FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

MESTRADO INTEGRADO EM MEDICINA

2017/2018

Beatriz Lousa Alves Riquito Marques

Morbidity and mortality in preterm infants less than 29 weeks of gestational age

Morbilidade e mortalidade em recém-nascidos pré-termo com menos de 29 semanas de idade gestacional

março, 2018

Beatriz Lousa Alves Riquito Marques

Morbidity and mortality in preterm infants less than 29 weeks of gestational age

Morbilidade e mortalidade em recém-nascidos pré-termo com menos de 29 semanas de idade gestacional

Mestrado Integrado em Medicina

Área: Neonatologia

Tipologia: Dissertação

Trabalho efetuado sob a Orientação de:

Professora Doutora Maria Hercília Ferreira Guimarães Pereira Areias

Trabalho organizado de acordo com as normas da revista:

Journal of Pediatric and Neonatal Individualized Medicine

março, 2018

U.PORTO
FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

Projeto de Opção do 6º ano - DECLARAÇÃO DE INTEGRIDADE

Eu, Beatriz Lousa Alves Riqueito Marques, abaixo assinado, nº mecanográfico 201204445, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter atuado com absoluta integridade na elaboração deste projeto de opção.

Neste sentido, confirmo que **NÃO** incorri em plágio (ato pelo qual um indivíduo, mesmo por omissão, assume a autoria de um determinado trabalho intelectual, ou partes dele). Mais declaro que todas as frases que retirei de trabalhos anteriores pertencentes a outros autores, foram referenciadas, ou redigidas com novas palavras, tendo colocado, neste caso, a citação da fonte bibliográfica.

Faculdade de Medicina da Universidade do Porto, 12/3/2018

Assinatura conforme cartão de identificação:
Beatriz Lousa Alves Riqueito Marques

U.PORTO
FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

Projecto de Opção do 6º ano – DECLARAÇÃO DE REPRODUÇÃO

NOME

Beatriz Lousa Alves Riquito Marques

NÚMERO DE ESTUDANTE | E-MAIL

201204445 | beatrizriquito@gmail.com

DESIGNAÇÃO DA ÁREA DO PROJECTO

Neonatologia

TÍTULO DISSERTAÇÃO/~~MONOGRAFIA~~ (riscar o que não interessa)

Morbidity and mortality in preterm infants less than 29 weeks of gestational age

ORIENTADOR

Professora Doutora Maria Hercília Ferreira Guimarães Pereira Areias

COORIENTADOR (se aplicável)

ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☒
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTE TRABALHO (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTE TRABALHO.	☐

Faculdade de Medicina da Universidade do Porto, 12/03/2018

Assinatura conforme cartão de identificação: Beatriz Lousa Alves Riquito Marques

Morbidity and Mortality in Preterm Infants Less than 29 Weeks of Gestational Age

Beatriz Riquito Marques*[1], Ana Clara Dinis[1], Gustavo Rocha[1,2], Filipa Flôr-de-Lima[1,2], Ana Cristina Matos[3,4]; Carla Henriques[3,5], Hercília Guimarães [1,2,6]

1 Faculty of Medicine, University of Porto, Porto, Portugal
2 Neonatal Intensive Care Unit, Centro Hospitalar São João, Porto, Portugal
3 School of Technology and Management, Polytechnic Institute of Viseu, Portugal
4 Center for the Study of Education, Technologies and Health, Viseu, Portugal
5 Center for Mathematics, University of Coimbra, Portugal
6 Cardiovascular R&D Unit of Faculty of Medicine, University of Porto, Porto, Portugal

***Corresponding author:**
Beatriz Riquito Marques (mimed12269@med.up.pt; beatrizriquito@gmail.com).
Department of Gynecology-Obstetrics and Pediatrics, Faculty of Medicine, University of Porto, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal.
Telephone number: +351 22 551 3600; Fax number: +351 22 551 3601.

Abstract

Background: Preterm birth is certainly a public health problem. Aside from being an important cause of mortality, prematurity increases the risk of serious lifetime disabilities.
Objective: To assess the overall survival, causes of death and neonatal morbidities associated with prematurity of newborns less than 29 weeks of gestational age (GA).
Methods: Retrospective study including all preterm infants less than 29 weeks of GA admitted to the level III NICU at Centro Hospital São João in Porto, Portugal, between January 1st 2005 and December 31st 2016. Newborns were grouped in three groups according to their GA: $G23^{+0}$-24^{+6}, $G25^{+0}$-26^{+6}, $G27^{+0}$-28^{+6}.
Results: In this 12-year-period, 160 preterm neonates less than 29 weeks of GA admitted to this NICU met our inclusion criteria. Overall deaths were 60 (37.5%), variating between 25 (92.6%) in the $G23^{+0}$–24^{+6}, 23 (46%) in the $G25^{+0}$-26^{+6} and 12 (14.5%) in the $G27^{+0}$–28^{+6}. Early neonatal mortality was 20.6% and the leading causes of death were intraventricular hemorrhage (IVH) and sepsis. Among survivors, 41% had bronchopulmonary dysplasia (BPD), 69% developed late sepsis, 56% retinopathy of prematurity (ROP), 44% IVH and 10% cystic periventricular leukomalacia (cPVL).
Conclusions: Mortality rates in this preterm group were high in spite of all the technological and scientific advances. Pulmonary conditions (respiratory distress syndrome and BPD), sepsis and neurologic outcomes (ROP, IVH and cPVL) were still major causes of morbidity. In line with other series, the limit of viability in this cohort of preterm infants is 25 weeks of GA. Prenatal, perinatal and postnatal care still all have a long road ahead, especially when it comes to these "gray zone" newborns.

Keywords: preterm infant, mortality, morbidity, limit of viability, neonatal intensive care unit, bronchopulmonary dysplasia

Introduction

Preterm birth is certainly a public health problem. According to the World Health Organization (WHO), prematurity is the leading cause of death among newborns and it comes in second between children bellow five years old, after pneumonia. Aside from being an important cause of mortality, premature birth increases the risk of serious lifetime disabilities.[1]

Prematurity, and its poor outcomes, not only occur at high rates in undeveloped countries but also have a significant impact in the more developed ones. In Portugal, for instance, 7.8% of all children born in 2016 were preterm, and 2.3/1000 babies died before 28 days of life.[2]

The limit of viability has been considerably decreasing from 31 weeks in 1960 to 23 weeks of gestational age (GA) nowadays [3], due to improvements in advanced life support technologies. However, this increase in survival rate has consequently raised the absolute number of premature infants with chronic morbidities.

There are numerous ways to fight these devastating outcomes of preterm newborns. One of them is to prevent preterm births through preconception and antenatal care; another one is to increase neonatal care quality, mainly in the Neonatal Intensive Care Units (NICU's).

A systematic review showed that there is still a wide variation of recommendations among countries, although with an overall agreement for comfort care at 22 weeks of GA and active care at 25 weeks of GA.[4]

The aim of this study was to assess the overall survival, causes of death and neonatal morbidities associated with prematurity of newborns less than 29 weeks of GA, in a level III NICU.

Methods

We conducted a retrospective study including all preterm infants born with less than 29 weeks of GA who were admitted to the level III NICU at hospital São João in Porto, Portugal. Data was collected from the past 12 years, between January 1st 2005 and December 31st 2016. We decided to exclude all newborns admitted after 72 hours of life and also those transferred to other centers before their first week of life. Clinical data, including demographic, obstetric and neonatal were collected through a retrospective search of the medical records available either on paper or electronic database.

GA was assessed by menstrual age (regular menstrual cycles), obstetric ultrasound examination[5] or, the New Ballard Score (in the absence of obstetric data).[6] Fetal growth restriction was defined as a birth weight below 10th percentile of Fenton's fetal growth charts.[7] In this center, antenatal steroid regimen is performed with betamethasone since 2003 in pregnancies below 25 weeks of GA, in which preterm labor is a possibility.[8]

We collected data on several conditions associated with prematurity. Respiratory distress syndrome (RDS) was diagnosed according to the European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome: PaO_2 <50 mmHg in room air, central cyanosis in room air, need for supplemental oxygen to maintain PaO_2 >50 mmHg or to maintain a pulse oximeter saturation >85% within the first 24 hours of life; and as well as the classical chest radiograph (including a ground-glass appearance and air bronchogram). Nonetheless, this classic patterns of RDS are rarely seen today due to early surfactant therapy and early continuous positive air pressure (CPAP).[9-11] Newborns were accessed at 36 weeks of GA or at discharge to determine whether they had bronchopulmonary dysplasia (BPD). BPD was defined as treatment with supplemental oxygen for at least 28 days and classified in mild, moderate or severe according to the National Institute of Child Health and Human Development (NICHD).[12] Pulmonary hemorrhage and pneumonia were diagnosed based on clinical and radiological findings, the latter being also based on a microbiological culture. Hemodynamically significant patent ductus arteriosus (PDA) was diagnosed between 24 and 72 hours of life based on clinical symptoms and echocardiographic findings. The infants were treated with indomethacin before 2010 and with ibuprofen afterwards or with surgical closure when medical treatment failed or was contraindicated. We defined and staged necrotizing enterocolitis (NEC) according to Bell's criteria.[13] Early and late-onset sepsis were considered when there was evident clinical symptoms of sepsis and a positive C-reactive protein, confirmed or not with a positive blood culture were present before or after the first 72 hours of life. The diagnosis and grading of

intraventricular hemorrhage (IVH) was based on Papile's [14] or Volpe's[15] classification depending on the year of birth (before or after 2010, respectively) and grade III and IV were considered severe. Cystic periventricular leukomalacia (cPVL) was classified according to De Vries.[16] Retinopathy of prematurity (ROP) was diagnosed and classified according to the international classification.[17]

We also registered all management and mortality information. Necropsy data of deceased neonates were also registered and analysed, whenever parents authorized it.

We divided the newborns in three groups of two weeks of age each according to their GA: $G23^{+0}$-24^{+6}, $G25^{+0}$-26^{+6} and $G27^{+0}$-28^{+6}. We focused our study on data after 2005 because there were a few major changes in the NICU concerning the management of preterm newborns. [8]

This study was approved by the Ethics Committee of Centro Hospitalar São João.

Data was statistically analysed using SPSS® version 24 IBM® software.

It was considered statistically significant a p-value ≤ 0.05. Categorical variables are presented as percentages and numerical variables as median with an inter-quartile range. Univariate analysis comprised the Mann–Whitney U-test or Kruskal-Wallis to compare groups for numerical variables and the Chi-square test or Fisher's exact test for categorical variables.

A multivariate analysis was conducted to identify predictors of death, with a 95% confidence interval (CI). Logistic regression models were constructed beforehand, including all covariates identified in the univariate analysis with p-value < 0.05.

Results

About 3000 newborns are born at Centro Hospital São João each year, and 450 are admitted to its level III NICU, including both inborn and outborn infants. In our 12-year-period, 160 preterm with less than 29 weeks of GA were admitted to the NICU and met our inclusion criteria.

Among the 160 neonates, 74 (46.3%) were female and 112 (70%) were singletons. Mother's median age was 31 years, and 60% of the babies were delivered by a cesarean section (C-section). Prenatal corticosteroids were administered to 141 (91.6%), Table 1.

Everyone received supplemental oxygen and ventilation, either with nasal continuous positive airway pressure (nCPAP) or with invasive mechanical ventilation (IMV). Surfactant therapy was administered to 150 (94.9%) preterm infants. Dopamine was administered to 16 (61.5%) and 26 (52.0%) in the first two groups ($G25^{+0}$–26^{+6} and $G27^{+0}$–28^{+6}, respectively), and to 26 (31.3%) in the third group ($G27^{+0}$-28^{+6}). All infants received antibiotics (Table 2).

Overall deaths were 60 (37.5%), variating between 25 (92.6%) in the $G23^{+0}$–24^{+6}, 23 (46%) in the $G25^{+0}$-26^{+6} and 12 (14.5%) in the $G27^{+0}$–28^{+6}. The leading causes of death were IVH and sepsis. Early neonatal mortality was 20.6%, and 45.5% of these newborns died more often because of pulmonary hypoplasia (Table 3).

In a logistic regression followed by a multivariable analysis, death was significantly associated with GA (B=0.355; 95% CI= 0.226-0.557; $p<0.0005$) and birth weight (B=0.996; CI= 0.993-0.999; $p<0.0005$) but not with prenatal steroids or surfactant ($p>0.05$). Based on the B value=0.355, the chances of death decrease 64.5% for each additional week of GA.

Global rates of RDS were close to 89% and BPD was seen in 35 (21.9%) of all infants included in the study. Nosocomial sepsis was present in 89 (55.6%) and PDA in 84 (52.8%). When it comes to brain damage, severe IVH occurred in 41 (59.4%), while 27 (16.9%) developed cPVL.

Among survivors, 41 (41%) had BPD, mostly mild or moderate. Between the 52 (52%) with PDA, 39 (78%) were treated medically. Twenty-four babies (42.9%) were discharged with severe ROP (grade 2 or higher), 16 of them born with 25 or 26 weeks. Severe NEC was diagnosed in 14 (14%) premature infants, 11 of them belonging to $G27^{+0}$–28^{+6}. Fourty-four (44%) had IVH, 19 (43.2%) of them classified as severe. Median NICU stay was around 70 days, ranging from 93 or 97 days in the first two groups to 63 days in the third group (Table 4).

Discussion

In this study, we analysed the neonatal mortality and morbidities of a cohort of preterm infants less than 29 weeks of GA.

A study comparing nine countries in Europe, showed that Portugal had one of the lowest preterm natality rates and it was ranked fifth in the adjusted neonatal death rate.[18]
Implementation of regionalized perinatal care and high quality NICU's, along with advances areas such as technology or delivery assistance have allowed major improvements in pediatrics life support.[19] Therefore, and as expected, the mortality rates have decreased over the years. Specifically in this level III NICU which belongs to the pedriatric service of a university hospital in Porto, Portugal, the mortality rates of premature infants less than 29 weeks of GA was around 52% in the nineties,[20] contrasting with the 37.5% verified in our 2005 to 2016 cohort. Nevertheless, this increase in survival does not necessarily come along with a reduction of morbidities, particularly neurological sequelae.[19]
Overall early neonatal mortality was 20.6%. We registered that in the $G23^{+0}$–24^{+6}, death was much more prevalent in the first week than afterwards (62.9% vs 25.9%). On the other hand, the majority of those born with 25 or 26 weeks of GA died after the first seven days (24.0% vs 14.0%). This might be explained by the causes of death observed in these groups with different GA's and consequently with different morbidities. The main cause death in neonates born with 23 or 24 weeks of GA in was pulmonary hypoplasia, which is a condition directly associated with their very low GA. The dominant cause of late neonatal death in the $G25^{+0}$–26^{+6} was sepsis, a condition not directly involved with the GA but significantly related with a longer stay in the NICU and of course, with the vulnerability of each newborn.[21] Among survivors, it is also clear that nosocomial sepsis decreases with GA, meeting our expectations. In 2010, this NICU changed some protocols in order to prevent nosocomial sepsis, and its rates have been decreasing since then.[21] In the management of these preterm infants we continue to implement better practices to increase more and more the survival without increasing their morbidities.
As mentioned before, the leading causes of death were IVH and sepsis, both contributing individually to 30% of all deaths. Infectious causes were also responsible for 30% of deaths in a cohort of extremely low birth weight (ELBW) infants from 1996 to 2014 in this tertiary care center.[22]
The limit of viability is considered to be the GA at which more than 50% of the newborns survive. The Portuguese Neonatal Society, based on the National Registry of Very Low Birth Weight (VLBW) infants has established this limit at 25 weeks since 2004 and sensitively at 500g of birth weight.[23] In this study, this limit was also at 25 weeks of GA. Below this GA, the so called "gray zone" of viability,[3] medical decisions vary intensively across countries and are somewhat controversial which is a reason why they require a careful and individualized analysis.[3, 4] In Portugal, palliative care is recommended for those born with less than 23 of GA.[23] In our study, premature infant born at $G23^{+0}$–24^{+6} had a 92.6% mortality rate, similar to other studies in this center[19, 22], and 44% of them died in the first 24 hours after admission in the NICU, in line with the EPIPAGE-2 group and other studies.[22, 24] This can be explained by decisions to withdraw intensive care, which can also justify the paradoxical low rates of morbidities in this group of patients. All these differences explain the great variability in mortality in preterm infants at the limit of viability.
Another important aspect is the limit of viability without major sequelae in more than 50% of survivors. In our study, limit was established at 27 weeks.
More than 50% of $G23^{+0}$–24^{+6} were twins. Multiple pregnancy is related with prematurity and in this study it was significantly associated with those with less than 24 weeks of GA.[25]
In this cohort, a C-section was performed in 60.6% of all deliveries, and the number increased with GA. C-section was not associated with higher survival when adjusted to GA, comparably with EPICure and EXPRESS groups.[26, 27]
Prenatal steroids were previously proven to be good for induction of fetal maturation and were introduced to medical practices around 1995[28]. Just like in the EXPRESS group study, steroids were almost universally administrated (91.6%), with 77.3% of mothers receiving a full cycle,[29] although significantly less at 23 and 24 weeks of GA probably due to the doubts about their efficacy in those born with 23 weeks of GA.
Extremely preterm newborns within "gray zone" GA ($G23^{+0}$–24^{+6}) were all immediately intubated after birth and started mechanical ventilation, just like in a study performed in this center.[19]

Surfactant therapy was commonly used in all neonates but its need in the first hour of life decreased with GA, from 78.9% ($G23^{+0}$–24^{+6}), to 51.1% ($G25^{+0}$–26^{+6}) to 40.3% in the last group ($G27^{+0}$–28^{+6}), as expected. We found no relation between this therapy and mortality, similar to EPICure and EPIBEL studies [25, 26] but in contrast with others.[27]

Death rates were not affected by surfactant therapy or prenatal steroids. However, and as expected, the chances of death decreased with an increase in GA and birth weight. Based on the B value=0.355, we can calculate and say that the chances of death decreased 64.5% for each additional week of GA.

Among survivors, care must be taken when interpreting data from the $G23^{+0}$–24^{+6}, as only two of them survived. The main morbidities were ROP (56%), IVH (44%) and BPD (41%). IVH is a major neurologic morbidity and was clearly a major cause of death at all ages, accounting for 30% of them. When comparing the prevalence of severe IVH on all patients with its prevalence among survivors, we can reinforce its contribution to mortality (59.4% vs 43.2%), also seen in the EPIBEL study.[25] This is one of many reasons why we should focus further research on how to prevent death and neurologic sequelae caused by this condition.

Between those who survived, infants born with less than 27 weeks of GA needed longer stays in the NICU, which can be a risk factor to many complications, particularly infectious ones.

One of the three major limitations is the retrospective design of the study. Another limitation is the small cohort size from a single center. We should not generalize the results, especially when comparing to larger studies like EPIcure, EPIBEL, EPIPAGE-2 or EXPRESS.[24-27] Large international studies are extremely more accurate to draw conclusion on all these practices.[30, 31]. Lastly, besides being a single center study, is also a tertiary one, which may hold some selection bias and we have to be aware when comparing it with data from a whole country.

Despite all these limitations, single-center studies are nonetheless extremely helpful to the physicians who work in NICU's allowing them to share experience and consequently improve the management of these preterm infants.

Conclusion

Mortality rates in this preterm group remained high in spite of all the technological and scientific advances. Pulmonary conditions (respiratory distress syndrome and BPD), sepsis and neurologic outcomes (ROP, IVH and cPVL) are still a major cause of morbidity. In line with other series, the limit of viability in this cohort of preterm infants is 25 weeks of GA. Prental, perinatal and postnatal care still all have a long road ahead, especially when it comes to these "gray zone" newborns.

Declaration of Interest Statement
The authors declare no conflicts of interest.

Funding Acknowledgement Statement
There was no funding to perform this study.

References

1. WHO. Born Too Soon: The Global Action Report on Preterm Birth. Howson C, Kinney M, Lawn J, editors. Geneva: Geneva, Switzerland : World Health Organization, 2012.; 2012.
2. INE. ESTATÍSTICAS DEMOGRÁFICAS. Instituto Nacional de Estatística (INE). 2016(76ª).
3. Seri I, Evans J. Limits of viability: definition of the gray zone. Journal of perinatology : official journal of the California Perinatal Association. 2008;28 Suppl 1:S4-8.
4. Guillen U, Weiss EM, Munson D, Maton P, Jefferies A, Norman M, Naulaers G, Mendes J, Justo da Silva L, Zoban P, Hansen TW, Hallman M, Delivoria-Papadopoulos M, Hosono S, Albersheim SG, Williams C, Boyle E, Lui K, Darlow B, Kirpalani H. Guidelines for the Management of Extremely Premature Deliveries: A Systematic Review. Pediatrics. 2015;136(2):343-50.
5. MacDonald H. Perinatal care at the threshold of viability. Pediatrics. 2002;110(5):1024-7.
6. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard Score, expanded to include extremely premature infants. The Journal of pediatrics. 1991;119(3):417-23.
7. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC pediatrics. 2013;13:59.
8. Flôr-de-Lima F, Rocha G, Guimaraes H. Impact of changes in perinatal care on neonatal respiratory outcome and survival of preterm newborns: an overview of 15 years. Critical care research and practice. 2012;2012:643246.
9. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Plavka R, Saugstad OD, Simeoni U, Speer CP, Halliday HL. European consensus guidelines on the management of neonatal respiratory distress syndrome in preterm infants - 2010 update. Neonatology. 2010;97(4):402-17.
10. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Plavka R, Saugstad OD, Simeoni U, Speer CP, Vento M, Halliday HL. European consensus guidelines on the management of neonatal respiratory distress syndrome in preterm infants--2013 update. Neonatology. 2013;103(4):353-68.
11. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Plavka R, Saugstad OD, Simeoni U, Speer CP, Vento M, Visser GH, Halliday HL. European Consensus Guidelines on the Management of Respiratory Distress Syndrome - 2016 Update. Neonatology. 2017;111(2):107-25.
12. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. American journal of respiratory and critical care medicine. 2001;163(7):1723-9.
13. Bell MJ, Ternberg JL, Feigin RD, Keating JP, Marshall R, Barton L, Brotherton T. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. Annals of surgery. 1978;187(1):1-7.
14. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. The Journal of pediatrics. 1978;92(4):529-34.
15. Volpe J, Inder T, Darras B, Vries Ld, Plessis Ad, Neil J, Perlman J. Volpe's Neurology of the Newborn. 6th Edition ed2017.
16. Vries LD, Rennie JM. Preterm Brain Injury. In: Rennie JM, Roberton N, editors. Textbook of Neonatology. 3rd ed. London: Churchill Livingstone; 1999.
17. The International Classification of Retinopathy of Prematurity revisited. Archives of ophthalmology (Chicago, Ill : 1960). 2005;123(7):991-9.
18. Field D, Draper ES, Fenton A, Papiernik E, Zeitlin J, Blondel B, Cuttini M, Maier RF, Weber T, Carrapato M, Kollee L, Gadzin J, Van Reempts P. Rates of very preterm birth in Europe and neonatal mortality rates. Archives of disease in childhood Fetal and neonatal edition. 2009;94(4):F253-6.
19. Rocha G, Guimaraes H. On the limit of viability extremely low gestational age at birth. Acta medica portuguesa. 2011;24 Suppl 2:181-8.
20. Rocha G, Rocha A, Martins A, Silva G, Guedes B, Guimarães H. Aspectos Clínicos da Prematuridade Extrema Parte I - Morbilidade e Mortalidade Neonatais. Acta Pediátrica Portuguesa. 2002;33(4):235-41.
21. Almeida CC, Pissarra da Silva SMS, Flôr-de-Lima F, Guimaraes Pereira Areias MHF. Nosocomial sepsis: evaluation of the efficacy of preventive measures in a level-III neonatal intensive care unit. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2017;30(17):2036-41.
22. Duraes MI, F. F-D-L, Rocha G, Soares H, Guimaraes H. Morbidity and mortality of preterm infants less than 26 weeks of gestational age. Minerva pediatrica. 2016.
23. Branco MR, Mimoso G. Limite da viabilidade 2014. Available from: www.spneonatologia.pt. Last access: March 1st, 2018

24. Ancel PY, Goffinet F, Kuhn P, Langer B, Matis J, Hernandorena X, Chabanier P, Joly-Pedespan L, Lecomte B, Vendittelli F, Dreyfus M, Guillois B, Burguet A, Sagot P, Sizun J, Beuchee A, Rouget F, Favreau A, Saliba E, Bednarek N, Morville P, Thiriez G, Marpeau L, Marret S, Kayem G, Durrmeyer X, Granier M, Baud O, Jarreau PH, Mitanchez D, Boileau P, Boulot P, Cambonie G, Daude H, Bedu A, Mons F, Fresson J, Vieux R, Alberge C, Arnaud C, Vayssiere C, Truffert P, Pierrat V, Subtil D, D'Ercole C, Gire C, Simeoni U, Bongain A, Sentilhes L, Roze JC, Gondry J, Leke A, Deiber M, Claris O, Picaud JC, Ego A, Debillon T, Poulichet A, Coline E, Favre A, Flechelles O, Samperiz S, Ramful D, Branger B, Benhammou V, Foix-L'Helias L, Marchand-Martin L, Kaminski M. Survival and morbidity of preterm children born at 22 through 34 weeks' gestation in France in 2011: results of the EPIPAGE-2 cohort study. JAMA pediatrics. 2015;169(3):230-8.
25. Vanhaesebrouck P, Allegaert K, Bottu J, Debauche C, Devlieger H, Docx M, Francois A, Haumont D, Lombet J, Rigo J, Smets K, Vanherreweghe I, Van Overmeire B, Van Reempts P. The EPIBEL study: outcomes to discharge from hospital for extremely preterm infants in Belgium. Pediatrics. 2004;114(3):663-75.
26. Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson AR. The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability. Pediatrics. 2000;106(4):659-71.
27. Fellman V, Hellstrom-Westas L, Norman M, Westgren M, Kallen K, Lagercrantz H, Marsal K, Serenius F, Wennergren M. One-year survival of extremely preterm infants after active perinatal care in Sweden. Jama. 2009;301(21):2225-33.
28. Effect of corticosteroids for fetal maturation on perinatal outcomes. NIH Consensus Development Panel on the Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes. Jama. 1995;273(5):413-8.
29. Incidence of and risk factors for neonatal morbidity after active perinatal care: extremely preterm infants study in Sweden (EXPRESS). Acta paediatrica (Oslo, Norway : 1992). 2010;99(7):978-92.
30. Zeitlin J, Manktelow BN, Piedvache A, Cuttini M, Boyle E, van Heijst A, Gadzinowski J, Van Reempts P, Huusom L, Weber T, Schmidt S, Barros H, Dillalo D, Toome L, Norman M, Blondel B, Bonet M, Draper ES, Maier RF. Use of evidence based practices to improve survival without severe morbidity for very preterm infants: results from the EPICE population based cohort. BMJ (Clinical research ed). 2016;354:i2976.
31. Edstedt Bonamy AK, Zeitlin J, Piedvache A, Maier RF, van Heijst A, Varendi H, Manktelow BN, Fenton A, Mazela J, Cuttini M, Norman M, Petrou S, Reempts PV, Barros H, Draper ES. Wide variation in severe neonatal morbidity among very preterm infants in European regions. Archives of disease in childhood Fetal and neonatal edition. 2018.

Figures and Tables

Table 1 - Maternal and newborn's demographics and perinatal clinical data

Gestational age (weeks)	Total (n=160)	23^{+0}–24^{+6} (n=27)	25^{+0}–26^{+6} (n=50)	27^{+0}–28^{+6} (n=83)	p
Mother's age, median (IQR)	31 (28-35)	32 (31-36)	31 (28-33)	31 (28-35)	0.246¥
Gender					0.683*
- Male, n (%)	86 (53.8)	16 (59.3)	28 (56.0)	42 (50.6)	
- Female, n (%)	74 (46.3)	11 (40.7)	22 (44.0)	41 (49.4)	
BW (g), median (IQR)	**835 (690-1000)**	**650 (560-700)**	**790 (700-880)**	**985 (805-1150)**	**<0.0005¥**
Fetal growth restriction, n (%)	30 (18.8)	3 (11.1)	8 (16.0)	19 (22.9)	0.330*
Parity					
- Single, n (%)	**112 (70.0)**	**12 (44.4)**	**37 (74.0)**	**63 (75.9)**	**0.006***
- Multiple, n (%)	**48 (30.0)**	**15 (55.6)**	**13 (26.0)**	**20 (24.1)**	
Delivery					
- C-section, n (%)	**97 (60.6)**	**3(11.1)**	**30 (60.0)**	**64 (77.1)**	**<0.0005***
Prenatal Steroids, n (%)	**141 (91.6)**	**19 (73.1)**	**44 (95.7)**	**78 (95.1)**	**0.004‡**
- Full cycle, n (%)	109 (77.3)	11 (57.9)	34 (77.3)	64 (82.1)	0,079*
Mother's Infection, n (%)	28 (17.6)	2 (7.4)	8 (16.0)	18 (22.0)	0.213*
Antibiotic use, n (%)	**63 (39.4)**	**6 (22.2)**	**16 (32.0)**	**41 (49.4)**	**0.019***
Mother's disease, n (%)					
- Autoimmune disease	4 (2.5)	0 (0.0)	0 (0.0)	4 (4.8)	0.293‡
- Arterial hypertension	10 (6.3)	1 (3.7)	1 (2.0)	8 (9.6)	0.195‡
- Gestational diabetes	**14 (8.8)**	**2 (7.4)**	**10 (20.0)**	**2 (2.4)**	**0.002‡**
- Preeclampsia	**24 (15.1)**	**1 (3.7)**	**5 (10.2)**	**18 (21.7)**	**0.035***
- Eclampsia	1 (0.6)	0 (0.0)	0 (0.0)	1 (1.2)	
- HELLP dyndrome	6 (3.8)	0 (0.0)	3 (6.0)	3 (3.6)	0.633‡
- Placental abruption	21 (13.1)	1 (3.7)	9 (18.0)	11 (13.3)	0.208*
ROM > 18 hours, n (%)	27 (17.0)	3 (11.1)	7 (14.0)	17 (20.7)	0.408*
Apgar Score, n (%)					
- 1st minute <7	**108 (68.4)**	**25 (100.0)**	**37 (74.0)**	**46 (55.4)**	**<0.0005***
- 5th minute <7	**58 (36.5)**	**15 (57.7)**	**21 (42.0)**	**22 (26.5)**	**0.01***
- 10th minute <7	**13 (9.8)**	**6 (42.9)**	**3 (7.7)**	**4 (5.1)**	**<0.001‡**

Abbreviations: BW – Birth Weight; ROM – Rupture of Membranes; IQR - Interquartile Range.
* - Chi-square test; ¥ - Kruskal-Wallis test; ‡ - Fisher's exact test.

Table 2 - Management data of the newborns

Gestational age (weeks)	Total (n=160)	23^{+0}–24^{+6} (n=27)	25^{+0}–26^{+6} (n=50)	27^{+0}–28^{+6} (n=83)	p
Resuscitation, n (%)	153 (95.6)	26 (96.3)	49 (98.0)	78 (94.0)	0.681‡
- Endotracheal tube, n (%)	141 (92.2)	26 (100)	45 (91.8)	70 (89.7)	0.258‡
Surfactant use, n (%)	150 (94.9)	27 (100)	49 (98.0)	74 (91.4)	0.118‡
- Nº of doses, median (IQR)	**2 (1-2)**	**2 (1.75-2.25)**	**2 (2-3)**	**2 (1-2)**	**0.028¥**
- <1st hour after birth, n (%)	**67 (49.3)**	**15 (78.9)**	**23 (51.1)**	**29 (40.3)**	**0.011***
Supplemental oxygen, n (%)	160 (100)	27 (100)	50 (100)	83 (100)	-
- Days O_2, median (IQR)	**15 (4-50)**	**5 (1-17)**	**34 (8-75)**	**15 (4-44)**	**<0.0005¥**
- FiO_2 max, median (IQR)	**45 (30-80)**	**100 (60-100)**	**60 (45-100)**	**30 (21-50)**	**<0.0005¥**
Ventilation, n (%)	160 (100)	27 (100)	50 (100)	83 (100)	-
- nCPAP, n (%)	**113 (70.6)**	**4 (14.8)**	**33 (66.0)**	**76 (91.6)**	**<0.0005***
- Days of therapy, median (IQR)	31 (17-45)	23 (4-44)	31 (12-45)	31 (22-46)	0.287¥
- IMV, n (%)	**143 (89.4)**	**27 (100)**	**48 (96.0)**	**68 (81.9)**	**0.038‡**
- Days of therapy, median (IQR)	**8 (4-25)**	**4 (1-17)**	**21 (8-35)**	**7 (4-17)**	**<0.0005¥**
Vasoactive amines use, n (%)	**68 (42.8)**	**16 (61.5)**	**26 (52.0)**	**26 (31.3)**	**0.007***
Antibiotic treatment, n (%)	156 (100)	25 (100)	49 (100)	82 (100)	-
- Nº of cycles, median (IQR)	**2 (1-4)**	**1 (1-2)**	**3 (2-4)**	**2 (2-4)**	**0.0005¥**
Transfusions					
- Erythocytes, n (%)	**115 (71.9)**	**18 (66.7)**	**44 (88)**	**53 (63.7)**	**0.009***
- Nº, median (IQR)	**3 (2-7)**	**3 (1-7)**	**5 (3-9)**	**3 (2-5)**	**<0.001¥**
- Platelets, n (%)	**57 (35.6)**	**10 (37.0)**	**29 (58.0)**	**18 (21.7)**	**<0.0005***
- Nº, median (IQR)	3 (1-5)	4 (2-7)	2 (1-5)	3 (1-4)	0.917¥

Abbreviations: nCPAP - Nasal Continuous Positive Airway Pressure; IMV - Invasive Mechanical Ventilation; IQR - Interquartile Range.
* - Chi-square test; ¥ - Kruskal-Wallis test; ‡ - Fisher's exact test;

Table 3 – Mortality and causes of death

Gestational age (weeks)	Total (n=160)	23^{+0}–24^{+6} (n=27)	25^{+0}–26^{+6} (n=50)	27^{+0}–28^{+6} (n=83)	p
Deceased, n (%)	**60 (37.5)**	**25 (92.6)**	**23 (46.0)**	**12 (14.5)**	**<0.0005***
Causes of Death					
- Pulmonary hypoplasia, n (%)	16 (26.7)	12 (48.0)	2 (8.7)	2 (16.7)	
- Pulmonary hemorrhage, n (%)	3 (5.0)	1 (4.0)	1 (4.3)	1 (8.3)	
- Pneumonia, n (%)	3 (5.0)	0 (0.0)	2 (8.7)	1 (8.3)	
- Sepsis, n (%)	18 (30.0)	6 (24.0)	8 (34.8)	4 (33.3)	
- Congenital heart disease, n (%)	2 (3.3)	0 (0.0)	1 (4.3)	1 (8.3)	
- IVH, n (%)	18 (30.0)	6 (24.0)	9 (39.1)	3 (25.0)	
Early Neonatal Mortality, n (%)	**33 (20.6)**	**17 (62.9)**	**7 (14.0)**	**9 (10.8)**	**<0.05****
Causes of Death					
- Pulmonary hypoplasia, n (%)	15 (45.5)	12 (70.6)	1 (14.3)	2 (22.2)	
- Pulmonary hemorrhage, n (%)	3 (9.1)	1 (5.9)	1 (14.3)	1 (11.1)	
- Pneumonia, n (%)	1 (3.0)	0 (0.0)	0 (0.0)	1 (11.1)	
- Sepsis, n (%)	3(9.1)	1 (5.9)	0 (0.0)	2 (11.1)	
- Congenital heart disease, n (%)	2 (3.3)	0 (0.0)	1 (14.3)	1 (11.1)	
- IVH, n (%)	9 (27.3)	3 (17.6)	4 (57.1)	2 (22.2)	
Late Neonatal Mortality, n (%)	**21 (13.1)**	**7 (25.9)**	**12 (24.0)**	**2 (2.4)**	**<0.05****
Causes of Death					
- Pulmonary hypoplasia, n (%)	1 (4.8)	0 (0.0)	1 (8.3)	0 (0.0)	
- Pneumonia, n (%)	2 (9.5)	0 (0.0)	2 (16.7)	0 (0.0)	
- Sepsis, n (%)	10 (47.6)	4 (57.1)	5 (41.6)	1 (50.0)	
- IVH, n (%)	8 (38.1)	3 (42.9)	4 (33.3)	1 (50.0)	
Postneonatal Mortality$^{\alpha}$, n(%)	6 (3.8)	1 (3.7)	4 (8.0)	1 (1.2)	>0.05**
Causes of Death					
- Sepsis, n (%)	5 (83.3)	1 (100)	3 (75.0)	1 (100)	
- IVH, n (%)	1 (16.7)	0 (0.0)	1 (25.0)	0 (0.0)	

Abbreviations: IVH – Intraventricular hemorrhage;
* - Chi-square test; ** - Chi-square test, using Bonferroni correction.
α – death occurring after the 28th day until discharge.

Table 4 – Neonatal morbidity among the survivors

Gestational age (weeks)	Total (n=100)	23^{+0}–24^{+6} (n=2)	25^{+0}–26^{+6} (n=27)	27^{+0}–28^{+6} (n=71)	p
RDS	89 (89.0)	2 (100)	25 (92.6)	62 (87.3)	0.780*
- Moderate, n (%)	**38 (38.0)**	**1 (50.0)**	**8 (38.1)**	**29 (47.5)**	**<0.0005‡**
- Severe, n(%)	**25 (25.0)**	**1 (50.0)**	**13 (61.9)**	**11 (18.0)**	
BPD, n (%)	**41 (41.0)**	**2 (100.0)**	**19 (70.4)**	**20 (28.2)**	**<0.0005‡**
- Mild, n (%)	24 (58.5)	1 (50.0)	9 (47.4)	14 (70.0)	
- Moderate, n (%)	14 (34.1)	1 (100)	8 (42.1)	5 (25.0)	0.561‡
- Severe, n(%)	3 (7.3)	0 (0.0)	2 (10.5)	1 (5.0)	
Pneumonia, n (%)	**9 (9.0)**	**0 (0.0)**	**8 (29.6)**	**1 (1.4)**	**<0.0005‡**
Pulmonary hemorrhage, n (%)	1 (1.0)	0 (0.0)	1 (3.7)	0 (0.0)	0.290‡
Pneumothorax, n(%)	4 (4.0)	0 (0.0)	3 (11.1)	1 (1.4)	0.136‡
Sepsis					
- Early, n (%)	5 (5.0)	0 (0.0)	2 (7.4)	3 (4.2)	0.652‡
- Late/Nosocomial, n (%)	69 (69.0)	2 (100)	20 (74.1)	47 (66.2)	0.663*
PDA, n (%)	52 (52.0)	2 (100)	17 (63.0)	33 (46.5)	0.108‡
- Medical Closure, n (%)	39 (78.0)	2 (100.0)	10 (58.8)	27 (87.1)	0.074‡
- Surgical Closure, n (%)	11 (22.0)	0 (0.0)	7 (41.2)	4 (12.9)	
NEC ≥ grade 2, n (%)	14 (14.0)	0 (0.0)	3 (11.1)	11 (15.5)	0.817‡
ROP, n (%)	**56 (56.0)**	**2 (100)**	**21 (77.8)**	**33 (46.5)**	**0.04‡**
- ≥ grade 2, n (%)	**24 (42.9)**	**1 (50.0)**	**16 (76.2)**	**7 (9.9)**	**<0.0005‡**
Brain damage					
- IVH, n (%)	**44 (44.0)**	**1 (50.0)**	**17 (63.0)**	**26 (36.6)**	**0.037‡**
- ≥ grade 3, n (%)	19 (43.2)	0 (0.0)	9 (52.9)	10 (38.5)	0.524‡
- cPVL, n (%)	10 (10.0)	0 (0.0)	5 (18.5)	5 (7.0)	0.298‡
NICU stay, median (IQR)	**70 (55-95)**	**93 (85-101)**	**97 (73-109)**	**63 (49-83)**	**<0.0005¥**

Abbreviation: RDS – Respiratory distress syndrome; BPD – Bronchopulmonary dysplasia; PDA – Patent ductus arteriosus; NEC - Necrotizing enterocolitis; ROP - Retinopathy of prematurity; IVH - Intraventricular hemorrhage; cPVL – cystic periventricular leukomalacia; NICU – Neonatal intensive care unit; IQR - Interquartile range.
* - Chi-square test; ‡ - Fisher's exact test; ¥ - Kruskal-Wallis test

Agradecimentos

Em primeiro lugar, queria agradecer à minha orientadora, a Professora Doutora Hercília Guimarães, por toda a disponibilidade e orientação que me deu, sem a qual este projeto não teria sido possível.

Em segundo lugar, à minha irmã, por toda a ajuda que me deu, principalmente nas alturas mais complicadas de todo este percurso.

Aos meus pais, pelo apoio incondicional que me deram todos os dias, pela preocupação, e pelas palavras que incentivo.

Por último, mas não menos importante, aos meus amigos da faculdade e ao Alexandre que, sem saberem, tornam tudo isto muito mais fácil.

ANEXOS

Author Guidelines for the Journal of Pediatric and Neonatal Individualized Medicine (JPNIM)

Papers must be written in English or Italian and must be **original** (not published elsewhere in whole or in part).

Text

Please submit the text in a Word file.

All acronyms in the text should be expanded at first mention, followed by the abbreviation in parentheses.

Please use the following font: Times New Roman, 11 pt.

For paragraph formatting, please use single spacing and full justification.

Do not use boldface or underline character formatting; use italics just for technical terms or not English words. Use quotation marks just for quotations or to underline a particular word meaning.

Do not insert footnotes. Divide the text in **paragraphs** and assign a title to each part.

Abstract and keywords

For every article, authors should send:

- an abstract of **250-300 words**, and
- **6** keywords.

Abstract and keywords must be in English also for Italian articles.

Figures and tables

Figures (graphs, charts, photographs, and illustrations) and tables should be submitted separately from the text file:

- **for graphs and charts**, use Excel files;
- **for photographs and illustrations**, use JPEG, PNG or TIFF files (or, at least, PowerPoint);
- **for tables**, use Excel or Word files.

Figures should be **high resolution** (300 dpi).

Please only use the following **fonts** in figures: **Helvetica or Arial**.

Authors should quote figures and tables in the text and should number them in the order in which they appear in the text. Each figure and table should be accompanied by a **short description**.

Figures and tables must be **original**.

Please note that editors and the publisher could evaluate the sent files overall and decide to modify the number of figures and tables.

Videos, audios and 3D illustrations

Starting from July 2014, we intend to accept also 3D illustrations, audios and videos (e.g., with slide presentations or demonstrations of clinical procedures) to integrate (as PDF-embedded multimedia) into each kind of article, and we are planning to start a new *Video* series, featuring the explanation of medical procedures. You are welcome to send your contributions for evaluation (see more here).

If you plan to send a video, please make sure to follow these guidelines:

- **file format: .mp4 (H.264 encoded)**;
- dimensions: 645x360 or smaller.

Videos, audios and 3D illustrations must be **original**.

References

Please list the references **in order of citation** in the text, in **square brackets**.

For each entry, please clearly indicate the following data: names of **all the authors**, title of the article/book, publication year. Moreover, for journal articles, indicate the abbreviated journal title, volume, issue, first and last page of the article; for websites, indicate the last access; for books, indicate the book publisher and its head office. If you want to quote a chapter within a book, please add information on the chapter (title and authors). Examples:

- **article (see and follow Pub Med citations)**: Mishra J, Dent C, Tarabishi R, Mitsnefes MM, Ma Q, Kelly C, Ruff SM, Zahedi K, Shao M, Bean J, Mori K, Barasch J, Devarajan P. Neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker for acute renal injury after cardiac surgery. Lancet. 2005;365(9466):1231-8.
- **book**: Cowan CP, Cowan PA. When partners become parents: the big life change for couples. New York: Basic Books, 1992.
- **chapter within a book**: Eyben E. Fathers and sons. In: Rawson B (Ed.). Marriage, divorce and children in ancient Rome. Oxford: Clarendon Press, 1991.
- **website**: http://guidance.nice.org.uk/CG54, last access: April 2012.

Author Listing

For each author, please list the following items: name, surname, institutional affiliations.

To facilitate the publisher's communication with authors, please list also the e-mail addresses.

Further requirements

Please indicate a conflict of interest statement and a funding acknowledgement statement.

In case of human experimentation, please indicate which ethical standards were followed and write an informed consent statement.

In experiments on animals, please indicate an animal rights statement.

180-17

Unidade de Investigação

Tomei conhecimento. Nada a opor.

09 de Agosto de 2017

A Coordenadora da Unidade de Investigação

(Prof.ª Doutora Ana Azevedo)

AUTORIZADO

CONSELHO DE ADMINISTRAÇÃO REUNIÃO DE 24 AGO 2017

Presidente do Conselho de Administração

(Dr. António Oliveira e Silva)

Diretor Clínico (Prof. Dr. [illegible] Artur Paiva) | Enfermeira Diretora (Enfª Filomena Caldeira) | Vogal Executivo (Dr. Luís Porto Gomes) | Vogal Executivo (Dr. [illegible] G. Matos)

DIRECÇÃO CLÍNICA

11/8/2017

Aprovado. Ao CA.

(Prof.ª Doutora Ana Azevedo)

Exmo. Senhor

Presidente da Comissão de Ética para a Saúde do Centro Hospitalar de S. João – EPE

Assunto: Pedido de apreciação e parecer para estudo/projecto de investigação

Nome do Investigador Principal: Beatriz Lousa Alves Riquito Marques

Título do projecto de investigação: Morbidity and mortality in preterm infants less than 29 weeks gestational age

Pretendendo realizar no(s) Serviço(s) de Neonatologia do Centro Hospitalar de S. João – EPE o estudo/projecto de investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, a sua apreciação e a elaboração do respectivo parecer.

Para o efeito, anexo toda a documentação referida no dossier dessa Comissão respeitante a estudos/projectos de investigação.

Com os melhores cumprimentos.

Porto, 1 / junho / 2017

O INVESTIGADOR/PROMOTOR

Beatriz Riquito

7. SEGURO

a. *Este estudo/projecto de investigação prevê intervenção clínica que implique a existência de um seguro para os participantes?*

SIM ☐ (Se sim, junte, por favor, cópia da Apólice de Seguro respectiva)

NÃO ☑

NÃO APLICÁVEL ☐

8. TERMO DE RESPONSABILIDADE

Eu, Beatriz Lousa Alves Riquito Marques,

abaixo-assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (com as emendas de Tóquio 1975, Veneza 1983, Hong-Kong 1989, Somerset West 1996 e Edimburgo 2000) e da Organização Mundial da Saúde, no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo no decurso do actual internamento ou da mesma consulta.

Porto, 1 / junho / 2017

A Comissão de Ética para a Saúde tendo aprovado o parecer do Relator, aguarda que o Investigador/Promotor esclareça as questões nele enunciadas para que possa emitir parecer definitivo.

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

Beatriz Riquito

O Investigador Principal

PARECER DA COMISSÃO DE ÉTICA PARA A SAÚDE DO CENTRO HOSPITALAR DE S. JOÃO

emitido na reunião plenária da CES de ___/___/___

Centro Hospitalar **São João**

CONSIDERADOS QUE FORAM COMO SATISFATÓRIOS OS ESCLARECIMENTOS PRESTADOS PELO(A) INVESTIGADOR(A), A CES APROVA POR UNANIMIDADE O PARECER DO RELATOR, PELO QUE NADA TEM A OPOR À REALIZAÇÃO DESTE PROJETO DE INVESTIGAÇÃO.

2017.07.17

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

Comissão de Ética para a Saúde do C.H.S.João e da FMUP

Parecer

Título do Projecto: Morbidity and mortality in preterm infants less than 29 weeks gestational age

Nome do Investigador Principal: Beatriz Lousa Alves Riquito Marques

Promotor do Estudo: NA

Serviço onde decorrerá o Estudo: Serviço Neonatalogia do Centro Hospitalar de S. João

Objectivo e Pertinência do Estudo: Com este estudo, que visa a realização de uma Tese de Mestrado Integrado de Medicina, pretende-se determinar a taxa de sobrevivência e de morbilidade em recém-nascidos pré-termo abaixo das 29 semanas de IG.

Trata-se de um estudo retrospectivo, que incluirá todos os RN PT com menos de 29 semanas de IG, admitidos na UCIN deste Centro Hospitalar entre janeiro 2005 e junho 2017.

Estão definidos critérios de inclusão e de exclusão.

É indicado que os dados serão acedidos por "uma equipa de investigação", a qual é constituída pela investigadora e pela orientadora do mestrado.

O Senhor Director de Serviço deu o seu aval à realização da investigação.

Benefício/risco: Não desproporcionado

Respeito pela liberdade e autonomia do sujeito de ensaio: NA

Confidencialidade dos dados: Os dados serão recolhidos em CRF's anonimizados.

Elo de ligação: Profª Doutora Hercília Guimarães

Indemnização por danos: É indicado serem os dados colhidos propriedade exclusiva do Promotor, mas prevista a publicação dos resultados a alcançar.

Continuação do tratamento: NA

Propriedade dos dados: NA

***Curriculum* do investigador**: NA

Data previsível da conclusão do estudo: 2018

Conclusão: Dada a natureza da investigação requerida, os seus objectivos, a metodologia que lhe está prevista e a clarificação efectuada pela investigadora, a CES nada tem a opor á sua realização.

Porto e C.H.S.João, 2017-07-14

O Presidente da CES

Doutor Filipe Almeida