

# Socioeconomic inequalities in children under 15 with medical complexity: A population-based study

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## Research article

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## Abstract

Background Health inequalities from the first stages of life onwards have consequences for children's health status and for their future development. Children's health is profoundly affected by the socioeconomic position (SEP) of their parents. The situation is even more disruptive in children with medically complex (CMC) conditions. The aim of this study is to describe the characteristics and related pathologies of CMC in Catalonia, and to assess the presence of socioeconomic inequalities.

Methods Cross-sectional study and cluster analysis of the diseases in the CMC population under the age of 15 in Catalonia in 2016 using administrative data. Each pathology cluster obtained was described and its association with socioeconomic position (SEP) determined. The Adjusted Morbidity Groups (Catalan acronym GMA) classification system was used to identify the CMC. Main outcome measures: SEP, GMA score, sex, and age distribution were recorded in both populations (CMC and non-CMC) and in each of the clusters identified.

Results 71% of the CMC population have at least one parent with no employment or an annual income of less than €18,000. Four comorbidity clusters were identified in CMC: respiratory (47%), neurodevelopmental (18%), hemato-oncological (12%), and perinatal disorders (23%). CMC experience higher levels of poverty and social disadvantage in all clusters. SES-cluster association results were: in the respiratory OR, 2.1 in boys and 2.1 in girls; in the neurodevelopmental disease, OR 2.0 in boys and 1.8 in girls; in the hemato-oncology OR, 1.7 in boys and 1.8 in girls; and in the perinatal OR, 1.7 in boys and 1.8 in girls.

Conclusions There are socioeconomic health inequalities in childhood across a broad spectrum of health outcomes. Children with lower SEP are more likely to have CMC conditions. All clusters showed SEP inequalities and respiratory and neurodevelopment clusters are the most prevalent.

## Introduction

Since the 1980s, when the Black Report drew attention to the gradient in health according to socioeconomic position (SEP), health inequalities have been a major social issue<sup>1</sup>. The report showed that poor health is more frequent among the most disadvantaged, even in childhood.

There is increasing scientific evidence, from both biology and the social sciences, of the importance of the first years of life (including *in utero* exposure) in the formation of the capacities that promote well-being throughout the life cycle<sup>2</sup>. Childhood is also a structural transmitter of inequalities<sup>3</sup>, in terms of both health and SEP. Naturally, children are affected by their socioeconomic environment<sup>4,5,6</sup>, and this impact becomes stronger as they grow older<sup>7</sup>.

One of the most vulnerable populations is "children with medical complexity"(CMC)<sup>8</sup> conditions. This denotes the profile of a child with intensive use of (and placing a high cost burden on) the health services and with special health and social needs. These children often have complex acute and chronic conditions, numerous comorbidities, a broad range of mental health and psychosocial needs, major functional limitations<sup>9</sup>, and a higher rate of mortality<sup>10</sup>. Family economic resources and social and health care support are identified as important external needs factors in CMC<sup>11,12</sup>.

Recent data from Catalonia (2015)<sup>13,14</sup> shows that children with the lowest SEP are twice as likely to be CMC than those at the next socioeconomic level. Clustering these patients by their different characteristics is a valuable tool for predicting children's future health and development, and also for planning healthcare services accordingly<sup>15,16</sup>. The aim of this study is to describe the characteristics and patterns of pathology on CMC patients and their association with socioeconomic position.

## Methods

### Study population criteria: Population-based risk assessment: GMA (Adjusted Morbidity Groups)

The CMC population was identified from the entire resident population of Catalonia under the age of 15 in 2016 (1,189,325, 52% boys). A morbidity, complexity, and risk score tool, Adjusted Morbidity Groups classification (Catalan acronym GMA)<sup>17</sup>, was used to identify the CMC population.

The GMA predicts an individual patient score according to their comorbidity and complexity. The higher the GMA score, the greater the individual's medically complex conditions. This scoring is used to stratify the population for the purposes of health planning<sup>17,18</sup>. It is more accurate and yields less variability than other health risk tools, such as Clinical Risk Group (CRG)<sup>18</sup>. Information on comorbidity and complexity to construct GMA was gathered from the Catalan Health Surveillance System (CCHS) database, for present and previous years, and so on.

A clinical complexity stratification has been established according to GMA percentiles (50% very low risk, 75% low risk, 85% moderate risk, 90% high risk, 99% very high risk, 99.5% extreme risk).

Those in the top 0.5% based on GMA score (5,950 children) were selected as CMC population since: 1) this is the level of highest complexity proposed by the GMA; 2) previous studies in Catalonia found that 0.3% of the population were CMC<sup>13</sup>; and 3) concordance with the prevalence of CMC in other population studies<sup>19</sup>. The 99.5% of the rest of the children, the non-CMC population, were used as a comparative group.

## Data

We used two main sources of data:

The central registry of insured persons (Catalan acronym RCA) was used to obtain the reference population (as of January 1, 2016), their income level, employment status, and Social Security benefits.

The CCHS database, for clinical purposes, includes detailed information on sociodemographic characteristics and medical diagnoses at an individual level in all contacts in primary care, emergency, mental health, long-term care services, and pharmacy prescription. It includes the total population of Catalonia, since all citizens are granted universal health coverage.

## Variables

Outcome variable:

The principal outcome variable was the different clusters obtained by grouping patients with similar patterns of comorbidity.

Medical diagnoses were obtained through CCHS (coded using the Agency for Healthcare Research and Quality's Clinical Classification Software (CCS))<sup>20</sup> and were considered in order to determine the comorbidities registered from 2014 to 2016 in each CMC child. Only the first diagnosis of each type within each individual was included.

Exposure variable and covariates:

SEP was created on the basis of the employment status, individual income, the receipt of welfare assistance of one of the child's parents or guardians from de RCA database. SEP was grouped into three categories: Low (no member of the household employed or in receipt of welfare support from the government, and an income <€18,000/year, considered poverty<sup>21</sup>); Middle (employed with an income <€18,000); and High (in employment, with income >€18,000).

Age was categorized based on clinical criteria for children's growth (0–1, 2–4, 5–11, 12–14). Sex was a stratification variable.

## Statistical analysis

A descriptive analysis was carried out of both the CMC and non-CMC populations.

Afterwards, in order to determine patterns of pathology in CMC population, diagnoses related to each individual, coded through CCS, were used. Homogeneous groups of patients with similar diseases were identified in CMC population via K-means cluster analysis using the Jaccard similarity index<sup>22</sup>, as in similar studies<sup>23</sup>.

Due to the large number of CCS in each individual, only the most disabling ones were selected based on the following criteria<sup>23</sup>: a prevalence > 0.5%, being five times more prevalent in the CMC than non-CMC, and a median of GMA >5 for the whole population. After this, a joint correspondence analysis was performed before the K-means procedure. CCS with correlations smaller than the median in each dimension were rejected or aggregated with similar<sup>24</sup>; some were recovered because of their clinical or socioeconomic relevance. In total, 93 of 279 CCS were selected (See Supplementary Table 1, Additional File 1).

The final number of clusters was determined by Calinsky-Harabasz's criterion<sup>25</sup>, which take into account minimum dispersion criteria to evaluate the optimal number of clusters. Each individual belonged to a single cluster. Finally, the clusters identified were interpreted and named under the supervision of a paediatrician. Logistic regression models, adjusted for age, were fitted for all children in Catalonia to test for association between SEP and to be allocated or not to each CMC cluster obtained by sex. Data analysis was conducted using STATA V.14/SE 2014<sup>26</sup>.

## Results

### Characteristics of the CMC population

The main characteristics of the CMC (0.5%) and non-CMC (99.5%) populations are described in Table 1. Both populations contained a higher proportion of boys (CMC 58.5% versus non-CMC 51.1%).

More of the CMC population was in early childhood than non-CMC. Almost a quarter of CMC were in the two first years of life (25.2% boys and 24.4% girls); compared with the non-CMC population, this rate was 2.2 times higher in boys and 2.1 times higher in girls. Around 50% of children of both sexes with CMC were aged under five; compared with non-CMC, this rate was 70.4% higher in boys and 65.9% higher in girls (see Table 1).

According to SEP, more than 60% of non-CMC (70.8% of CMC) had at least one parent with an annual income of less than €18,000 (Low and Middle SEP). Low SEP had a prevalence of 13% in CMC (9% in non-CMC); 44.3% higher in boys and 46.7% higher in girls than in the non-CMC.

### Cluster analysis of CMC

Four clusters with different disease profiles were identified; their prevalence rates in the whole population of children in Catalonia were as follows: respiratory (2.37‰), neurodevelopmental (0.89‰), hemato-oncological (0.59‰), and perinatal disorders (1.16‰). The statistics of the most prevalent CCS (>20%) in the four clusters and other characteristics are summarized in Table 2 and Figure 1, and their distribution during childhood is shown in Figure 2.

Cluster 1 (respiratory comorbidities): this cluster included 2,815 children, representing 47% of the CMC population. Its maximum distribution was between the ages of two and 11 (67%). This cluster of comorbidities was more prevalent in girls than boys in ages 12–14 ( $p = 0.011$ ). The main diseases were allergic reaction (71% boys, 73% girls), chronic obstructive pulmonary disease and bronchiectasis (58% boys and 53% girls), and asthma (52% boys and 44% girls).

Cluster 2 (neurodevelopmental disorders): this cluster included 1,058 children representing 18% of the CMC population. Its distribution was highest between the ages of five and 11 (49%). The most prevalent diseases were other nervous system disorders (74% boys, 72% girls), developmental disorders (57% boys, 51% girls), and epilepsy and convulsions (53% boys, 54% girls).

Cluster 3 (hemato-oncology): this cluster included 699 children representing 12% of the CMC population. Its distribution was highest between the ages of five and 11 (49%). A high proportion had deficiency and other anaemia (57% boys, 58% girls), white blood cell diseases (49% boys, 53% girls), and chemotherapy and radiotherapy (33% boys, 35% girls).

Cluster 4 (perinatal disease): this cluster included 1,378 children representing 23% of the CMC population. Its distribution was highest below the age of two (49%). The most prevalent diseases were other perinatal conditions (73% boys, 68% girls), cardiac and circulatory congenital anomalies (60% boys, 63% girls), other congenital anomalies (47% boys, 47% girls), and short gestation, low birth weight, and foetal growth retardation (36% boys, 37% girls).

## Socioeconomic inequalities

SEP inequalities in the four clusters are displayed in Table 2 and Figure 3. There were socioeconomic inequalities in all clusters, for both sexes. Children in the Middle or Low SEP groups were more likely to belong to one of the disease clusters than High SEP children.

The respiratory cluster showed an association with Low SEP ([OR, 2.1; CI, 1.7–2.4 in boys] and [OR, 2.1; CI, 1.7–2.5 in girls]) compared to the High SEP category. The second was the neurodevelopment disease cluster ([OR, 2.0; CI, 1.5–2.6 in boys] and [OR, 1.8; CI, 1.3–2.5 in girls]), followed by the hemato-oncology cluster ([OR, 1.7; CI, 1.3–2.4 in boys] and [OR, 1.8; CI, 1.2–2.6 in girls]), and finally the perinatal cluster ([OR, 1.7; CI, 1.3–2.1 in boys] and [OR, 1.8; CI, 1.4–2.5 in girls]).

## Discussion

Four different comorbidity clusters in CMC were obtained with different prevalence rates according to sex and age. All of them showed inequalities for SEP, being the most disadvantaged who had a higher probability to belong in all CMC clusters and moreover a lack of economic support within their family to have the best development and care.

In both populations (CMC and non-CMC) and sexes, >60% of children were Low and Middle SEP. Like other reports of childhood poverty in Spain<sup>27</sup>, this finding highlights the fact that children are subjected to inequalities from the very beginning of their lives.

Common characteristics of all clusters were a high prevalence of allergic reaction (>30%) and a higher proportion of boys, of around 58%. This data supports the contribution of sex to the origin and development of health and disease. Male foetuses mature slower than female; and, after birth, males have more perinatal issues. This vulnerability may persist for up to five years<sup>28</sup>, coinciding with the time of maximum prevalence of the respiratory and perinatal clusters (57% and 71%, respectively).

The respiratory cluster involves mainly pulmonary diseases and allergic reactions. In accordance with the natural development of most respiratory diseases, its prevalence is highest in the mid-age range. Risk factors known to be related to social and economic inequalities are: exposure to air pollution<sup>29</sup>, *in utero* exposure to tobacco<sup>30</sup>, maternal stress<sup>31</sup> and low weight at birth and prematurity<sup>32</sup>. Age distribution varied according to sex. The presence of boys was more marked under the age of 11, related to adverse birth outcomes<sup>28</sup>, while at the age of 12 to 14 girls presented a more chronic profile<sup>33</sup>.

The neurodevelopmental disorders cluster includes two related types of disease: on the one hand, nervous system and developmental disorders such as paralysis and epilepsy, and on the other hand, congenital, perinatal and degenerative anomalies. Their prevalence increases as the child grows older; they have a chronic, cumulative profile due to the difficulty of healing and they may be precursors of future complications in other systems<sup>4</sup>. The aetiology of nervous system anomalies may be related to social inequalities such as exposure to certain environmental factors<sup>34</sup>, maternal stress during pregnancy, or adverse gestational and delivery outcomes<sup>35,36</sup>. All these events occur in the pre-natal and perinatal period but their impact may be felt at a later stage.

The hemato-oncology cluster had the highest median GMA, since the prognosis and development of the pathology entail a high risk. This profile includes all cancers, where leukaemia is the most prevalent (30% boys, 26% girls), along with related hematological diseases. Its association with SEP is weaker than that of the other clusters. There is general agreement that oncology is influenced less by SEP<sup>37</sup> and more by exposure to environmental contaminants<sup>38</sup>.

The perinatal disease cluster comprises mainly perinatal and congenital diseases and cardiac and circulatory congenital anomalies. Its maximum prevalence was seen in the first two years of life (49%). In this short time, socioeconomic and social determinants influence the child mainly through the mother: maternal behaviour during pregnancy has been identified as a risk factor<sup>31,39,40</sup>. It should also be noted that advances in perinatal care have increased the likelihood of survival for extremely preterm infants, who are likely included in this cluster.

The age distribution of each cluster shows the ages of maximum expression of each of the patterns (see Figure 2). Diseases are not static, and prognosis may mean that individuals move from cluster to cluster.

All clusters showed SEP inequalities, thus corroborating the previous analyses carried out in Catalonia<sup>13,14</sup> and elsewhere<sup>41</sup>. Respiratory and neurodevelopmental clusters (see Figure 3) slightly showed a higher SEP inequality, in line with similar studies in the US<sup>4</sup> and the UK<sup>5</sup>.

Having to care for CMC may negatively affect families' economic position and health<sup>12</sup>. In addition, stressful factors affecting the parents, such as poverty or poor mental health, impose heavy developmental burdens on young children<sup>42</sup>. In contrast, families with more economic resources are able to provide more active stimulation, alternative treatments, and an environment that is safer and more conducive to maintaining good health in childhood. This phenomenon has been termed the "buffering effect of income" in chronic conditions<sup>4,5</sup>. The family's SEP is related to CMC, thus impacts on the development of this vulnerable population.

## Strengths and limitations

The criteria for defining CMC population presented certain limitations. The GMA classification was originally created for adults. Nevertheless, CRG takes the same point of view and has been successfully used in CMC populations.<sup>43</sup>

Because of the limited data available on income, we were unable to obtain a more detailed segmentation of the SEP variable. This was especially true of the High SEP category, which includes a wide range of income levels. A more segmented category would have given a more accurate approximation of the SEP gradient.

The health status data is based on the use of public healthcare resources, and data from private healthcare was not available. Even so, the bias is presumably very low, as CMC patients require highly specialized care and, for this reason, are mainly treated in the universal Catalan Healthcare System.

The main strength of this population-based study is the use of robust individual records and databases. Another advantage is that it includes all the children in Catalonia and thus provides a realistic view of the current health status of the population.

Some studies have used maternal education as a proxy for SEP, or self-reported outcomes<sup>7,44</sup>; the present study, like other influential studies in the US<sup>4</sup> and the UK<sup>5</sup>, goes further by using population-based economic, employment, and health data to determine the health status of individuals, making it less vulnerable to response bias.

## Conclusion

This study confirms the existence of an SEP gradient in childhood health for a broad spectrum of health outcomes. Children from lower socioeconomic backgrounds are more likely to have CMC conditions. Respiratory and neurodevelopment diseases are the most prevalent, and show the most prominent socioeconomic inequalities.

Daily life for CMC and their families is not only complex from the perspective of healthcare; every area of life is complex. Introducing policies to support both healthcare and financial will have implications beyond children's health itself; it will become a catalyst to reduce social inequalities and to break the vicious circle of poverty and ill-health.

## Declarations

- Ethics approval and consent to participate: Not applicable
- Consent for publication: The authors declare that they have no competing interests
- Availability of data and materials: The data that support the findings of this study are not publicly available due to them containing personal information that could compromise research participant privacy. The anonymised and unidentified data will be accessible to the research staff of the research centers accredited by the institution Research Centers of Catalonia (CERCA), SISCAT agents and public university research centers, as well as the same health administration (for example, groups of investigation of the master plans of the Department of Health of Catalonia).
- Competing interests: None declared
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- Authors' contributions: Neus Carrilero had full access to all the data in the study and vouches for the integrity of the data and the accuracy of the data analysis. Study concept and design: Anna García-Altés. Acquisition, analysis, or interpretation of data: Neus Carrilero, Cristina Colls and Albert Dalmau-Bueno. Drafting of the manuscript: Neus Carrilero. Critical revision of the manuscript for important intellectual content: Neus Carrilero, Dolores Ruiz-Muñoz and Anna García-Altés. Study supervision: All authors.
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- Authors' information (optional): This work has been conducted within the framework of the PhD in Biomedics of the University Pompeu Fabra.

## Abbreviations Used

Socioeconomic position (SEP)

Children with medically complex (CMC)

The Adjusted Morbidity Groups (Catalan acronym GMA)

Clinical Risk Group (CRG)

Catalan Health Surveillance System (CCHS)

Central registry of insured persons (Catalan acronym RCA)

Clinical Classification Software (CCS)

## References

1. Gray AM. Inequalities in health. The Black report: a summary and comment. *Int J Heal Serv.* 1982;12(3):349–380.
2. Heckman JJ. The developmental origins of health. *Health Econ.* 2012;21(1):24–9.
3. Irwin L, Siddiqi A, Hertzman G. Early child development?: a powerful equalizer final report. Geneva (Switzerland): World Health Organization WHO; 2007.
4. Case A, Lubotsky D, Paxson C. Economic status and health in childhood: The origin of the gradient. *Am Econ Rev.* 2002;92(5):1308–34.
5. Currie A, Shields MA, Price SW. The child health/family income gradient: Evidence from England. *J Health Econ.* 2007;26(2):213–32.
6. Flores M, García-Gómez P, Zunuzegui MV. Crisis económica, pobreza e infancia. ¿Qué podemos esperar en el corto y largo plazo para los “niños y niñas de la crisis”? Informe SESPAS 2014. *Gacet Sanit.* 2014;28(S1):1–146.
7. Currie J, Stabile M. Socioeconomic status and health: why is the relationship stronger for older children? *Am Econ Rev.* 2003;93(5):1813–23.
8. Optimizing health care for children with medical complexity. Alexandria, VA (USA): Children’s Hospital Association; 2013. <http://www.childrenshospitals.org>. Accessed 23 Sep 2019.
9. Simon TD, Cawthon ML, Popalisky J, Mangione-Smith R, Center of Excellence on Quality of Care Measures for Children with Complex Needs (COE4CCN). Development and Validation of the Pediatric Medical Complexity Algorithm (PMCA) Version 2.0. *Hosp Pediatr.* 2017;7(7):373–7.
10. Feudtner C, Christakis DA, Connell FA. Pediatric deaths attributable to complex chronic conditions: a population-based study of Washington State, 1980–1997. *Pediatrics.* 2000;106:205–9.
11. Cohen E, Kuo DZ, Agrawal R, Berry JG, Bhagat SKM, Simon TD, et al. Children with medical complexity: an emerging population for clinical and research initiatives. *Pediatrics.* 2011;127(3):529–38.
12. Thomson J, Shah SS, Simmons JM, Sauers-Ford HS, Brunswick S, Hall D, et al. Financial and social hardships in families of children with medical complexity. *J Pediatr.* 2016;172:187–93.
13. Observatori del Sistema de Salut de Catalunya. Desigualtats socioeconòmiques en la salut i la utilització de serveis sanitaris públics en la població de Catalunya. Observatori sobre els efectes de la crisi en la salut de la població. Barcelona: Agència de Qualitat i Avaluació Sanitàries de Catalunya. Departament de Salut. Generalitat de Catalunya; 2017.
14. García-Altés A, Ruiz-Muñoz D, Colls C, Mias M, Martín Bassols N. Socioeconomic inequalities in health and the use of healthcare services in Catalonia: analysis of the individual data of 7.5 million residents. *J Epidemiol Community Health.* 2018;72(10):871–9.
15. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet.* 2012;380:37–43.
16. Hesketh KR, Fagg J, Muniz-Terrera G, Bedford H, Law C, Hope S. Co-occurrence and clustering of health conditions at age 11: cross-sectional findings from the Millennium Cohort Study. *BMJ Open.* 2016;6(11):e012919.
17. Monterde D, Vela E, Clèries M. Los grupos de morbilidad ajustados: nuevo agrupador de morbilidad poblacional de utilidad en el ámbito de la atención primaria. *Aten Primaria.* 2016;48(10):674–82.
18. Dueñas-Espín I, Vela E, Pauws S, Bescos C, Cano I, Cleries M, et al. Proposals for enhanced health risk assessment and stratification in an integrated care scenario. *BMJ Open.* 2016;6(4):e010301.
19. Kuo DZ, Melguizo-Castro M, Goudie A, Nick TG, Robbins JM, Casey PH. Variation in child health care utilization by medical complexity. *Matern Child Health J.* 2015;19(1):40–8.
20. Healthcare Cost and Utilization Project (HCUP) A Federal-State-Industry Partnership in Health Data CLINICAL CLASSIFICATIONS SOFTWARE (CCS); 2015. <http://www.ahrq.gov/data/hcup/>. Accessed 14 Nov 2017.
21. Idescat. Enquesta de condicions de vida. Llindar de risc de pobresa segons la composició de la llar. Catalunya [Internet]. <https://www.idescat.cat/pub/?id=ecv&n=7623>. Accessed 4 May 2019.
22. Rezanková H. Cluster analysis and categorical data. *Statistika: Statistics and Economy Journal.* 2009. [https://www.researchgate.net/profile/Hana\\_ezankova/publication/228758935\\_Cluster\\_analysis\\_and\\_categorical\\_data/links/5709146308aed09e916f90f1](https://www.researchgate.net/profile/Hana_ezankova/publication/228758935_Cluster_analysis_and_categorical_data/links/5709146308aed09e916f90f1) Accessed 4 May 2019.
23. Turino C, Bertran S, Gavalda R, Teixidó I, Woehle H, Rué M, et al. Characterization of the CPAP-treated patient population in Catalonia. *PLoS One.* 2017;12(9):e0185191.
24. Greenacre M, Blasius J. Statistics in the social and behavioral sciences. In: Greenacre M, Blasius J, editors. Multiple correspondence analysis and related methods. New York (USA): Chapman and Hall/CRC; 2006.
25. Calinski T, Harabasz J. A dendrite method for cluster analysis. *Commun Stat-Theor M.* 1974;3(1):1–27. <https://doi.org/10.1080/03610927408827101>

26. STATA V.14/SE 2014 | StataCorp LLC [software]. 2014. <https://www.stata.com/company>. Accessed 20 Dec 2018.
27. Marcos L, Ubrich T. DESHEREDADOS: Desigualdad infantil, igualdad de oportunidades y políticas públicas en España. Madrid (Spain): Save the Children; 2017. [https://www.savethechildren.es/sites/default/files/imce/docs/desheredados\\_pobreza\\_infantil\\_vlq.pdf](https://www.savethechildren.es/sites/default/files/imce/docs/desheredados_pobreza_infantil_vlq.pdf). Accessed 20 Dec 2018.
28. DiPietro JA, Voegtline KM. The gestational foundation of sex differences in development and vulnerability. *Neuroscience*. 2017;342:4–20.
29. Li S, Williams G, Jalaludin B, Baker P. Panel studies of air pollution on children's lung function and respiratory symptoms: a literature review. *J Asthma*. 2012;49(9):895–910.
30. McEvoy CT, Spindel ER. Pulmonary effects of maternal smoking on the fetus and child: effects on lung development, respiratory morbidities, and life long lung health. *Paediatr Respir Rev*. 2017;21:27–33.
31. Wright RJ, Visness CM, Calatroni A, Ms M, Grayson MH, Gold DR, et al. Prenatal maternal stress and cord blood innate and adaptive cytokine responses in an inner-city cohort. *Am J Respir Crit Care Med*. 2010;182(1):25–33.
32. Skromme K, Vollsæter M, Øymar K, Markestad T, Halvorsen T. Respiratory morbidity through the first decade of life in a national cohort of children born extremely preterm. *BMC Pediatr*. 2018;18(1):102.
33. Almqvist C, Worm M, Leynaert B, working group of GA2LEN WP 2.5 Gender. Impact of gender on asthma in childhood and adolescence: a GA 2 LEN review. *Allergy*. 2008;63(1):47–57.
34. González-Alzaga B, Lacasaña M, Aguilar-Garduño C, Rodríguez-Barranco M, Ballester F, Rebagliato M, et al. A systematic review of neurodevelopmental effects of prenatal and postnatal organophosphate pesticide exposure. *Toxicol Lett*. 2014;230(2):104–21.
35. Kelly R, Ramaiah S, Sheridan H, Cruickshank H, Rudnicka M, Kissack C, et al. Dose-dependent relationship between acidosis at birth and likelihood of death or cerebral palsy. *Arch Dis Child Fetal Neonatal Ed*. 2018;103(6):F567-F572.
36. Himmelmann K, Ahlin K, Jacobsson B, Cans C, Thorsen P. Risk factors for cerebral palsy in children born at term. *Acta Obstet Gynecol Scand*. 2011;90(10):1070–81.
37. Pan I-J, Daniels JL, Zhu K. Poverty and childhood cancer incidence in the United States. *Cancer Causes Control*. 2010;21(7):1139–45.
38. Filippini T, Heck JE, Malagoli C, Giovane C Del, Vinceti M. A review and meta-analysis of outdoor air pollution and risk of childhood leukemia. *J Environ Sci Heal Part C*. 2015;33(1):36–66.
39. Stothard KJ, Tennant PWG, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies. *JAMA*. 2009;301(6):636.
40. Martínez-Frías ML, Bermejo E, Rodríguez-Pinilla E, Frías JL. Risk for congenital anomalies associated with different sporadic and daily doses of alcohol consumption during pregnancy: A case-control study. *Birth Defects Res Part A Clin Mol Teratol*. 2004;70(4):194–200.
41. Spencer NJ, Blackburn CM, Read JM. Disabling chronic conditions in childhood and socioeconomic disadvantage: a systematic review and meta-analyses of observational studies. *BMJ Open*. 2015;5(9):e007062.
42. Shonkoff JP. Building a new biodevelopmental framework to guide the future of early childhood policy. *Child Development*. 2010;81(1):357–67.
43. Neff JM, Sharp VL, Muldoon J, Graham J, Popalisky J, Gay JC. Identifying and classifying children with chronic conditions using administrative data with the clinical risk group classification system. *Ambul Pediatr*. 2002;2(1):71–9.
44. Propper C, Rigg J, Burgess S. Child health: Evidence on the roles of family income and maternal mental health from a UK birth cohort. *Health Econ*. 2007;16(11):1245–69.

## Tables

**Table 1. Characteristics of children under 15 by population (CMC<sup>a</sup> and non-CMC<sup>b</sup>) and sex in Catalonia, 2016.**

	Boys					Girls				
	Non-CMC		CMC		P Value <sup>y</sup>	Non-CMC		CMC		P Value <sup>y</sup>
	N=609 015	51.4%	N=3480	58.4%		N=574 360	48.6%	N=2470	41.6%	
<b>Ages (years)</b>										
<2	70 465	11.6	878	25.2	<.001	66 591	11.6	604	24.4	<.001
2 to 4	113 705	18.7	916	26.3		107 284	18.7	636	25.8	
5 to 11	303 127	49.8	1256	36.1		285 247	49.7	848	34.3	
12 to 14	121 718	20.0	430	12.4		115 238	20.1	382	15.5	
<b>SEP</b>										
Low	53 360	8.8	440	12.6	<.001	50 261	8.8	317	12.8	<.001
Middle	321 762	52.8	2030	58.3		303 039	52.8	1428	57.8	
High	233 197	38.3	1001	28.8		220 437	38.4	713	28.9	
<b>GMA* (score)</b>	2.3	(0.8-4.1)	16.7	(15.1-20.5)	<.001	2.1	(0.7-3.8)	16.7	(15.0-20.0)	<.001

Note: GMA = Morbidity Adjusted Group, SEP=Socioeconomic Position. Low (none member of the household employed, receiving welfare support from the government and an income <18 000€/year), Middle (employed and an income <18,000€/year), High (employed and an income >18,000€/year).

<sup>a</sup>Children Medically Complex population= top 0.5% of GMA score of all entire population under 15.

<sup>b</sup>Non Children Medically Complex population= 99.5% bottom of GMA score of all entire population under 15.

Values are absolute numbers (percentages) for categorical variables. \*Median (IQR).

<sup>y</sup> P Value  $\chi^2$  test for categorical variables and Mann-Whitney U-test for continuous variables. Differences between CMC and Non-CMC populations according to sex groups.  $\alpha=0.005$ .

**Table 2. Socioeconomic characteristics of each comorbidity cluster among the CMC and association between SEP and prevalences by cluster. Catalonia, 2016.**

	Respiratory <sup>II</sup>				P	Neurodevelopment <sup>II</sup>				P	Hemato-Oncology <sup>II</sup>				P	Perinata <sup>II</sup>				P
	Boys		Girls			Boys		Girls			Boys		Girls			Boys		Girls		
	N	%	N	%		N	%	N	%		N	%	N	%		N	%	N	%	
<b>Ages (years)<sup>Y</sup></b>																				
<2	380	23.3	271	22.8	0.011 <sup>II</sup>	58	9.2	36	8.4	0.648 <sup>II</sup>	35	8.6	32	11.0	0.195 <sup>II</sup>	405	49.9	265	46.8	0.313 <sup>II</sup>
2 to 4	560	34.4	384	32.4		106	16.8	64	15.0		69	16.9	58	19.9		180	22.2	131	23.1	
5 to 11	554	34.0	388	32.7		310	49.2	209	48.8		214	52.5	129	44.3		178	21.9	122	21.6	
12 to 14	135	8.3	143	12.1		156	24.8	119	27.8		90	22.1	72	24.7		49	6.0	48	8.5	
<b>SEP<sup>X</sup></b>																				
High	454	27.9	335	28.2	0.876 <sup>II</sup>	184	29.2	125	29.2	0.752 <sup>II</sup>	125	30.6	99	34.0	0.411 <sup>II</sup>	238	29.3	154	27.3	0.703 <sup>II</sup>
Middle	959	58.8	686	57.8		358	56.8	247	57.7		232	56.9	150	51.5		481	59.2	345	61.0	
Low	215	13.2	162	13.7		84	13.3	50	11.7		50	12.3	40	13.7		91	11.2	65	11.5	
<b>SEP OR (CI)<sup>#</sup></b>																				
High	1		1			1		1			1		1			1		1		
Middle	1.5 (1.3-1.6)		1.4 (1.2-1.6)			1.4 (1.2-1.7)		1.5 (1.2-1.8)			1.3 (1.1-1.7)		1.1 (0.9-1.4)			1.3 (1.1-1.6)		1.5 (1.2-1.8)		
Low	2.1 (1.7-2.4)		2.1 (1.7-2.5)			2.0 (1.5-2.6)		1.8 (1.3-2.5)			1.7 (1.3-2.4)		1.8 (1.2-2.6)			1.7 (1.3-2.1)		1.8 (1.4-2.5)		
<b>GMA<sup>Δ</sup> (score)</b>	15.9 (14.7-17.9)		16.0 (14.8-18.2)		0.252 <sup>Y</sup>	17.9 (15.6-22.7)		17.3 (15.5-21.2)		0.074 <sup>Y</sup>	19.4 (16.0-24.9)		19.6 (16.2-27.6)		0.251 <sup>Y</sup>	17.8 (15.5-21.8)		17.1 (15.2-21.1)		0.080 <sup>Y</sup>

Note: GMA = Morbidity Adjusted Group, SEP=Socioeconomic Position. Low (none member of the household employed, receiving welfare support from the government and an income <18,000€/year), Middle (employed and an income <18,000€/year), High (employed and an income >18,000€/year).

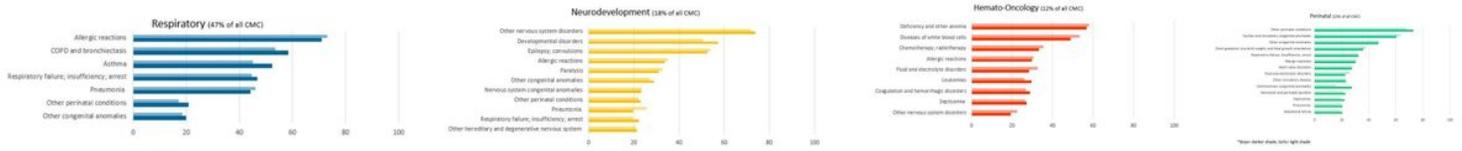
II Prevalences of each cluster (%): (num of individuals in cluster/num individuals in all CMC)\*100.

Y Values are absolute numbers and percentages in each cluster for categorical variables. \*Median (IQR) for continuous variables.

P Value for categorical variables: π χ<sup>2</sup> Test. For continuous variables: γ Mann-Whitney U-test. α=0.005.

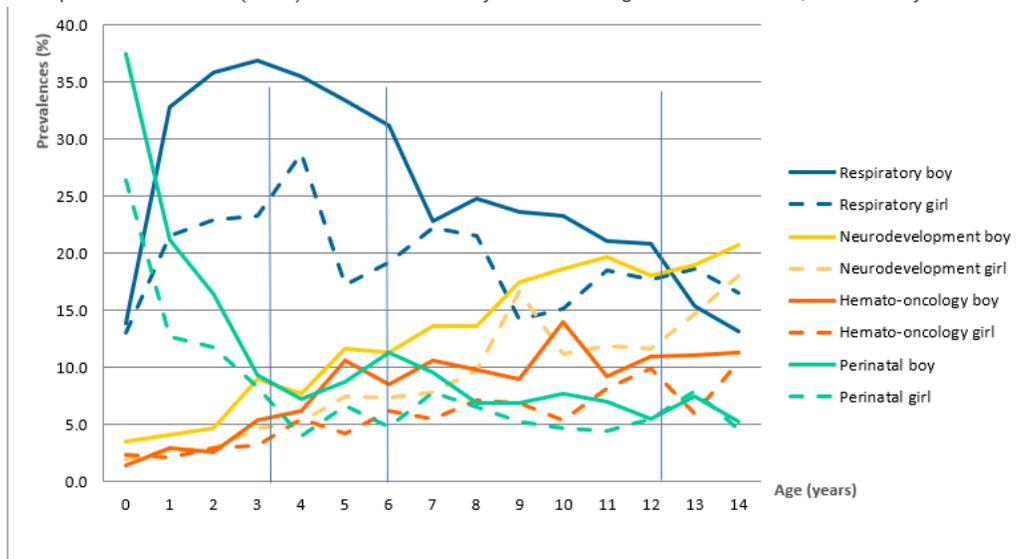
#Odds Ratio, adjusted by age. CI, 95% confidence intervals of the odds ratio.

## Figures



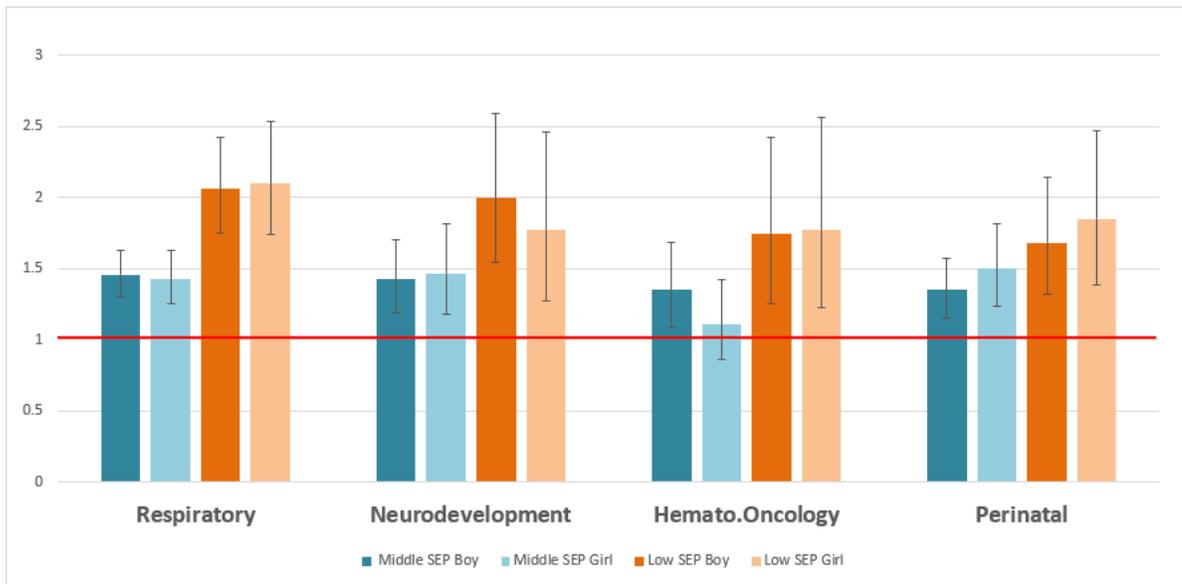
**Figure 1**

More prevalent diseases (>20%) in each comorbidity cluster among CMC in Catalonia, 2016. \* Boys= darker shade, Girls= light shade



**Figure 2**

Prevalences of comorbidity clusters among CMC by age and sex. Catalonia, 2016.



**Figure 3**

Odds ratio between socioeconomic position (SEP) and each comorbidity cluster among CMC by sex. Catalonia, 2016.\* \*Models were adjusted by age. Odds ratio and 95% Confidence Interval. High SEP was the reference category.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [ADDITIONALFILEINFORMATION.docx](#)
- [Additionalfile1SEPCMC.xlsx](#)