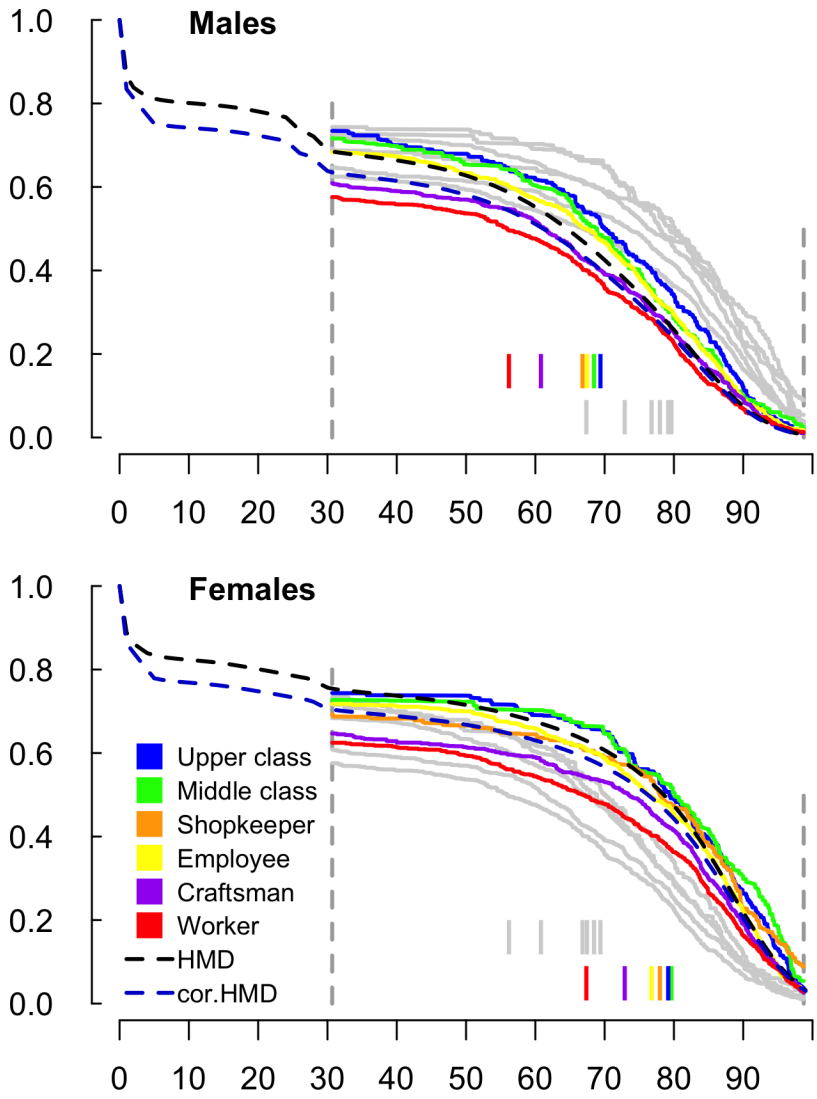

Fig 2. Survival curves by sex and occupation of the father. The survival functions are based on the pooled 10 completed datasets created by multiple imputation. In each plot, grey lines are survival functions for the other sex. Estimates of median ages at death based on B = 500 bootstrap samples are drawn in the lower part of the plots. The survival functions of the French 1915 male and female cohorts as given by the Human Mortality Database (HMD) are also drawn. Child mortality was known to be higher in the "departement" (district) of Paris than nationwide at the beginning of the XXth century. Also drawn are HMD survival functions corrected for this excess child mortality (cor. HMD), based on the quotients of mortality ${}_1q_0$ and ${}_4q_1$ as given by ref. 20, which relate to the 1901–1905 female cohort. 1915 HMD ${}_1q_0$ and ${}_4q_1$ were corrected assuming that the percent excess Parisian mortality for both sexes was the same in 1915 as in 1901–1905.

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MAD of illegitimate children was 18.9 y [13.3–32.3] years below that of legitimate children (illegitimate: 53.2 y [47.9–66.6]; legitimate: 72.1 y [71.0–73.4]). MAD also varied according to maternal occupation in both sexes (S1 Fig).

Survival to 31 years

Survival to 31 y was significantly associated with paternal occupation in all 10 datasets completed by multiple imputation (analysis of deviance: median of the 10 p-values (p) = 7.8 x 10^{-6}; maximum p = 5.3 x 10^{-4}). This was largely due to low survival in worker's offspring: indeed,

the pooled adjusted odds ratio (OR, with craftsmen as the group of reference) was 0.77 [0.63–0.94] for those born to a worker. Though not significant, there was a trend for higher survival for those born to a middle class father (OR = 1.33 [0.89–2.00]) and upper class father (OR = 1.23 [0.87–1.74]). The offspring of craftsmen, employees and shopkeepers experienced intermediate survival (Table 2 and S2 Fig). Consistent with the idea that association between paternal occupation and survival to 31 y was largely driven by the high mortality in workers' offspring, the analysis of deviance was not significant when they were excluded from the dataset (median p = 0.14).

Survival to age 31 y was also strongly decreased in illegitimate children: the adjusted OR with legitimate children was 0.54 [0.46–0.62] (Table 2).

Maternal occupation had no effect (median p = 0.31, minimum p = 0.14). The age of the mother was found to be linearly associated with survival in all datasets (effective degree of freedom of f_2 after penalization ≈1). There was a 1.09 [1.02–1.16] fold increase in survival associated with each 5-year increase in the age of the mother.

The results remained unchanged when the analysis was restricted to legitimate births alone. In particular, paternal occupation was still found associated with survival (analysis of deviance: $p = 1.3 \times 10^{-4}$), again due to low survival in worker's offspring (S2 Fig).

Survival after 31 years

The hazard ratio (HR) was associated with paternal occupation (median $p = 9.0 \times 10^{-3}$; maximum $p = 7.8 \times 10^{-2}$). In the by-sex analysis, the effect of paternal occupation was found to be

Table 2. Parametric terms from model (1) and model (2).

	OR of survival to 31 y (95% CI)	HR on [31; 99 y] (95% CI)
Fatherly occupation		
Worker	0.77 (0.63–0.94)	1.06 (0.94–1.19)
Craftsman	1 (ref)	1 (ref)
Employee	1.18 (0.94–1.46)	1.01 (0.89–1.14)
Shopkeeper	1.06 (0.81–1.38)	0.83 (0.69–1.00)
Middle class	1.33 (0.89–2.00)	0.87 (0.72–1.06)
Upper class	1.23 (0.87–1.74)	0.94 (0.78–1.12)
Motherly occupation		
Worker	0.82 (0.65–1.04)	1.07 (0.93–1.24)
Servant	0.85 (0.68–1.07)	0.98 (0.86–1.13)
Craftswoman	1 (ref)	1 (ref)
Employee	0.96 (0.73–1.25)	0.89 (0.76–1.04)
Shopkeeper	1.04 (0.75–1.45)	1.16 (0.95–1.42)
Housekeeper	0.91 (0.73–1.13)	1.01 (0.89–1.15)
Housewife	1.05 (0.84–1.31)	0.97 (0.86–1.09)
Middle & upper class	1.32 (0.77–2.29)	0.94 (0.71–1.24)
Sex		
M	0.84 (0.74–0.95)	1.63 (1.52–1.76)
F	1 (ref)	1 (ref)
Legitimacy		
Legitimate	1 (ref)	1 (ref)
Illegitimate	0.54 (0.46–0.62)	1.06 (0.96–1.16)

Probability of survival to age 31 y (model 1) and the hazard ratio on [31; 99 y] (model 2) were modeled with Generalized Additive Models on each of the 10 datasets completed by multiple imputation. Adjusted odds ratios (OR) and hazard ratios (HR) obtained on each dataset were then combined by Rubin's rules.

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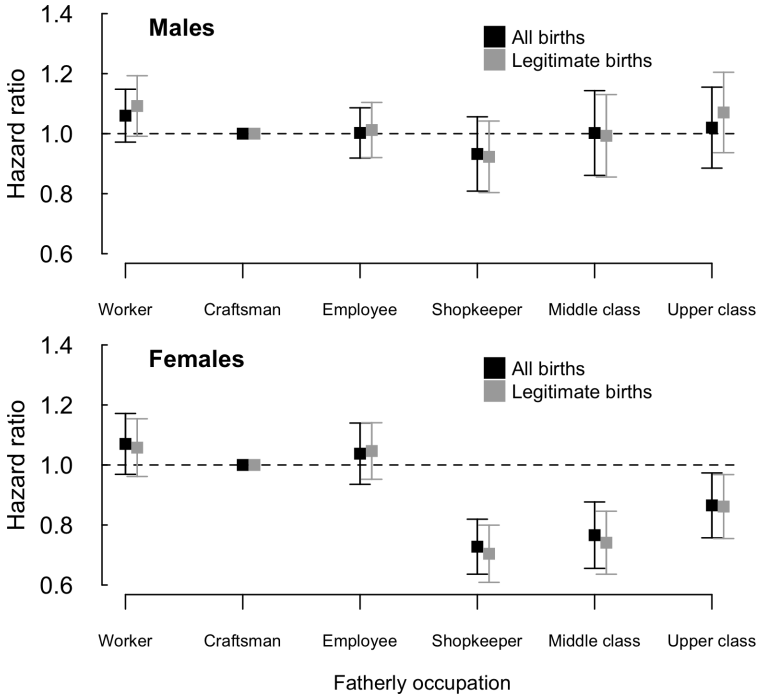

Fig 3. Adjusted hazard ratio according to sex and paternal occupation. The effect of paternal occupation on the hazard ratio on [31; 99 y] is estimated for each completed dataset thanks to a Cox proportional hazard model, and then combined following Rubin's rules. Also given are estimates on legitimate children alone, for whom no imputation of paternal occupations is needed. For both sexes, the reference group is that of craftsmen' children. Estimated effects are given ± standard error.

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significant for females (median $p = 5.2 \times 10^{-4}$), not for males (median $p = 0.73$). As shown on Fig 3, the HR among males was very close in all groups. In contrast, a clear difference was visible among women between the three lower status groups (worker, employee, craftsman) and the three highest (shopkeeper, middle and upper class). The life expectancy analysis was consistent with these results (S3 Fig).

The results held true when the analysis was restricted to legitimate births alone. In particular, an association was found between paternal occupation and survival after age 31 y in females ($p = 3.2 \times 10^{-3}$), but not in males (median $p = 0.74$; see Fig 3).

Discussion

This study reports that parental occupations and legitimacy are strongly associated with whole life mortality for a cohort born a century ago in Paris. The association was observed for mortality after age 31 y as well as before age 31 y.

Because birth registers do not indicate the date of death when it occurred before 1945, the probability of survival to 31 y was our indicator of mortality from birth to young adulthood. Unskilled paternal occupation ('workers' category, which forms the lowest quarter of paternal occupations) and illegitimacy were independently associated with a strong excess risk of death before 31 y. We observed no effect of maternal occupation on survival to 31 y after adjustment for paternal occupation. It is likely that most of the differences in survival to 31 y according to paternal occupation and legitimacy relate to early life mortality, since the main contributors to the probability of death before 31 y in our study were infant (0–1 y) and child (1–5 y) mortalities, and to a lesser extent World War II (WW2) (see Fig 2, HMD survival curves).

In the context of 1914 Paris, both paternal occupation and illegitimacy were likely to influence many environmental factors, including pre and postnatal nutrition, risk of infections (in particular during the 1918 influenza pandemic) and access to healthcare. About 20% of infants were left to wet-nurses mainly residing outside Paris [20]. Illegitimacy increased the probability of being sent to a wet-nurse [21]. Quality of wet-nursing was known to depend directly on the household income [22], and in turn was critical to child's health. Risk of diarrheas (~ 25% of infant deaths nationwide [23]) was increased for bottle-fed infants if sterilization was not performed by the parents or wet-nurse. It may also be the case that the father's environmental exposures affected the offspring's biological vulnerability in early life through transgenerational epigenetic modifications [24–26].

Lack of effect of maternal occupation on survival to 31 y was unexpected. Our interpretation is that it is due to the fact that 43% of mothers are recorded on birth certificates as "housekeeper" or "housewife", a status that may indeed mask heterogeneous socioeconomic conditions and wealth. This is evidenced by the diversity of paternal occupations associated with a "housekeeper" or a "housewife" (see S1 Table). Interestingly, survival was not improved when the mother was a "housekeeper" or a "housewife" compared with employed mothers although they were more available for direct childcare (notably breastfeeding). It may also be noted that the offspring of workers, among whom were women working in war factories, had a survival to 31 y close to that of servants' offspring, a fact that supports the idea that work in a war factory during pregnancy was not a key factor in infant mortality, contrary to what was held by some leading pediatricians of the time [27]. The association found between low maternal age and early life mortality is still observed in contemporary populations [28], despite changes in the distribution of maternal ages, and has been attributed to decreased maternal care [29] and biological immaturity resulting in low birth weight [30].

For those people who survived WW2, knowledge of the exact date of death after 1945 allowed classical survival analysis through two different approaches to study mortality after 31 y (modeling the hazard ratio on [31; 99 y] and modeling the life expectancy at 31 y). Both approaches showed an association between paternal occupation at birth and mortality for females, but not for males. Neither legitimacy nor maternal occupation showed an association with mortality after 31 y.

Loose classification or loose imputation of paternal occupations cannot account for this absence of differences among men after 31 y, given that we do find differences according to paternal occupation for both sexes before 31 y, and among women after 31 y. Moreover, results were not changed when the analysis was restricted to legitimate children alone. One hypothesis is that the men of the cohort encountered in adulthood risk factors that were strong enough to overcome the effects of paternal SES. Indeed, smoking and stress are likely to have been stronger mortality "equalizers" among males than among females. In 1953, 72% of French men (only 17% of women) were regular smokers [31]. On the other side, most females born 1914–1916 into middle and upper class families never entered the workforce [23], thereby remaining protected from the physical and psychosocial stress associated with employed work, contrary to women of the working class.

Although the current study allows no identification of its causes, we wondered if the sexual dimorphism observed for mortality after 31 y could relate in part to the wartime conditions at the time of the birth. Most young women had their husband called to arms in the early months of the conflict. These women had to face loneliness during pregnancy, fear for husband's death and the day-to-day challenges of single life, exposing their offspring to socially dependent degree of early life adversity and childhood stress. Altered perinatal maternal behavior is known to modify the offspring's stress response durably [32, 33], and to yield increased susceptibility to diseases in adulthood [34–36]. Some consequences of prenatal maternal stress

have been shown to vary according to sex on animal models [37–39], and occasionally in humans [40]. Disentangling their potential contribution to that of the aforementioned conditions lived later in life could be achieved by studying individuals born shortly before the War, e.g. around 1910.

In conclusion, the observation of this cohort over its entire lifetime found large differences in median ages at death between children of both sexes born to parents of high and low socioeconomic status. Most of these differences were due to mortality occurring during youth, likely to be due to direct environmental accidents hitting more vulnerable offspring of both sexes. Differential mortality was also observed after 31 y for women only, an unexpected observation that calls for further studies of extinct cohorts in other historical contexts. While our results show that social inequalities in the early 20th century translated in decreased longevity in offspring of those unprivileged, nobody can predict how these findings can be extrapolated to children born in contemporary countries. Some of the signals generated by the lowest SES situations may still act on infants in contemporary societies through biological, educational, or behavioral pathways comparable to that which prevailed for those born in 1914 France. In contrast, newly appeared conditions that have today strong links with SES, such as obesity [41], may affect offspring's longevity through socially dependent mechanisms that were not prevalent a century ago. Causal mechanisms for such long-term differences in longevity may involve the developmental effects of socially dependent environmental cues on phenotypic plasticity.

Supporting information

S1 Fig. Median age at death according to maternal occupation and sex. Median ages at death are computed separately for males and females according to maternal occupation at the time of birth. For both sexes, those born of a middle & upper class mother have the highest median age at death. Dotted line: Males = Females.
(PDF)

S2 Fig. Survival to 31 y by paternal occupation (all births / legitimate births). Probability of survival to 31 y was modeled with a Generalized Additive Model (GAM) on each of the 10 datasets completed by multiple imputation. The model was fitted for all births and for legitimate births only (which do not necessitate imputation of paternal occupations). Association of survival to 31 y with paternal occupation was not changed when the analysis was restricted to legitimate births alone. Plotted standard errors are those for the all births estimates and are computed thanks to the delta method.
(TIFF)

S3 Fig. Life expectancy at 31 y by paternal occupation. The life expectancy at 31 y was modeled with a Generalized Additive Model separately for each sex on each completed dataset and then combined. Since March 29th 1945, dates of deaths have been notified on birth certificates. [31; 99 y] is the age range on which the deaths of all the members of the cohort were observed. Those with no date of death on their birth certificate may have died before March 29th 1945 or be alive at the end of the observation period. Those with no life event (marriage, divorce, guardianship) after March 29th 1945 were considered dead before March 29th 1945. Conversely, those with no date of death but at least one life event after March 29th 1945 were considered alive at age 99 y. To test the effect of this indirect means of classification, the analysis of life expectancy at 31 y was performed on all those considered alive at 31 y (black) and was then restricted to those who died on [31; 99 y] (grey), with hardly any difference in the results. These results are in line with those obtained from the modeling of the hazard ratio on the age span [31; 99 y]: increased variability according to paternal occupation is found among females.

Estimated effects are given ± standard error.
(TIFF)

S1 File. Dataset used.
(CSV)

S1 Table. Contingency table for parental occupations of legitimate children. Both paternal and maternal occupations are available on the birth certificate of virtually all legitimate children. 0.93% of all legitimate children (N = 32) with at least one missing or unclassified parental occupation were excluded from the contingency table. Cramer's V is 0.29.
(DOCX)

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Investigation: Nicolas Todd.

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Writing – review & editing: Nicolas Todd, Sophie Le Fur, Pierre Bougnères, Alain-Jacques Valleron.

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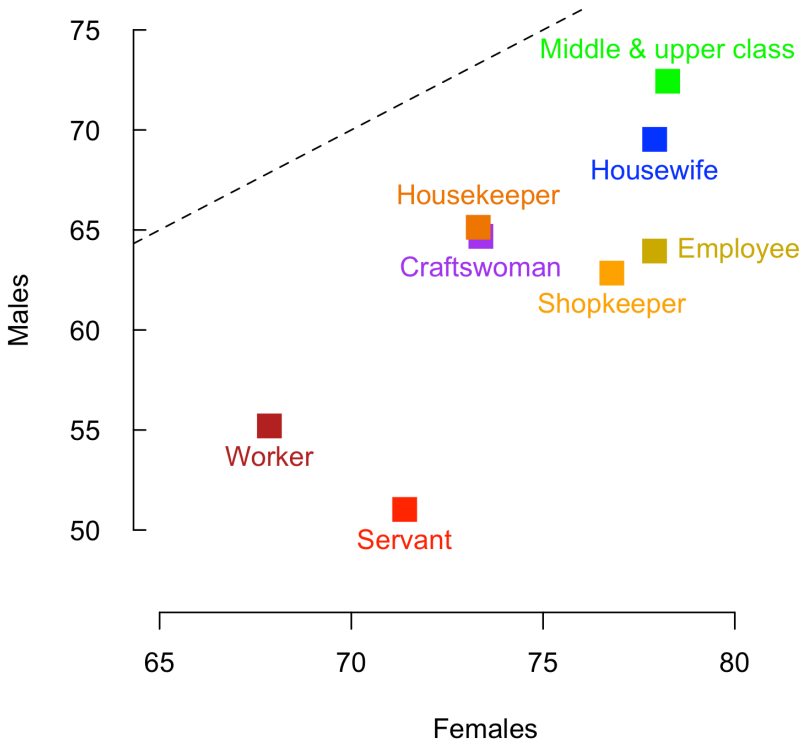
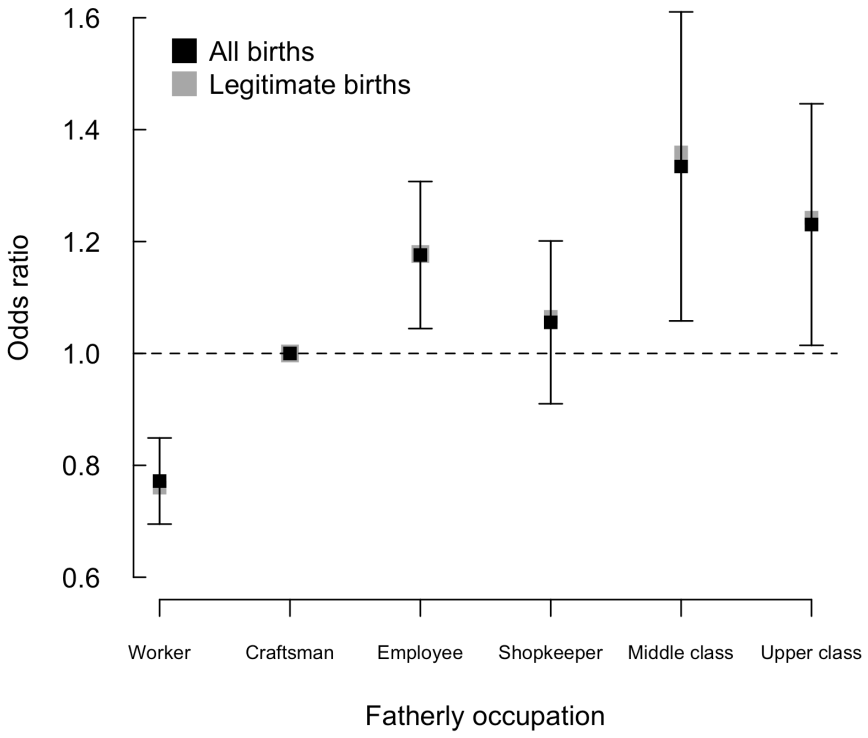
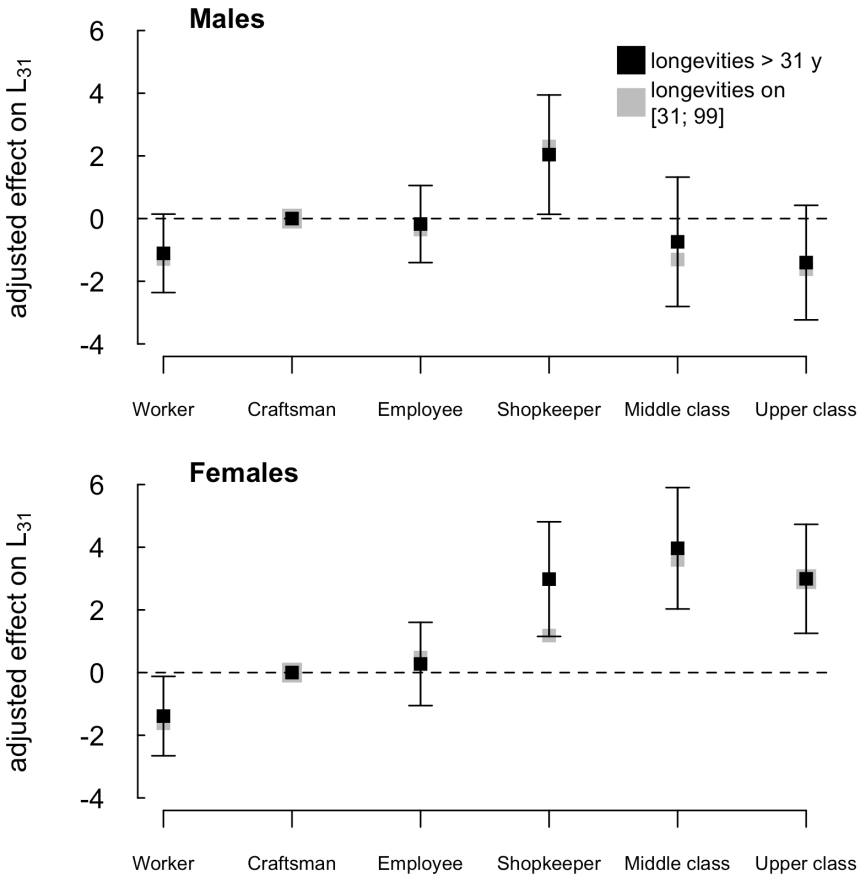
S1 Fig. Median age at death according to maternal occupation and sex.



S2 Fig. Survival to 31 y by paternal occupation (all births / legitimate births)



S3 Fig. Life expectancy at 31 y by paternal occupation



S1 Table. Contingency table for parental occupations of legitimate children

Father **Mother**	Worker	Craftsman	Employee	Shopkeeper	Middle Class	Upper Class
Worker	199 (20.2%)	84 (14.3%)	54 (5.5%)	16 (5.1%)	8 (4.1%)	1 (0.3%)
Servant	76 (7.7%)	26 (4.4%)	119 (12.2%)	14 (4.5%)	4 (2.0%)	0
Craftswoman	159 (16.2%)	148 (25.2%)	157 (16.1%)	30 (9.6%)	30 (15.2%)	2 (0.6%)
Employee	45 (4.6%)	39 (6.6%)	118 (12.1%)	25 (8.0%)	15 (7.6%)	5 (1.5%)
Shopkeeper	37 (3.8%)	20 (3.4%)	26 (2.7%)	102 (32.8%)	5 (2.5%)	3 (0.9%)
Housekeeper	259 (26.3%)	116 (19.7%)	175 (17.9%)	39 (12.5%)	17 (8.6%)	3 (0.9%)
Housewife	206 (21.0%)	148 (25.2%)	309 (31.7%)	85 (27.3%)	106 (53.8%)	307 (90.8%)
Middle & Upper class	2 (0.2%)	7 (1.2%)	17 (1.7%)	0 (0.0%)	12 (6.1%)	17 (5.0%)

Percentage are in column.

Prenatal loss of father during World War One is predictive of a reduced lifespan in adulthood

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Although early-life stress is known to alter health, its long-term consequences on mortality remain largely unknown. Thanks to unique French legislation established in 1917 for war orphans and children of disabled soldiers, we were able to study the adult mortality of individuals born in 1914–1916 whose fathers were killed during World War 1. Vital information and socio-demographic characteristics were extracted manually from historical civil registers for 5,671 children born between 1 August 1914 and 31 December 1916 who were granted the status of "*pupille de la Nation*" (orphan of the Nation). We used a database comprising 1.4 million deceased soldiers to identify war orphans and collect information on their fathers and then paired each orphan with a nonorphan from the same birth register matched for date of birth, sex, and mother's age at the infant's birth. Mortality between ages 31 and 99 y was analyzed for 2,365 orphan/nonorphan pairs. The mean loss of adult lifespan of orphans who had lost their father before birth was 2.4 y (95% CI: 0.7, 3.9 y) and was the result of increased mortality before age 65 y. Adult lifespan was not reduced when the father's death occurred after the infant's birth. These results support the notion that intrauterine exposure to a major psychological maternal stress can affect human longevity.

intrauterine programming | maternal bereavement | adult mortality | historical cohort | World War One

Multiple lines of evidence indicate that exposure to adverse environmental cues in the early stages of development may have durable effects on biological vulnerability at older ages (1, 2). Following D. J. Barker's seminal observations ("the womb may be more important than the home") in children born during 1911–1930 (3), the Fetal Origins of Adult Disease hypothesis (4) and the Developmental Origin of Health and Disease (DOHaD) hypothesis (5) have developed. Two main kinds of early-life adversities, undernutrition and psychic maternal stress, have been studied in humans. Indeed, exposure to famine during pregnancy can have long-range consequences on offspring's morbidities including cardiovascular, metabolic, and mental diseases (6–8). Psychic suffering of pregnant mothers has been associated with functional alteration in the offspring's hypothalamo–pituitary–adrenal (HPA) axis (9, 10) that may pave the way for psychic vulnerabilities (11), obesity (12), diabetes (13), and cardiovascular diseases (14).

Stressors in critical periods of development induce both immediate, reversible homeostatic mechanisms and whole-life modifications of the response to environmental challenges (15). The mechanisms implicated in early programming of adult disorders remain largely unknown, although epigenetics is likely involved (16, 17). The intrauterine and early postnatal periods are characterized by high epigenetic plasticity (18); thus, as shown in laboratory rodents, early-life stress can affect development by durably imprinting specific brain regions and other tissues through epigenetic modifications (19). Restraint stress (20) or repeated exposure of pregnant dams to an aggressive congener (21), poor maternal care (22), or separation of recently born pups from the mother (23, 24) were shown to result in tissue-specific changes in DNA methylation and in the activity of genes involved in the stress response (22–25); some of these effects are sexually dimorphic (26). Epigenetics, however, is only one of the many effectors of early-life stress that can act on brain development (19); for example, prenatal stress in rats induces a reduction of neurogenesis in specific brain regions (27).

Few studies have investigated the mortality consequences of early-life conditions, including caloric deprivation during gestation (28, 29), economic conditions at birth (30), and season of birth (31). For instance, males born at the height of the Finnish famine lost ∼1 y of life expectancy at age 40 y (29). To our knowledge, only two studies have related early psychological stress and adult mortality (32, 33). No increased mortality between age 27 and 69 y was found in the 1,726 members of the Helsinki Birth Cohort (born 1934–1944 and followed from 1971–2003) who were separated as children from their parents during the Second World War (32). In the 1958 British birth cohort, increased all-cause mortality before age 50 y was found for the 4,543 individuals who experienced events such as parental divorce or bereavement in early life (33).

World War I (WWI) has been described as a "vast human experiment in stress" (34). Based on universal conscription, the French army suffered heavy losses (∼1.4 million deaths). The great majority of casualties were men aged 18–35 years old in 1914 and were caused mainly by artillery bombardments (35). Every day, about 350 French women lost their husbands, an event found to top a list of 43 stressful life events (36).

We studied the adult mortality of individuals whose fathers were killed during WWI. Our working hypothesis was that the father's death, known to be associated with maternal stress of extreme psychic intensity, could program orphans for various disorders, leading to an increased mortality in adulthood. Further, we hypothesized that if specific in utero programming did take place, it could be revealed by a decreased lifespan observed only in orphans whose fathers died before they were born (prenatal orphans). Depending on the mechanisms involved, male and female offspring might not have been equally affected.

Significance

The First World War was a historical experiment for early-life stress. Fathers of hundreds of thousands of children of all ages were killed during the conflict. The Developmental Origins of Health and Disease hypothesis predicts long-term effects of early-life stress. We collected historical data on French orphans born 1914–1916 and their fathers' military records and compared the orphans' mortality in adulthood (age 31–99 y) with that of matched nonorphans. We found a strong decrease in lifespan, reflecting increased mortality before age 65 y, in persons whose fathers died before, not after, their birth. These results support the notion that maternal psychological stress in pregnancy decreases adult longevity in offspring.

Author contributions: N.T., A.-J.V., and P.B. designed research; N.T. performed research; N.T., A.-J.V., and P.B. analyzed data; and N.T., A.-J.V., and P.B. wrote the paper.

The authors declare no conflict of interest.

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MEDICAL SCIENCES

We chose the design of a historical (non-concurrent) cohort study to test the relation between the loss of father and the mortality outcome. We took advantage of a specific legal status created in July 1917 and granted upon request to war orphans from 1918 onwards (37) that enabled state assistance and financial support if needed. The children, named "*pupilles de la Nation*" (orphans of the Nation), were said to be "adopted by the Nation," an event noted on their birth certificate (Fig. 1*A*). By law, adoption, marriage, divorce, and, since 1945, death also were systematically inscribed on birth certificates, no matter where they occurred. Any French city hall continuously updates its birth registers, receiving systematic notifications from the ~36,000 other city halls covering France and consulates abroad (death and marriage notifications) and from civil tribunals and law firms (adoptions and divorces).

We identified and computerized the birth certificates of 5,671 *pupilles de la Nation* born between 1914 and 1916 in two large cities, Paris and Bordeaux. The dates of death of *pupilles* who died after 1945 were known by the notifications on their birth certificates. For the 3,210 *pupilles* identified as war orphans, we retrieved the dates and causes of paternal death in the publicly available database of all military deaths that occurred between 3 August 1914 and 1 June 1919 (Fig. 1*B*). After we excluded those whose father died from disease, we compared the adult lifespan of orphans with that of non-*pupille* individuals (i.e., matched nonorphans, MNOs) drawn from the same birth registers. An orphan and an MNO were matched by sex, mother's age (± 2 y), district, and date of birth. The flowchart of the study is shown in Fig. S1. The adult lifespan of 2,365 orphan/MNO pairs alive at age 31 y was analyzed. Lifespan comparisons with MNOs were performed separately for prenatal and postnatal orphans.

Results

Baseline Characteristics of Subjects. Table 1 shows the characteristics of the 2,365 pairs (see Table S1 for detailed characteristics); 27.7% (95% CI: 25.9, 29.6%) of orphans were prenatal orphans, and 72.3% (95% CI: 70.4, 74.1%) were postnatal orphans.

Dates of birth of MNOs matched those of orphans. The distribution of dates of birth of prenatal and postnatal orphans showed differences (Fig. S2). The monthly number of orphans fell in May 1915. Although the dates of birth of postnatal orphans were uniformly distributed before May 1915, a peak in prenatal orphans occurred in February–April 1915 (see legend of Fig. S2).

The paternal occupation score (range: 1–6) was 2.60 (95% CI: 2.46, 2.74) in prenatal orphans and 2.70 (95% CI: 2.58, 2.82) in their MNOs (median P of the χ^2 test over the 10 datasets obtained by multiple imputation = 0.02). This orphan/MNO difference was similar in postnatal orphan/MNO pairs [postnatal orphans: 2.62 (95% CI: 2.55, 2.69); MNOs: 2.75 (95% CI: 2.68, 2.83)]. The illegitimacy rate was lower in orphans than in MNOs (Table 1): 4.0% (95% CI: 2.7, 5.8%) in prenatal orphans, 11.7% (95% CI: 10.2, 13.3%) in postnatal orphans, and 15.9% (95% CI:13.2. 18.9%) and 17.3% (95% CI:15.6, 19.2%) in their respective MNOs.

Difference in Adult Lifespan Between Orphans and MNOs. Adult lifespan was different in prenatal orphans and their MNOs (Wilcoxon test: $P = 8.1 \times 10^{-3}$). No difference was found between postnatal orphans and their MNOs (Wilcoxon test: $P = 0.99$). Prenatal and postnatal orphans had different losses of lifespan (permutation test: $P = 0.03$). Mean lifespan was 75.9 y (95% CI: 74.6, 77.1 y) in prenatal orphans vs. 78.2 y (95% CI: 77.1, 79.3 y) in their MNOs and was 76.7 y (95% CI: 76.0, 77.4 y) in postnatal orphans vs. 77.0 y (95% CI: 76.3, 77.7 y) in their MNOs. The mean lifespan of prenatal orphans was 2.4 y (95% CI: 0.7, 3.9 y) less than that of their MNOs. The difference was 0.3 y (95% CI: −0.8, 1.3 y) in postnatal orphans. Using a Generalized Additive Model (GAM) to control for legitimacy, parental occupation, and age, the adjusted difference between orphans and MNOs was 2.0 y (95% CI: 0.1, 4.0 y) higher in prenatal than in postnatal pairs.

The observed difference lifespan in orphan/MNO prenatal pairs was stronger in males [males: 3.1 y (95% CI: 0.8, 5.4 y); females: 1.3 y (95% CI: −1.1, 3.5 y)]. However, the male/female difference in effects did not achieve significance (permutation test: $P = 0.29$).

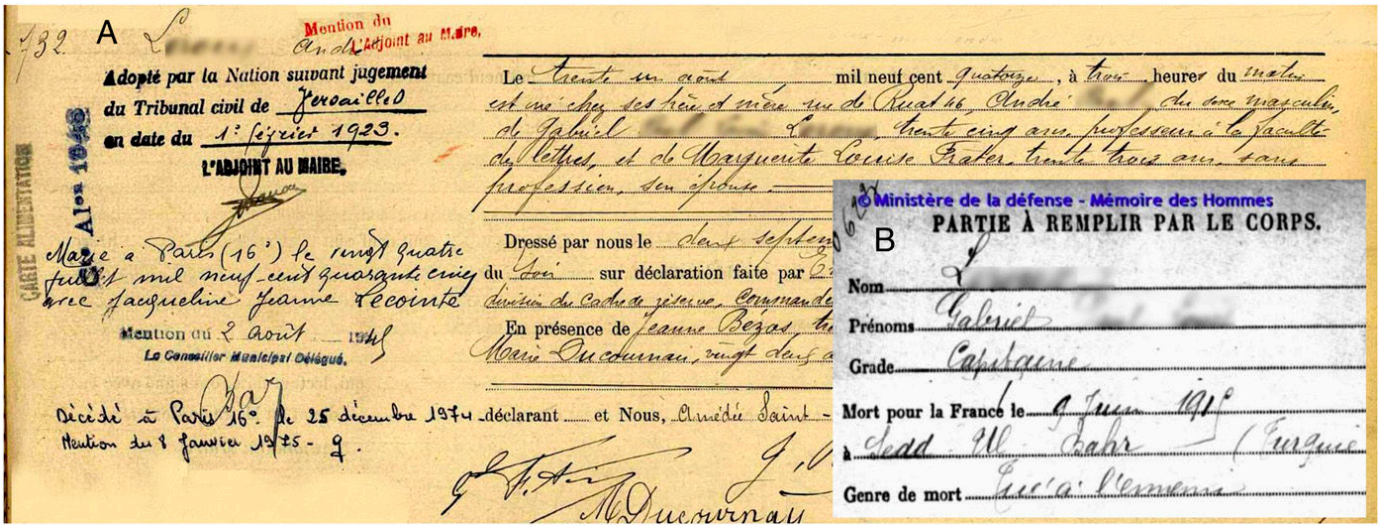

Fig. 1. Historical material used: Examples of an orphan's birth certificate (*A*) and the military record of the orphan's father (*B*). (*A*) Birth certificate of a *pupille de la Nation*, André L., born of Gabriel L. on 31 August, 1914, in Bordeaux. The tribunal of the city of Versailles granted him *pupille de la Nation* status in 1923. That information was automatically transmitted by the Versailles tribunal to the city hall of Bordeaux and was transcribed by a civil servant in the upper left margin of the birth certificate. Similarly, notification of André L.'s marriage (in 1945) and death (in 1974) were transmitted (both by the city hall of the 16th district of Paris) to the city hall of Bordeaux, which noted these life events on the left margin of the birth certificate a few days after they occurred (© archives Bordeaux métropole – Bordeaux 1 E 427). (*B*) We searched for the father of André L., Gabriel L., by name and age in the database of French soldiers who died during WW1 (available at www.memoiredeshommes.sga.defense.gouv.fr/en/article.php?larub=80). The database yielded the image of the father's record (selected sections are shown). Gabriel L. was killed in action on 9 June 1915.

Table 1. Baseline characteristics of the 2,365 studied orphan/MNO pairs

Variable	Prenatal orphans (n = 656)	MNOs (n = 656)	Postnatal orphans (n = 1,709)	MNOs (n = 1,709)
Date of birth, mean	28 April 1915	27 April 1915	1 April 1915	2 April 1915
Sex, n (%)				
Female	319 (48.6)	319 (48.6)	814 (47.6)	814 (47.6)
Male	337 (51.4)	337 (51.4)	895 (52.4)	895 (52.4)
Legitimacy, n (%)				
Legitimate	630 (96.0)	552 (84.1)	1,509 (88.3)	1,413 (82.7)
Illegitimate	26 (4.0)	104 (15.9)	200 (11.7)	296 (17.3)
Paternal OS (95% CI)	2.60 (2.46, 2.74)	2.70 (2.58, 2.82)	2.62 (2.55, 2.69)	2.75 (2.68, 2.83)
Maternal OS (95% CI)	4.42 (4.26, 4.59)	4.70 (4.53, 4.86)	4.44 (4.34, 4.54)	4.62 (4.52, 4.72)
Maternal age, mean (SD)	25.8 (4.3)	26.2 (4.5)	25.6 (4.9)	26.4 (5.0)
Paternal age, mean (SD)	28.7 (4.3)	30.4 (5.7)	28.5 (4.9)	30.6 (6.2)
Status at age 99, n (%)				
Dead	630 (96.0)	637 (97.1)	1,645 (96.3)	1,632 (95.5)
Alive	26 (4.0)	19 (2.9)	64 (3.7)	77 (4.5)

OS, occupation score (*Methods*).

We examined the possibility of an increased effect of father's death in early pregnancy (first trimester vs. pooled second and third trimesters) or late pregnancy (third trimester vs. pooled first and second trimesters). No difference in orphan/MNO lifespan was found when the father's death occurred during early pregnancy (permutation test: $P = 0.80$), but the orphan/MNO difference reached 4.1 y (95% CI: 1.5, 6.7 y) when the father's death occurred during the third trimester vs. 1.2 y (95% CI: −0.8, 3.2 y) when the father's death occurred during the first/second trimester (permutation test: $P = 0.07$) (Fig. 2). For postnatal orphans, the mean difference between the orphans and the MNOs was similar when the father's death occurred in the first year of postnatal life or after age 1 y (permutation test: $P = 0.59$) (Fig. 2) and when the father's death occurred before or after 6 mo of age (permutation test: $P = 0.94$).

Evolution of Differences in Lifespan with Age. A larger proportion of prenatal orphans (150/656) than their MNOs (107/656) died before age 65 y ($P = 3.5 \times 10^{-3}$). No difference was found in remaining lifespan for prenatal orphans and MNOs alive at age 65 y (Fig. 3), indicating that the 2.4-y difference in remaining life expectancy at age 31 y reflected increased mortality between the ages of 31 and 65 y.

Sensitivity Analyses. Because of the difference in the proportion of legitimate children in orphans and MNOs, the analyses were performed on the subset of orphan/MNO pairs in which both members were legitimate. The difference between prenatal and postnatal pairs was maintained: The mean loss of lifespan of orphans was 2.7 y (95% CI: 0.9, 4.4 y) in prenatal legitimate pairs and was 0.2 y (95% CI: −0.9, 1.4 y) in postnatal legitimate pairs (permutation test: $P = 0.03$). In the multivariate analysis restricted to legitimate pairs, the difference with MNOs was 2.6 y (95% CI: 0.4, 4.7 y) greater in prenatal than in postnatal orphans.

Results remained consistent when rematched pairs were removed (*Methods*), when the analysis was restricted to Paris, when median, not mean, differences were analyzed, when only pairs born before May 1915 (i.e., conceived before the beginning of the war) were included, or when the longevity of those still alive at age 99 y was imputed and included in the analyses.

Discussion

All persons in the current study were born in 1914–1916, at a time when most mothers faced uncertainty about safety and nutrition and an increased workload. Those whose spouse survived may have lost a brother or friend. Those who lost their spouse were not always informed immediately (*SI Text*). Our main finding was a large difference of 2.4 y in adult lifespan between prenatal orphans and MNOs because of increased mortality before age 65 y. In contrast, postnatal orphans and their MNOs had quasi-identical lifespans. Both findings are of interest in the context of the DOHaD hypothesis.

It is known that early mortality selection may mask the negative long-term effects of an early-life adversity by enriching the proportion of more robust individuals in the studied population (30). A striking example is the Finnish famine, when selection induced by the immediate threefold increase in mortality was strong enough to mask a 1-y decrease in adult life expectancy (28, 29). Had preferential mortality been present among WWI

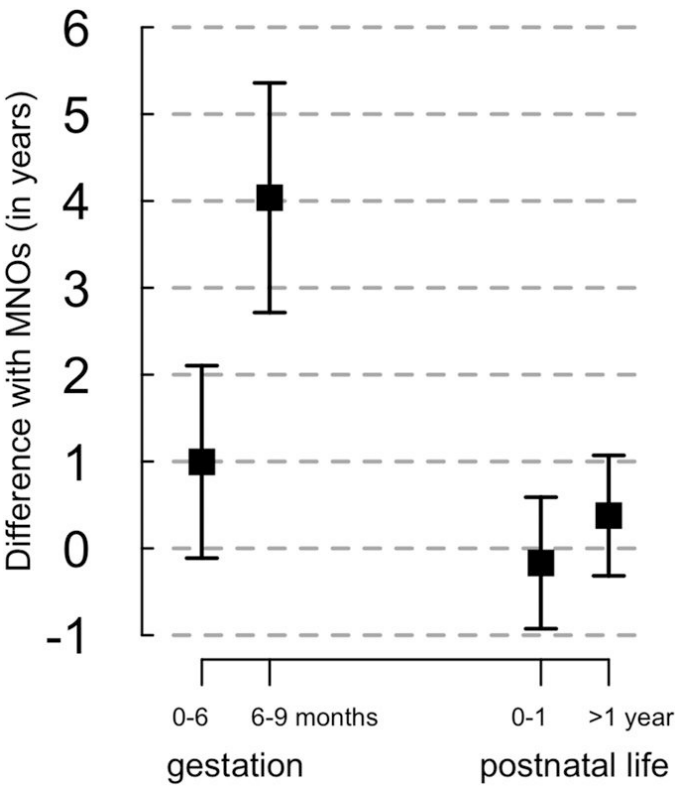

Fig. 2. Mean difference in lifespan between war orphans and MNOs according to age at father's death. Data are shown as mean ± SE.

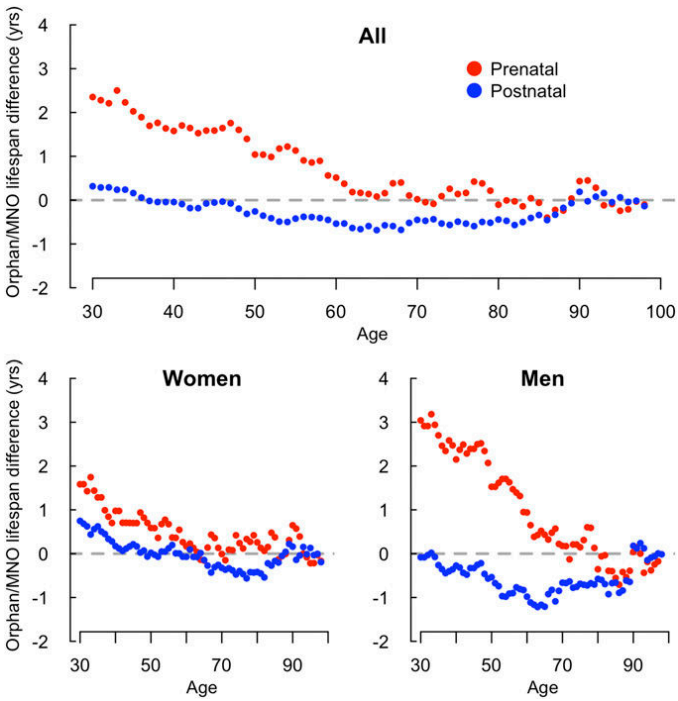

Fig. 3. Variation with age of the difference between orphan and MNO remaining lifespans, by sex.

orphans before they reached age 31 y, a more robust proportion of them would have been selected, strengthening our finding of a loss of lifespan in prenatal orphans.

In fact, orphans and MNOs followed a similar path of adversities except for the father's death. Because adoptions by the Nation started in 1918, only orphans alive in 1918 could become *pupilles*, precluding a direct study of infant and child mortality. However, there is no evidence for any selective pressure comparable to a famine in the early life of WWI orphans. When the Spanish influenza pandemic started in France in August 1918 (38), the studied orphans and MNOs were 1.5–4 y old. We see no reason to postulate that the Spanish flu struck significantly more war orphans than MNOs. Indirect evidence against a significant early-mortality selection also comes from the examination of paternal occupations. The odds ratio of survival in the Finnish famine was ~2.5 between rich and poor families (39). In contrast, we observed only minimal differences in the occupations of the fathers of the war orphans who survived to adulthood and the fathers of their MNOs (Table 1 and Table S1).

Our rule for recruiting MNOs aimed at limiting confounding factors. An orphan and the MNO were born in the same district. In 87.8% of the orphan/MNO pairs, the difference in dates of birth was less than 2 wk, guaranteeing that an orphan and the MNO faced a comparable external environment and food supply at the earliest stages of development. Matching of date and district of birth also was critical because of the migrations induced by the war. In particular, refugees from the invaded regions of the northeast, including pregnant women, progressively settled in Paris (40), thereby modifying the area of recruitment (Fig. S3*C*).

We searched for variables that might have influenced both the offspring's lifespan and the paternal risk of death at war. The risk of death affected all strata of society because of universal conscription and depended on three key factors: age, health, and occupation. Men aged ≥35 y in 1914 were assigned to less exposed units (territorial regiments) (35). Because paternal age was not always available on birth certificates, we matched MNOs and orphans by maternal age, with which paternal age is associated. This matching ensured that mean paternal age was comparable in MNOs and orphans (Table 1). After thorough medical examination, French men in poor health were declared unfit for military service or were assigned to units not involved in combat. Thus fathers of orphans were men in good health. Another source of confounding might be that specific occupations at all levels of the social ladder protected a fraction of citizens from combat (e.g., railroad workers, policemen, physicians). Our detailed classification of paternal occupations in six socioeconomic categories showed only minimal differences between fathers of orphans and of MNOs (Table 1). Heterogeneity that might remain within categories is unlikely to be different in prenatal and postnatal pairs, so it could not account for the observed difference in loss of adult lifespan.

Because the *pupille de la Nation* status was granted upon request, we checked to confirm that the non-*pupille* individuals initially drawn to serve as MNOs were not war orphans (Fig. S1). We found that only 1% of the MNOs alive at age 31 y actually were war orphans who did not become *pupilles* (Table S2). There was also the question of legitimacy. A strikingly low illegitimacy rate (4.0%) was observed in prenatal orphans (Table 1), perhaps because, for unmarried couples, the early death of the partner made recognition of the child impossible. For mothers who had no definite proof of paternity (letters or other evidence), the lack of recognition made application to the *pupille* status impossible. We found that legitimacy cannot explain the difference in lifespan, because this difference also was observed in the analysis performed on legitimate children only.

Our main argument for our belief that potential confounding factors were unlikely to explain our observation is that we observed no association between postnatal father's death and reduced lifespan. Similarly, the decreased lifespan found in prenatal orphans could not be explained by degraded familial socioeconomic status, because we observed no loss of lifespan in the postnatal orphans, who faced comparable conditions in childhood and adolescence.

Finally, maternal stress during pregnancy appears the most plausible cause for the reduced lifespan of prenatal orphans. Glucocorticoids are a major candidate for programming the womb and the fetal HPA axis during prenatal stress (41). The maternal HPA axis undergoes dramatic changes during pregnancy. Although cortisol levels rise threefold by the third trimester, placental 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) maintains low concentrations of cortisol in the fetal circulation until late in gestation (42). This hypocortisolic fetal milieu seems crucial for fetal HPA axis maturation and regulation of steroidogenesis (43). Placental 11β-HSD2 is more active in females (44) and is sensitive to maternal stress, which causes a greater transfer of glucocorticoids from mother to fetus. A reduction in placental levels of 11β-HSD2 occurs during late gestation, allowing an increased transfer of maternal glucocorticoids to the fetus and exacerbation of the effects of maternal stress on the fetus (45, 46). Because maternal cortisol levels are much higher than fetal levels, even moderate changes in placental 11β-HSD2 can significantly modify the glucocorticoid exposure of the fetus. The increase in fetal glucocorticoid levels can lead to fundamental changes in gene regulation and fetal development in many developing organs and in the HPA axis, in particular (47, 48).

Some of these changes may relate to the powerful effects of glucocorticoids on the epigenome (49), which can imprint male and female fetuses for life. Indeed, durable epigenetic imprints involving genes expressed in regions of the HPA axis may have a long-lasting influence on the expression of these genes and cause an altered cortisol reactivity to future stress in later life (50). Human studies have shown that maternal psychological trauma during pregnancy can influence the offspring's epigenome, notably the human glucocorticoid receptor gene (*NR3C1*) that mediates the effects of fetal cortisol on HPA-axis development. Precisely, the *NR3C1* locus was found to be hypermethylated in children whose mothers suffered from depression and anxiety during the third trimester of their pregnancy (51). Women's experience of

intimate partner violence during pregnancy also has been associated with increased *NR3C1* methylation in their adolescent offspring (52). When women were exposed to the Tutsi genocide during pregnancy, their children had higher methylation of the *NR3C1* exon 1F than offspring from nonexposed women (53). *NR3C1* is not the only locus where DNA methylation is modified by maternal stress. Other methylation changes in offspring exposed to maternal depression were detectable in the immune system at birth and persisted until adulthood in the hippocampus, a known regulator of HPA activity (54).

Remarkably, the methylation status of the *NR3C1* promoter was found to be more sensitive to maternal depression in late pregnancy (55). This finding is consistent with our observation of a trend for a greater increase in adult mortality when the father's death occurred during the third trimester of intrauterine life. Trimester-specific early-life adversities may have differential effects on particular systems. In this respect, psychic maternal stress is unlikely to have the same effects on offspring health as famine, which is known to favor late development of diseases if it occurs during early gestation. It is important to note that programming mechanisms remain out of reach in humans, notably with regard to the tissue-specific nature of epigenetic modifications, because the tissues of interest, such as the hippocampus, hypothalamus, or pituitary, escape investigation. Nevertheless epigenetic imprints probably represent a critical component of the programming process and could be partly responsible for the long-range effects of antenatal glucocorticoid exposure on neurologic, cardiovascular, and metabolic function through their persistent effects on the HPA axis (56). Epigenetic programming of neuroendocrine and behavioral phenotypes has some sex specificity (26). It is conceivable that imprints in the HPA axis following the father's death could be perpetuated in subsequent generations through the female lineage and pregnancies.

In conclusion, our study of the consequences of maternal bereavement during WWI, a single stress of extreme psychic intensity, allowed us to study the effects of the loss of the father at specific moments of child development and to compare the whole-life adult mortality of persons whose mothers had experienced this stress with that of matched individuals born at the same time and place to mothers who had not experienced this particular stress. Although we were not able to dissect the causes of the increased mortality in orphans, our study contributes to the assessment of the health impact of severe maternal psychic stress during pregnancy.

Methods

Identification of *Pupilles de la Nation* on the Birth Registers. All *pupilles de la Nation* born in 17 districts of Paris between 1 August 1914 and 31 December 1916 and in the four districts of Bordeaux from 1 August 1914 to 31 December 1915 (Table S3) were identified by the "adopted by the Nation" notification that was systematically inscribed on their birth certificates following adoption. Vital information available on birth certificates was computerized; see *SI Text* for details. The Commission Nationale de l'Informatique et des Libertés (57) authorized us to access and analyze those data (registration number 915774).

Choice of MNOs. MNOs were used for comparison of orphans' lifespans. Because MNOs were selected before the identification of war orphans among *pupilles* (see below), an MNO was paired to each *pupille*, whether the *pupille* was an orphan or the child of a disabled soldier. The MNO of a *pupille* was selected from the same birth register and was the closest (going upward in the birth register, from the *pupille*'s certificate) non-*pupille* same-sex birth with an age difference ≤2 y between the MNO's mother and the *pupille*'s mother.

Claiming the status of *pupille de la Nation* required a proof of dead soldier's paternity of the child. Therefore, a child whose father's identity was unknown could not become a *pupille*, whatever his father's war experience. *Pupilles* were legitimate children or children who were born illegitimate but later were recognized by their father or by judgment (in cases in which the father died before recognition but where definite proof of paternity existed). MNOs with an unknown father therefore were excluded from the analysis.

Longevity Information Available on Birth Certificates. The date of death has been systematically recorded on French birth certificates since 29 March 1945. Wherever and whenever death occurs, the civil registration service at the place of death notifies the civil registration service at the place of birth, so that the birth certificate is updated within a few weeks, at most, after death. For individuals who die abroad, the information is transmitted to the place of birth by the local French consulate. Thus 31–99 y is the range within which the age at death is known for all included individuals, from the youngest (born December 1916) to the oldest (born August 1914) (see *SI Text* for details).

Identification of War Orphans Among *Pupilles de la Nation*. A *pupille de la Nation* is the child of a soldier who died or was disabled (injured or ill) during the war. To identify orphans, we searched for the father of each *pupille de la Nation* in an online database (58) (available at www.memoiredeshommes.sga.defense.gouv.fr/en/article.php?larub=80), which records all French soldiers who died during WWI (see *SI Text* and Fig. S4). We similarly searched for the father of each MNO in the database of French soldiers who died during WWI. The 35 MNOs alive at age 31 y who were identified as war orphans were excluded from the analysis (Fig. S1).

Rematching. A total of 987 orphans alive at age 31 y were rematched to an available MNO of same sex and same district of birth (Fig. S1) because the initial MNO had died before age 31 y, was identified as a war orphan, or had an unknown father. When several MNOs were available for rematching, we selected the one with the date of birth closest to that of the orphan. Each available MNO was used only once in rematching. Rematching was performed after a random permutation of the 987 orphans. Rematching was successful for 985 of the 987 orphans, yielding 2,365 orphan/MNO pairs in the final dataset analyzed.

Classification of Parental Occupations. We computed an ordinal score of paternal occupations based on the following six categories: *i*) worker; *ii*) craftsman; *iii*) employee; *iv*) shopkeeper; *v*) middle class, and *vi*) upper class. Similarly, we defined eight categories of maternal occupations: *i*) servant; *ii*) worker; *iii*), craftswoman; *iv*) employee; *v*) housekeeper; *vi*) shopkeeper; *vii*) housewife, and *viii*) middle and upper class. The maternal occupation at the time of birth was available on 99.4% of birth certificates. The paternal occupation was available for 97.2% of legitimate children.

Statistical Analysis. To impute the unavailable paternal and maternal occupations and those we could not classify, we performed multivariate imputation by chained equations (MICE) (59) using district and date of birth, sex, status (alive/dead) at age 31 y, parental occupations, legitimacy, and maternal age. We created 10 completed datasets. The parental occupation scores and regression coefficients obtained on the 10 datasets then were combined following Rubin's rules (60).

The main outcome analyzed was the lifespan of those died between the ages of 31 and 99 y. We tested for differences in the distribution of lifespans between orphans and MNOs using paired Wilcoxon signed-ranked tests on pairs in which the lifespan of both members was measured (i.e., both died between the ages of 31 and 99 y). The presence of differences was assessed separately for prenatal orphan/MNO and postnatal orphan/MNO pairs. We computed the mean lifespan of each group: prenatal orphans, MNOs of prenatal orphans, postnatal orphans, and MNOs of postnatal orphans. Bootstrapped 95% CIs were based on B = 1,000 replicates. To test the hypothesis that mean losses of lifespan were different in prenatal orphans and postnatal orphans, permutation tests were performed on prenatal and postnatal pairs. For each orphan/MNO pair, prenatal or postnatal, in which both members died between the ages of 31 and 99 y, an orphan/MNO difference in lifespan, δ, was determined. We ran $P = 10{,}000$ permutations on the prenatal/postnatal variable to estimate the null distribution of differences of means between prenatal and postnatal pairs.

Finally, the δs were regressed in a GAM (61) on status (postnatal/prenatal pair) with control for six categorical variables (paternal occupation, maternal occupations, legitimacy) and paternal and maternal ages (modeled by cubic regression splines with 5 df and evenly spaced knots; smoothing parameters determining the effective df were selected to minimize the unbiased risk estimator score).

Analyses were repeated for prenatal orphans according to the prenatal trimester of the father's death, and six sensitivity analyses were performed (*SI Text*).

All analyses were performed in R v3.0.3, with the package *mice* for multiple imputation (62) and the package *mgcv* for GAM regressions (63).

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Supporting Information

Todd et al. 10.1073/pnas.1617911114

SI Text

Identification of *Pupilles de la Nation* on the Birth Registers. Both Paris and Bordeaux remained protected from the frontline during WWI. Paris' city halls were readily accessible. Bordeaux is one of the few French cities for which images of its 1914 and 1915 birth registers are already online (available at archives.bordeaux-metropole.fr). The distribution of births by district reflected the distribution of hospitals and midwives' houses (Fig. S3 and Table S1). A total of 91,728 certificates were manually examined for the presence of the "Adopted by the Nation" notification, and 5,671 *pupilles* were identified thereby. Information collected and computerized from the handwritten birth registers were date of birth, sex, parental age (level of precision: year) and occupation at the time of the birth, legitimacy status (i.e., whether the parents were married at the time of the birth), date of death, and date of other life events (marriages, divorces, guardianships) noted in the margin of birth certificates (Fig. 1*A*). The presence of possible new life events was rechecked at the end of the data-collection process (8 October 2015) on the birth certificates of all included individuals (*pupilles de la Nation* and MNOs).

Longevity Information Available on Birth Certificates. Included individuals were born between 1 August 1914 and 31 December 1916. Dates of death have been recorded on birth certificates since 29 March 1945, so that 31–99 y is the range for which the age at death is known for all included individuals. The individuals fall into three categories: those who died at an unknown age before age 31 y, those who died between age 31 and 99 y (with known age at death), and those alive at age 99 y.

An individual with no life event recorded on the birth certificate after 29 March 1945 (i.e., with no notification of marriage, divorce, guardianship, or death after this date) was considered to have died before age 31 y. Conversely, an individual without the notification of death but at least one other life event recorded after 29 March 1945 was considered to be alive at age 99 y.

Identification of War Orphans Among *Pupilles de la Nation*. The "Morts pour la France" database (available at www.memoiredeshommes.sga.defense.gouv.fr/en/article.php?larub=80) is searchable by name. To each soldier is attached an image of his record (see Fig. 1*B* for an example). We computerized the necessary available information on the image, e.g., date and type of death (killed in action, missing in action, died of wounds, disease, other). To ensure that a given soldier was actually the father, not a homonymous person, positive identification was achieved as described in Fig. S4. This search yielded 3,210 orphans (56.6% of the 5,671 *pupilles*). The 489 orphans whose father had died of disease were removed from the analysis.

Statistical Analysis: Trimester-Specific Effects. To investigate specific effects of paternal death early (first trimester) or late (third trimester) in pregnancy, we compared (with the same procedure used for the prenatal/postnatal orphans comparison) those orphans whose father died in the first trimester with those whose father died later in the pregnancy (second and third trimester loss) and compared orphans whose father died in the third trimester with those whose father died earlier in the pregnancy (first and second trimester loss). Similarly, among postnatal orphans we compared those who had experienced loss of father before and after age 1 y and those who had lost their father before and after age 6 mo.

Statistical Analysis: Sensitivity Analyses. Six sensitivity analyses were performed. We compared median lifespans instead of mean lifespans. We restricted the analysis to legitimate children. We restricted the analysis to the Paris districts (Bordeaux was excluded). Also, rematched pairs were removed from the analysis. Only orphan/MNO pairs born before May 1915 (conceived before August 1914) were analyzed. Finally, we conducted the analysis after imputation of the lifespan of those alive at age 99 y; their lifespans were set to $99 + e_r$, where e_r is the life expectancy remaining at age 99 y for the French 1915 cohort (2.10 y for men and 2.52 y for women) given by the Human Mortality Database (64).

Announcement of Father's Death to the Mother. The official notification of a soldier's death to his family could take weeks, sometimes months. A frequent channel of information to the mothers was a direct letter from the comrades of the dead soldier to the spouse. Because of its very nature, evidence for this second channel of information is qualitative (65).

To check that the women who lost their husbands during pregnancy were actually informed of their husbands' deaths before delivery, we analyzed the transmission of the father's first name. Among the 337 male orphans who lost their father before birth, 40.7% were given their father's first name, compared with 17.2% of the 895 male orphans who lost their father after birth ($P = 1.1 \times 10^{-17}$) and 12.4% of the 1,232 male MNOs ($P = 6.8 \times 10^{-32}$).

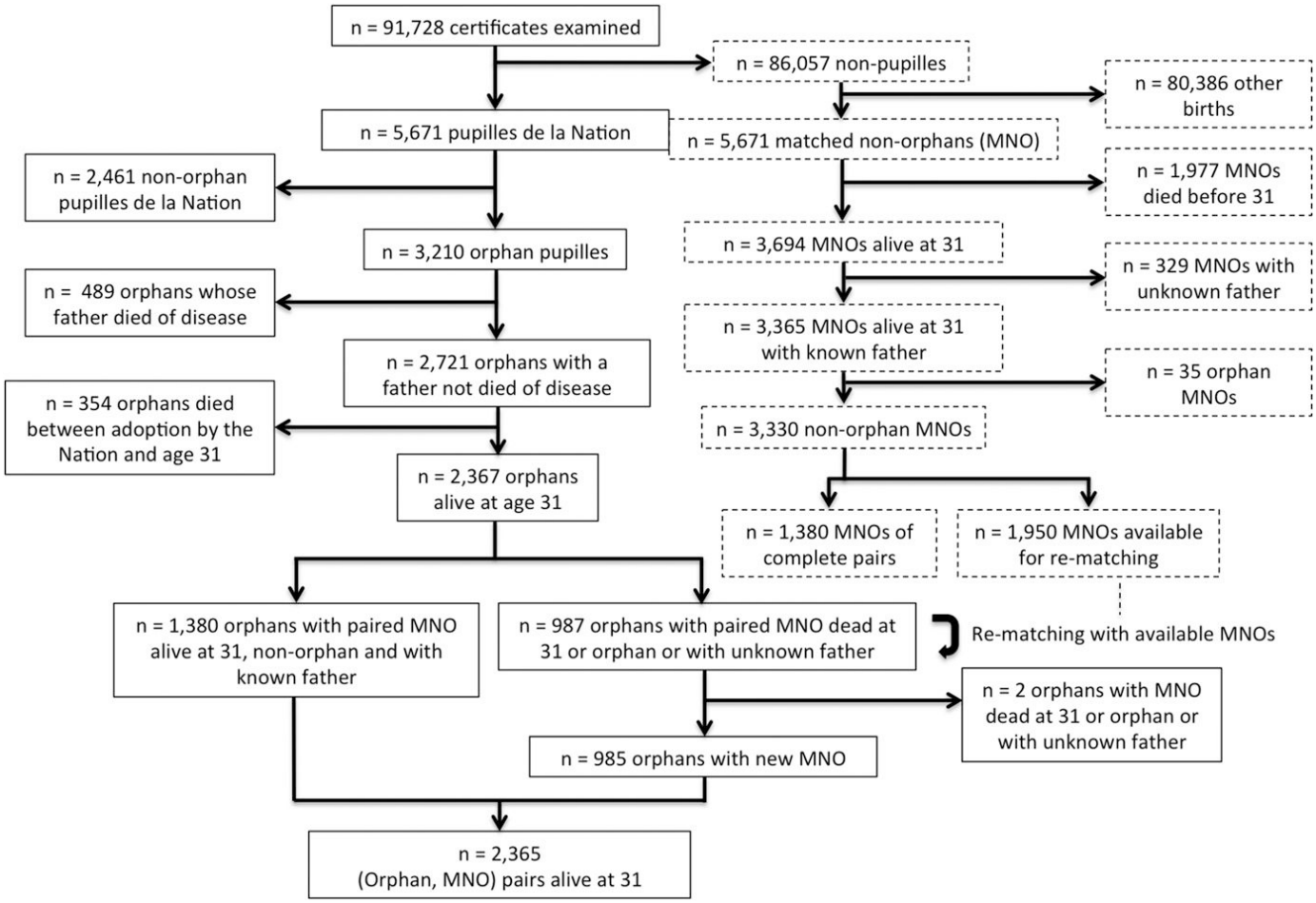

Fig. S1. Flowchart showing the definition of the cohorts of war orphans and MNOs. *Pupilles* were by definition children who survived from birth to their being adopted by the Nation at some point in childhood (on average at ~ age 5 y). Their probability of death before age 31 y is conditional on having being adopted (354/2721 = 13%) and therefore was expected to be lower than the unconditional probability of death before age 31 y measured in MNOs (1,977/5,671 = 34.9%).

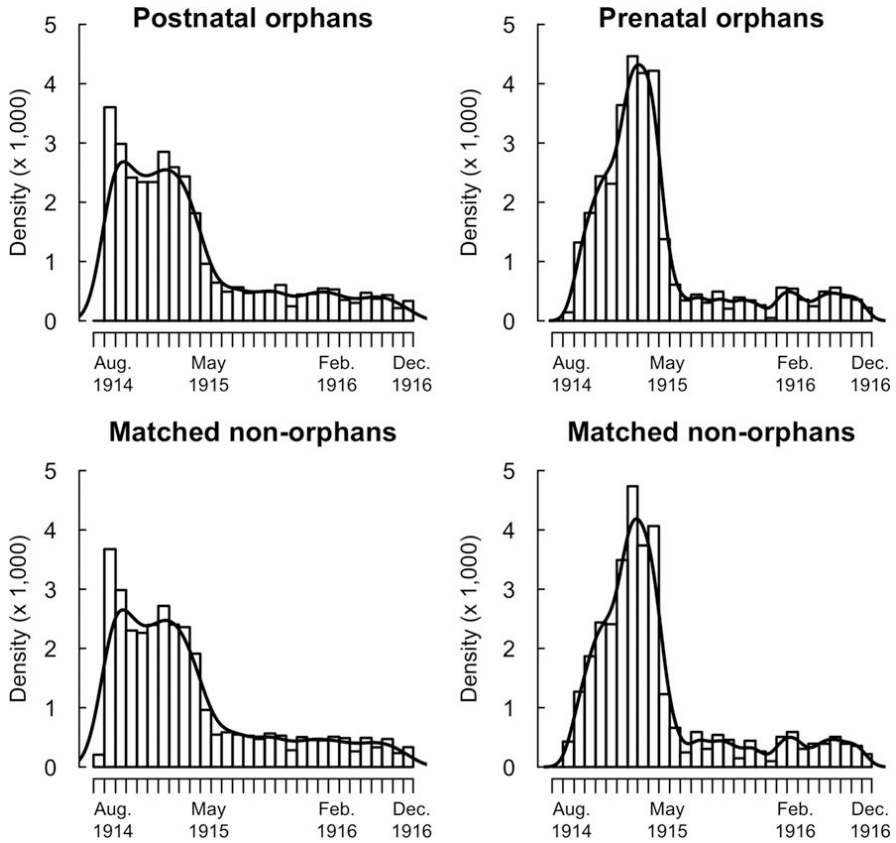

Fig. S2. Birth dates of prenatal and postnatal orphans and MNOs. The majority of orphans were conceived before August 1914 (the beginning of the war) and thus were born before May 1915. The observed abrupt decline in the monthly number of orphan births in May 1915 paralleled the decline observed at the country level (66). The distributions of dates of birth were different in prenatal and postnatal orphans. By design, the distribution of dates of birth is identical in orphans and MNOs for both types of orphans. The number of prenatal orphans born in a given month was determined by both the number of conceptions 9 mo before and the father's risk of death during pregnancy. Men who impregnated women just before the war began had a prewar fertility and were at risk during the woman's entire pregnancy. The observed peak in the birth of prenatal orphans in February–April 1915 therefore was expected. In contrast with prenatal orphans, the monthly number of postnatal orphans was approximately constant before May 1915. MNOs are matched to orphans by district and date of birth, so any cofounding associated with the place and date of birth (e.g., changing disease environment) is removed in the comparison of orphans and MNOs. The solid line shows the Gaussian kernel density estimate.

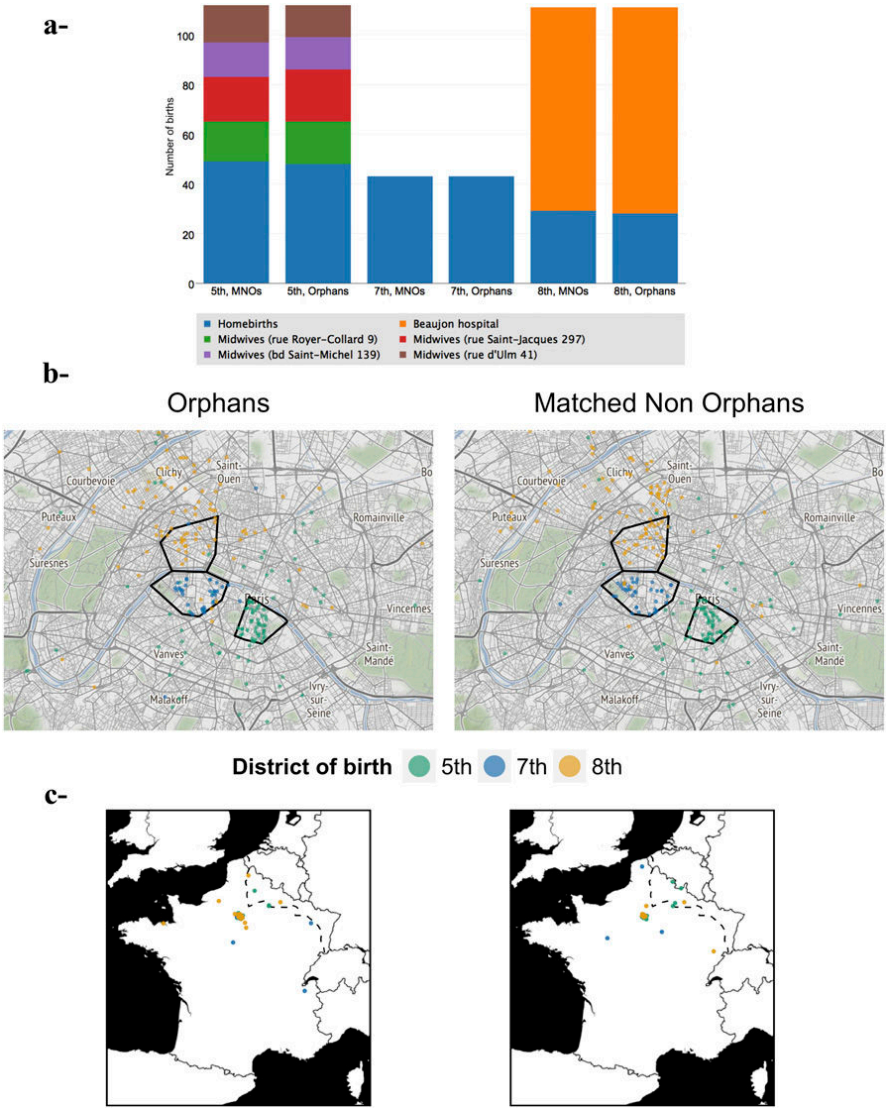

Fig. S3. Type of birth and home address of parents for orphans and MNOs born in three contrasted districts of Paris. For orphan/MNO pairs born in three districts of Paris (fifth, $n = 112$; seventh, $n = 43$; and eighth, $n = 111$) with contrasted delivery modes (hospital, midwife's house, at-home births), the home address of the parents was computerized ($n = 532$). Addresses were geocoded using Google Maps API, called from R with the *geocode* function of the *ggmap* package (67). The addresses for which this geocoding failed were examined manually ($n = 52$): 33 streets whose name had changed since 1914 were identified by comparing 1914 and modern-day maps, and the Google Map geocoding was relaunched accordingly. Addresses in streets that had disappeared were geocoded manually ($n = 7$). Finally, addresses in streets that we failed to identify on 1914 maps were set at the district/town center ($n = 12$). (*A*) Number of hospital births, homebirths, and births at midwives' houses for orphans and MNOs. (*B*) Districts with hospitals or midwives' houses (i.e. the fifth and eighth districts) recruited women living in neighboring districts and suburban towns. In the seventh district all births were homebirths. The three selected districts are outlined in black. (*C*) Among parents domiciled outside Paris were war refugees who had settled in Paris but were still domiciled in their region of origin. (The dotted line shows the stabilized frontline from October 1914.)

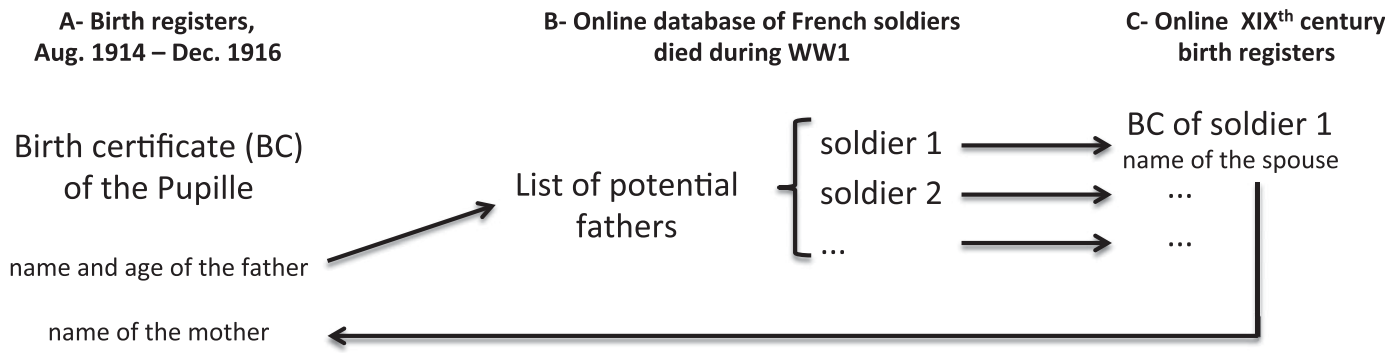

Fig. S4. Process for the identification of orphans' fathers. We manually searched for the father of each of the 5,671 included *pupilles de la Nation* (*A*) in the online database of soldiers who died during WW1 (*B*) (available at www.memoiredeshommes.sga.defense.gouv.fr), based on the father's name and age, to determine whether the *pupille* was an orphan and to retrieve the father's date and cause of death. The record of each soldier also contains his date and place of birth. In the cases where the search yielded several candidates, or when uncertainty remained as to whether the soldier found was indeed the father of the *pupille*, we took advantage of the fact that the birth certificates of candidate fathers found in the database (commonly born 1880–1895) (*C*) are available on the websites of the local archives ("Archives départementales") of their place of birth. We manually examined the birth certificate of each candidate to check whether his wife (whose name is given on the marriage notification on the birth certificate) was named as the mother of the *pupille* on the *pupille*'s birth certificate. This method yielded certain identification for all *pupilles de la Nation* whose parents married, whether before or after birth. Because of a recent digitization program, images of >90% of birth registers before 1900 (*C*) are now available online (current completion by region may be seen at www.archivesdefrance.culture.gouv.fr, from which local websites may be reached). Marriages began to be noted on the birth certificates of those marrying in 1897, thus providing a simple, systematic, positive method of verifying the linkage between birth registers and the WWI military deaths database. For a *pupille de la Nation* whose parents never married but who was recognized by his father, the act of recognition (which mentions the date and place of birth of the father and thus yields positive identification) was examined, provided that the recognition took place in one of the districts included in the study.

Table S1. Detailed characteristics of the studied 2,365 orphan/MNO pairs

Variable	Prenatal orphans (n = 656)	MNOs (n = 656)	Postnatal orphans (n = 1,709)	MNOs (n = 1,709)
Date of birth, mean	28 April 1915	27 April 1915	1 April 1915	2 April 1915
Sex, *n* (%)				
Female	319 (48.6)	319 (48.6)	814 (47.6)	814 (47.6)
Male	337 (51.4)	337 (51.4)	895 (52.4)	895 (52.4)
Legitimacy, *n* (%)				
Legitimate	630 (96.0)	552 (84.1)	1509 (88.3)	1413 (82.7)
Illegitimate	26 (4.0)	104 (15.9)	200 (11.7)	296 (17.3)
Paternal occupation, *n* (%)				
Worker	190 (29.0)	168 (25.6)	493 (28.9)	456 (26.7)
Craftsman	117 (17.9)	151 (23.0)	329 (19.3)	367 (21.5)
Employee	224 (34.1)	190 (28.9)	535 (31.3)	455 (26.6)
Shopkeeper	55 (8.3)	54 (8.2)	153 (8.9)	165 (9.7)
Middle class	30 (4.6)	46 (7.0)	81 (4.8)	110 (6.5)
Upper class	41 (6.2)	48 (7.4)	118 (6.9)	156 (9.1)
Paternal occupation score (95% CI)	2.60 (2.46, 2.74)	2.70 (2.58, 2.82)	2.62 (2.55, 2.69)	2.75 (2.68, 2.83)
Maternal occupation, *n* (%)				
Servant	57 (8.7)	61 (9.3)	164 (9.6)	158 (9.2)
Worker	87 (13.2)	60 (9.2)	212 (12.4)	190 (11.1)
Craftswoman	122 (18.6)	109 (16.7)	318 (18.6)	284 (16.6)
Employee	68 (10.3)	50 (7.7)	146 (8.5)	121 (7.1)
Housekeeper	100 (15.2)	115 (17.6)	284 (16.6)	297 (17.4)
Shopkeeper	35 (5.4)	37 (5.6)	92 (5.4)	101 (5.9)
Housewife	178 (27.1)	212 (32.3)	448 (26.2)	526 (30.8)
Middle and upper class	10 (1.5)	11 (1.7)	44 (2.6)	31 (1.8)
Maternal occupation score (95% CI)	4.42 (4.26, 4.59)	4.70 (4.53, 4.86)	4.44 (4.34, 4.54)	4.62 (4.52, 4.72)
Age of the mother, mean (SD)	25.8 (4.3)	26.2 (4.5)	25.6 (4.9)	26.4 (5.0)
Age of the father, mean (SD)	28.7 (4.3)	30.4 (5.7)	28.5 (4.9)	30.6 (6.2)
Status at age 99 y, *n* (%)				
Dead	630 (96.0)	637 (97.1)	1,645 (96.3)	1,632 (95.5)
Alive	26 (4.0)	19 (2.9)	64 (3.7)	77 (4.5)

Paternal occupations and age at birth for illegitimate births were multiply imputed using MICE (*Methods*). Ten completed datasets were created. Figures by paternal occupation are averaged over the 10 completed datasets and are rounded to the nearest integer.

Table S2. Paternal occupations in the 35 prospective MNOs that were identified as war orphans compared with *pupille* orphans

Group	Worker	Craftsman	Employee	Shopkeeper	Middle class	Upper class
MNOs, $n = 35$ (%)	6 (17)	3 (8)	12 (34)	2 (5)	2 (6)	11 (30)
Pupille orphans, $n = 2{,}791$ (%)	828 (30)	521 (19)	879 (32)	244 (9)	130 (5)	190 (7)

Initially 5,671 non-*pupille* births were drawn from birth registers to serve as MNOs. Among the 3,365 MNOs with a known father that were alive at 31 y, 35 (1.0%) identified as war orphans were subsequently removed from the analysis. Paternal occupations of orphan MNOs were different from those of orphan *pupilles* alive at 31 y (median P value of Fisher's exact test over the 10 completed datasets: 2.5×10^{-4}). No difference was found between MNOs and orphan *pupilles* after the removal of those born of an upper class father (median $P = 0.25$). The excess upper class paternal occupation in orphan MNOs suggests a lower propensity of upper class families to apply for the *pupille de la Nation* status. Figures by occupation are averaged over the 10 completed datasets and are rounded to the nearest integer.

Table S3. Districts included in the study and period covered

Civil registration service	Region	Period covered	Orphan/MNO pairs, $n = 2{,}365$
1st arrondissement	Paris	1 August 1914–31 December 1916	17
2nd arrondissement	Paris	1 August 1914–31 December 1916	18
3rd arrondissement	Paris	1 August 1914–31 December 1916	26
5th arrondissement	Paris	1 August 1914–31 December 1916	112
6th arrondissement	Paris	1 August 1914–31 December 1916	170
7th arrondissement	Paris	1 August 1914–31 December 1916	43
8th arrondissement	Paris	1 August 1914–31 December 1916	111
9th arrondissement	Paris	1 August 1914–31 December 1916	35
12th arrondissement	Paris	1 August 1914–31 December 1916	180
13th arrondissement	Paris	1 August 1914–31 December 1916	239
14th arrondissement	Paris	1 August 1914–31 December 1916	708
15th arrondissement	Paris	1 August 1914–31 December 1916	184
16th arrondissement	Paris	1 August 1914–31 December 1916	36
17th arrondissement	Paris	1 August 1914–31 December 1916	99
18th arrondissement	Paris	1 August 1914–31 December 1916	195
Le Kremlin Bicêtre	Paris	1 August 1914–31 December 1916	5
Neuilly-sur-Seine	Paris	1 August 1914–31 December 1916	23
1st section	Bordeaux	1 August 1914–31 December 1915	56
2nd section	Bordeaux	1 August 1914–31 December 1915	41
3rd section	Bordeaux	1 August 1914–31 December 1915	37
4th section	Bordeaux	1 August 1914–31 December 1915	30

Conclusion and perspectives

World War One proves a relevant model for the study of early life psychological stress in humans. Casualties of the French army, at the time based on universal conscription, were unprecedented. Exposure to risk was assuredly not fully homogenous: an advanced age protected from combat, while the infantry was a far more dangerous assignment than any other arm. Specific occupations at all levels of the social hierarchy were at least partially protective: railroad workers or physicians appear as extreme cases. Some tried and find a cushy posting. A small fraction of each generation remained exempted because of bad health after careful medical examinations. In short, many individual characteristics modulated the specific hazard each soldier experienced. It should yet be kept in mind that these phenomena, while they belong to the meticulous description of the war, should not mask the essence of the situation, in which randomly selected French infants lost their father at various stages of development. Moreover, the most important risk-modifiers can be controlled for: matching on maternal age yields comparable paternal ages, while matching on place of birth contributes to pairing orphans and MNOs on SES. On the whole, SES was of little relevance in our study, as reflected by the balanced distribution of occupations in orphans and MNOs. Good health of those mobilized – that relates to the "healthy soldier effect" set forth in other contexts [87], if of any importance, would tend to bias downward, not upward, the estimated effect of father's loss on adult lifespan.

As our search for sources revealed, high-quality quantitative data is available, especially thanks to the serendipitous pupille de la Nation status and its being notified on birth certificates. We could construct a simple observation system that, because it mainly relied on military records established at the time of the war as well as on data continuously processed over the past hundred years by the ~36,000 civil registration services that cover France, demanded a reasonable amount of collection work. The use of WW1 as a historical model for early life stress obviously comes at a supplementary cost: it demands a study, brief and elementary as it may be, of the historical conditions of the time. Those include: the position in society and rights of illegitimate children, the war-induced migrations, short-term changes in nutrition and disease environments, as well as the potential delays in soldier's death

announcement to his family. On these questions, we tried to bring as often as possible quantitative evidence relating directly to our cohort.

The main result of the study is that an orphan-MNO difference in adult longevity of ~2.5 years was found for prenatal orphans, but that no difference in adult longevity could be measured between postnatal orphans and their MNOs.

The absence of evidence for a loss of lifespan in the case of a postnatal loss suggests that the psychological and financial consequences of the fatherly loss were at least partially buffered. Other family members, grandparents in particular, could provide alternative postnatal care and financial help [88]. The State and charities provided subsidies to women who had just lost their husband at war. Permanent pensions, as well as specific allowances, were paid to orphans' mothers by the State [69,85]. Remarriages occurred for ~ 40% of war widows [89]. Interestingly, remarriage of the remaining parent has been shown to be associated with improved survival to childhood in other contexts [64]. All these elements highlight that familial and social support are critical elements of the response to postnatal psychological stress. Postnatal stress today may preferentially strike individuals lacking such support, causing impaired health in adulthood. In this perspective, both postnatal stress and low resilience to it are public health issues.

The loss of lifespan in prenatal orphans is unlikely to be explained by long-running socioeconomic consequences of the early loss of father, which must have been experienced by both prenatal and postnatal orphans. It rather suggests early trauma in utero has programming effects on biological susceptibility in adulthood strong enough to significantly alter longevity. Having found a strong decrease in adult life expectancy of prenatal orphans, it is enticing to try and determine the reasons of this increased mortality. Though animal models provide hints at the biological mechanisms involved, the study of causes of death appears fruitful, and indeed indispensable. Causes of death can be retrieved for deaths that occurred after 1968: orphans of the cohort were aged about 53 y. The exploratory analysis of the age-span at which the 2.5 y longevity difference was established suggests the critical period was 31-65 y, so that causes of death would open a narrow but essential window on the mechanisms underlying our observation.

Because the pupille status started to be granted in 1918, the early life mortality of orphans escaped our investigation. Early selection has been shown a major issue in the case of

famines, where it may be potent enough to fully mask the true effect of debilitation on those surviving the early life adversity. It must be stressed that for such a significant selection to act, a high immediate mortality must be at play in the exposed group. While famine is evidently a mortality crisis, there is no evidence to suggest children exposed to loss of father during WW1 experienced an early-life mortality that even remotely compared with the mortality of those exposed to a famine. Therefore, selection, that is achieved if a high mortality is unevenly distributed according to frailty, seems to be much less of a problem in the context of WW1 orphans. In addition, a signature of early selection would be an uneven distribution of SES in orphans and MNOs who attained adulthood, with orphans displaying higher SES, a disequilibrium that is not observed. A case-control study would probably be the most straightforward way to tackle the issue of early life mortality of orphans using civil registration services. Cases would be those with no notification after 1945 (classification errors left aside, they are those died beforehand), while controls would be chosen among those with known date of death (thus having survived to 1945). Fathers of cases and controls would be searched for in the BMF, so as to establish the proportion of orphans in both groups. Similarly, one would hope to determine the potential consequences of the loss of husband on the mothers themselves, e.g. premature death, which in turn could have had consequences on the offspring's health.

Another potential continuation of this work relates to the transgenerational consequences of WW1 traumas. Recent animal research has shed light on non-genetic germline inheritance in mammals [90]. Both methylation at various loci in DNA and miRNA content of sperm cells have been shown to be sensitive to environmental factors, including stress [91,92]. Stress experienced in postnatal life was found to alter phenotype in second and third generations after that exposed [93]. HPA axis is reprogrammed by paternal traumatic experience: offspring of males stressed in puberty or adulthood display significantly blunted corticosterone responses to acute stress [94]. It might therefore be the case that the still-alive offspring of severely traumatized soldiers carry epigenetic marks brought about by the First World War.

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Appendices

Appendix 1. Civil registration services included.

Service d'état civil	Period covered	MNOs	Pupilles identified (n = 7,250)
Paris – 1st arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	39
Paris – 2nd arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	37
Paris – 3rd arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	66
Paris – 5th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	228
Paris – 6th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	377
Paris – 7th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	75
Paris – 8th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	240
Paris – 9th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	88
Paris – 12th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	485
Paris – 13th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	573
Paris – 14th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	1 711
Paris – 15th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	500
Paris – 16th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	93
Paris – 17th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	242
Paris – 18th arr.	Aug. 1st 1914 – Dec. 31st 1916	Yes	477
Le Kremlin Bicêtre	Aug. 1st 1914 – Dec. 31st 1916	Yes	18
Neuilly-sur-Seine	Aug. 1st 1914 – Dec. 31st 1916	Yes	41
Bordeaux – 1st sec.	Aug. 1st 1914 – Dec. 31st 1915	Yes	108
Bordeaux – 2nd sec.	Aug. 1st 1914 – Dec. 31st 1915	Yes	107
Bordeaux – 3rd sec	Aug. 1st 1914 – Dec. 31st 1915	Yes	92
Bordeaux – 4th sec.	Aug. 1st 1914 – Dec. 31st 1915	Yes	74
Lyon – 1st arr.	Aug. 1st 1914 – Dec. 31st 1915	No	33
Lyon – 2nd arr.	Aug. 1st 1914 – Dec. 31st 1915	No	483
Lyon – 3rd arr.	Aug. 1st 1914 – Dec. 31st 1915	No	60
Lyon – 4th arr.	Aug. 1st 1914 – Dec. 31st 1915	No	133
Lyon – 5th arr.	Aug. 1st 1914 – Dec. 31st 1915	No	49
Lyon – 6th arr.	Aug. 1st 1914 – Dec. 31st 1915	No	54
Lyon – 7th arr.	Aug. 1st 1914 – Dec. 31st 1915	No	60
Chartres	Aug. 1st 1914 – Dec. 31st 1915	No	50

Dijon	Aug. 1st 1914 – Dec. 31st 1915	No	147
Lorient	Aug. 1st 1914 – Dec. 31st 1915	No	114
Nîmes	Aug. 1st 1914 – Dec. 31st 1915	No	113
Orléans	Aug. 1st 1914 – Dec. 31st 1915	No	145
Tarbes	Aug. 1st 1914 – Dec. 31st 1915	No	58
Versailles	Aug. 1st 1914 – Dec. 31st 1915	No	80

Appendix 2. Paternal age and proportion of orphans in those born 1914

Simple computations using nationwide data make it possible to estimate the proportion of orphans among those born 1914, as well as age of orphans' and non-orphans' fathers. The sources are:

- number of deaths at war (until August 1st 1919) by year of birth : [85], p. 290. The very small number of deaths for those born before 1867 (n=1,800) was given by [85] in aggregate form; we evenly distributed these n=1,800 deaths between years of birth 1854 to 1867;

- distribution of the male population in 1914 according to age: Human Mortality Database;

- age specific male fertility rate: Insee (available at: insee.fr/fr/statistiques/).

Combining these three sources of data, it is straightforward to compute the probability of death during the war according to year or birth, as well as the number of 1914 births for each paternal year or birth. Making the assumption that given the father's year of birth, fertility in 1914 and death during the war were independent yields:

- a theoretical proportion of orphans among those born 1914: 13.1%;

- a theoretical distribution of paternal ages in orphans and non-orphans among those born 1914, shown on Figure b.

These elementary computations predict a 3.8-year difference in paternal ages between orphans and non-orphans born 1914 (μ_{NO} - μ_{O}; see Figure b). By contrast, the difference in paternal ages between orphans and MNOs analysed in Chapter 6 is 2.0 years, and virtually no MNO is the offspring of a father above 45 years of age (Figure c): comparison of Figures b and c shows that high paternal ages are 'skimmed' on Figure c, likely thanks to matching on maternal age.

It must also be stressed that the nationwide death numbers used include deaths by disease, that struck preferentially older soldiers: for instance, among the 3,210 orphans identified in Paris and Bordeaux, the mean paternal age at the infant's birth was 30.6 y when the father died of disease and 28.6 y otherwise ($p = 2.2 \times 10^{-16}$). Nationwide, orphans born to

a father not died of disease therefore had a mean paternal age below $\mu_O = 29.7$ y. Accordingly, the nationwide difference in paternal ages between the type of orphans considered in the analysis (those whose father died not died of disease) and non-orphans is in fact larger than 3.8 years. This further points to the efficiency of our matching rule (that relies on maternal age) to maintain comparability of paternal ages between orphans analysed and MNOs: it is likely that the orphan-MNO difference in paternal ages would have been much more than 2.0 years had we chosen MNOs at random.

As stressed in Chapter 3, the probability of becoming an orphan is difficult to assess using our cohort, due to the fact that the pupille status was attributed conditional on having escaped infant-child mortality, that the number of births given by the *Annuaire statistique* is that for Paris as a whole (which comprises the five arrondissements not included in our study), and that a fraction of illegitimate children were excluded from the pupille status (especially those who would still not have been recognized by their father had the war been avoided : ~ 8.9% of those alive at 31 y – see Chapter 6, Fig. S1). Based on the number of acts registered in 1914 in each arrondissement (births + recognitions), the five arrondissements not included represent 27.7% of Paris. It is known from previous research that probability of survival to age 5 was 75.8% for females born 1901-1905 in the Seine département [95]. Using these numerical values, the rate of orphans given in Chapter 3 (n_m/N_m; p. 71, Figure 23), which is 5.5% for the August 1914 – April 1915 period as a whole, becomes: 5.5 / (1-0.277) / 0.758 / 0.911=11.0%, which seems, given the very approximate nature of the computations, reasonably close to the nationwide estimate of 13.1%[30].

[30] In particular, the potential *a priori* differences in male age-specific fertility rates between Paris and France as a whole as well as the unescapable uncertainties on nationwide death counts make direct comparability difficult. Also, the excess male infant-child mortality (see Chapter 5) and illegitimate children who would have been recognized by their father had he not died at war (not taken into account in our correction of the 5.5% crude rate) tend to bias downward the estimate our cohort yields.

Figure a- Age-specific fertility and war mortality.

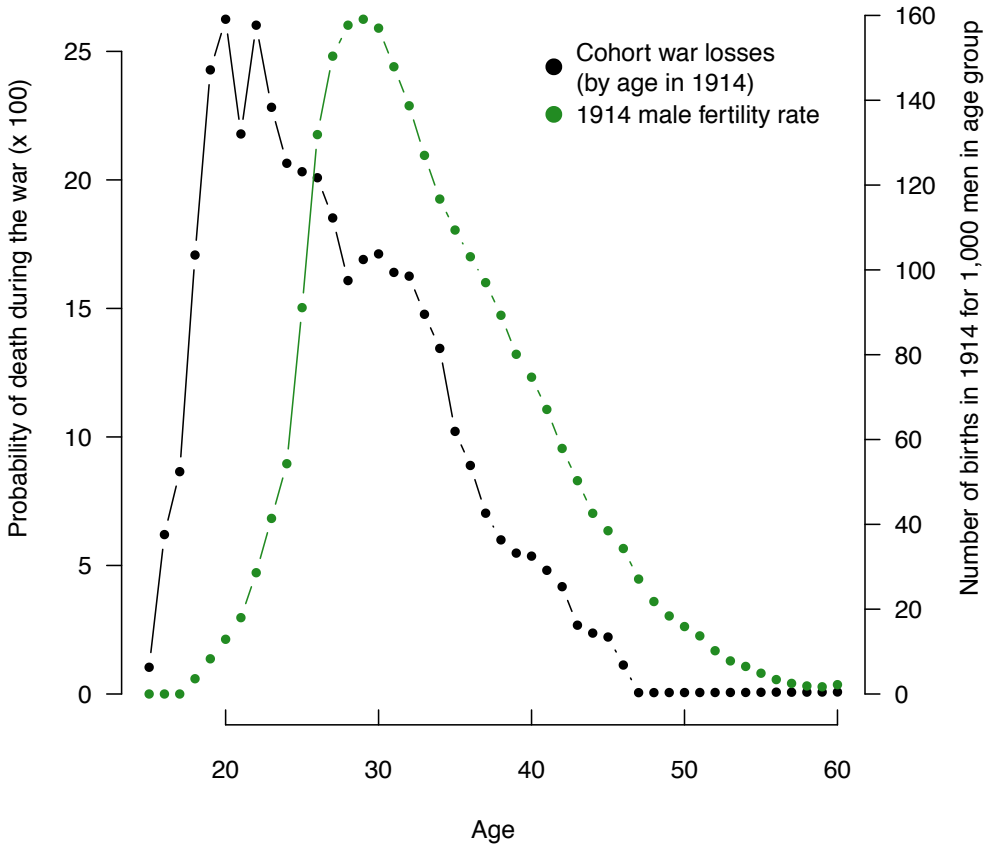


Figure b- Predicted distribution of paternal ages in orphans and non-orphans born 1914

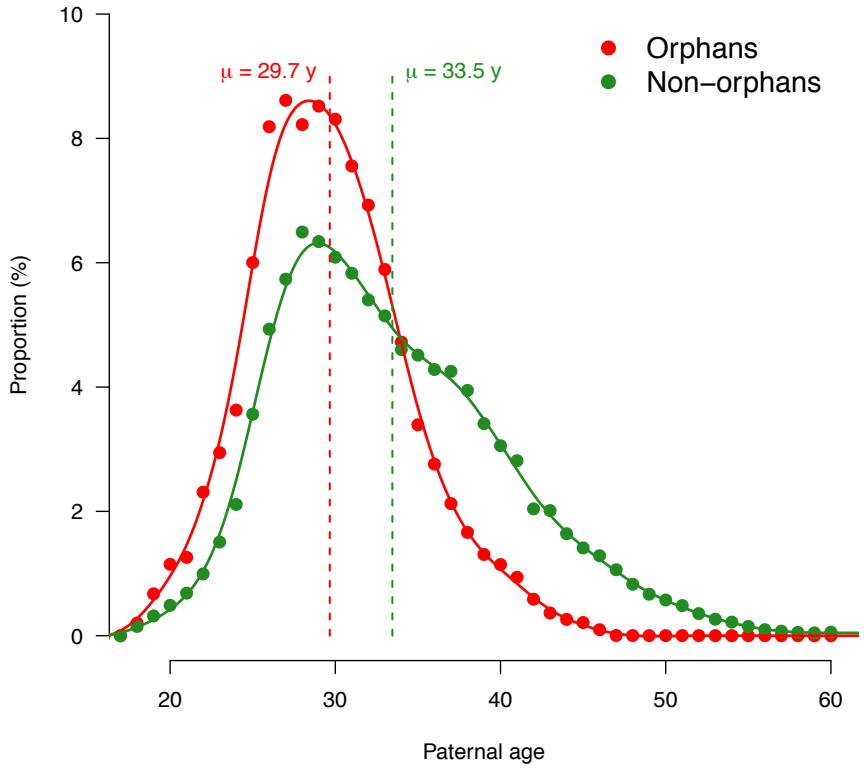
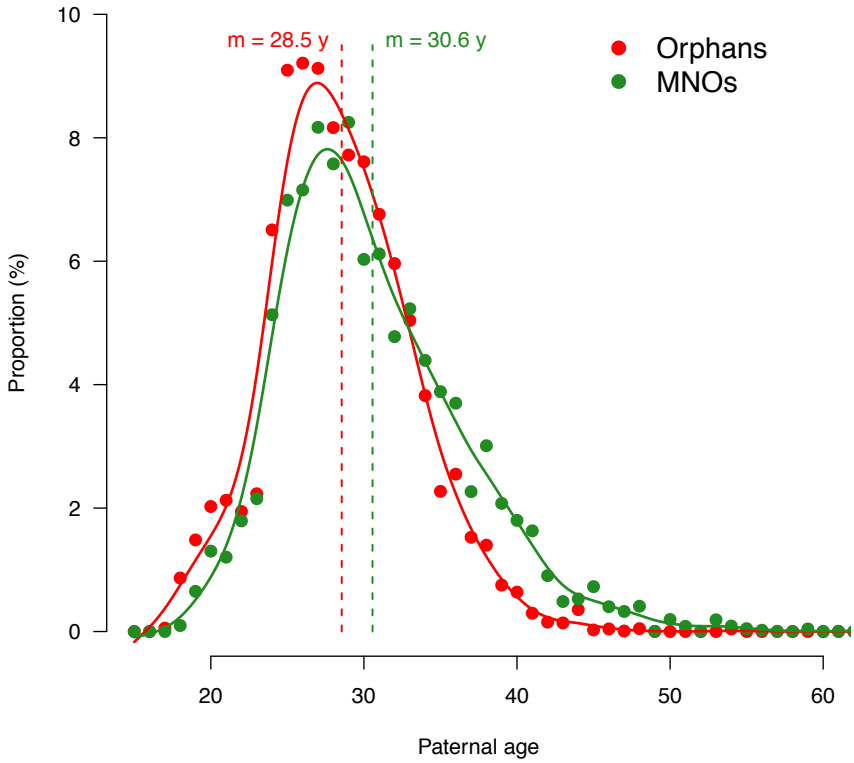


Figure c- Distribution of paternal ages in orphans and MNOs analysed in Chapter 6.



Line: cubing smoothing spline.