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Global Prevalence of Bronchopulmonary Dysplasia in Very Low Birth Weight Neonates:

A Systematic Review and Meta-Analysis

Jooby Joy, BS, Michelle Noronha, BS, Aina Tarriela, Altha Naqvi, Sarah Zoretic, DO, Maxwell Jones, Ali Marotta, Taylor Valarie, Grace Lee, Sunil K. Ahuja, Alvaro Moreira, MD



Introduction

- Bronchopulmonary dysplasia (BPD) is a chronic lung disease that is characterized by arrest of lung growth and development n preterm neonates exposed to long periods of supplemental oxygen and positive pressure ventilation.
- Evolving interventions have led to survival of smaller and younger infants, however treatments for BPD are still limited.
- Early preventive measures and treatment are warranted to attenuate disease
- To accomplish this endeavor, a global understanding of the disease and its impact over time is necessary.
- Valid and consistent estimates of the prevalence of BPD around the globe are largely lacking.

Objectives

 To estimate global trends in the prevalence of BPD, to examine temporal changes of BPD rates, and to stratify BPD rates according to definition, birth weight, gestational age, setting, continent, and gross domestic product.

Materials and Methods

- We conducted a systematic review and meta-analysis according to the Cochrane Handbook for Systematic Reviews of Interventions and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria.
- Two investigators systematically searched MEDLINE from January 1990 to September 30th, 2019. Search terms included (bronchopulmonary dysplasia OR chronic lung disease) AND a list of each country.
- Records Identified Through Database Search (n = 4582)ecords Screened by Title Records Excluded and Abstract (n = 2264)(n = 4582) Records Excluded Full - Text Records Evaluated for Eligibility (n = 2318) 66 Overlapped Countries Figure 1. PRISMA Records Included for Flowchart of Literature Systematic Analysis (n = 82) Identification and Study
- Articles were filtered to include children between the age range of birth and 1 month, limited to articles written in English and Spanish, and refined to remove review articles.
- Two groups of investigators independently reviewed the titles and abstracts of all citations to determine suitability
- Male and female neonates with a birth weight of less than or equal to 1,500 grams or a gestational age of less than 32 weeks were included in this study. Case report, editorials, and commentaries were excluded.
- Study specifics included country, BPD definition, BPD rates, total number of neonates in the study, years of observation, inclusion criteria, and study design.
- BPD was defined by three categories: (i) BPD28- supplemental oxygen or positive pressure ventilation at 28 days, (ii) BPD36- supplemental oxygen or positive pressure ventilation at 36 weeks postmenstrual age, (iii) AnyBPD- combination of studies that defined BPD as either BPD28 or BPD36.
- If the study used both definitions, we inserted BPD28 as the prevalence.
- Prespecified subgroup analyses included birth weight categories, gestational age (GA), years, setting, continent, and gross domestic product (GDP).
 - GA: extremely low gestational age (ELGA) (≤28 weeks) vs. very low gestational age (VLGA) (<32 weeks)
 - Study setting: international, national, regional, or community
 - Study years: 1990-1999, 2000-2009, 2010-2019
 - Birth weight: extremely low birth weight (<1,000 grams), very low birth weight (≤1,500 grams), and modifications of these terms (e.g., 501-750 grams, 751-1000 grams, 1001-1250 grams, and 1251-1500 grams).

Results

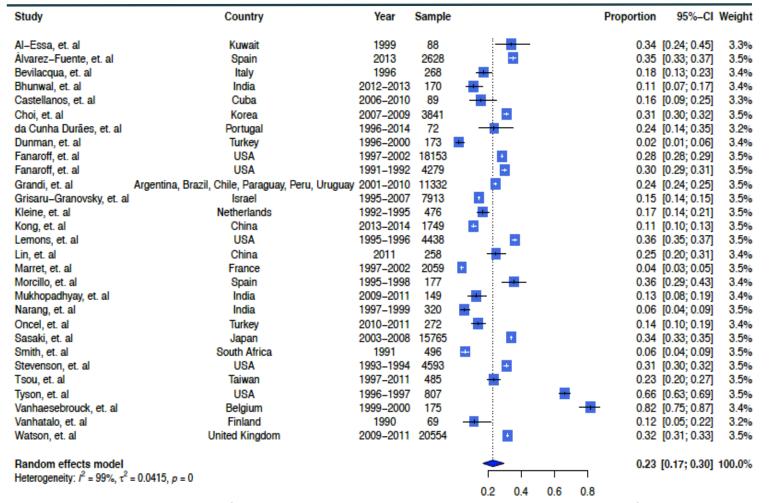


Figure 2. Pooled Prevalence for BPD28. Forest plot demonstrating pooled prevalence for BPD28 and 95% CI with a random-effects meta-analysis model. The pooled prevalence for BPD28 with 29 studies and 101,848 neonates was 23% (95% CI, 0.17-0.30).

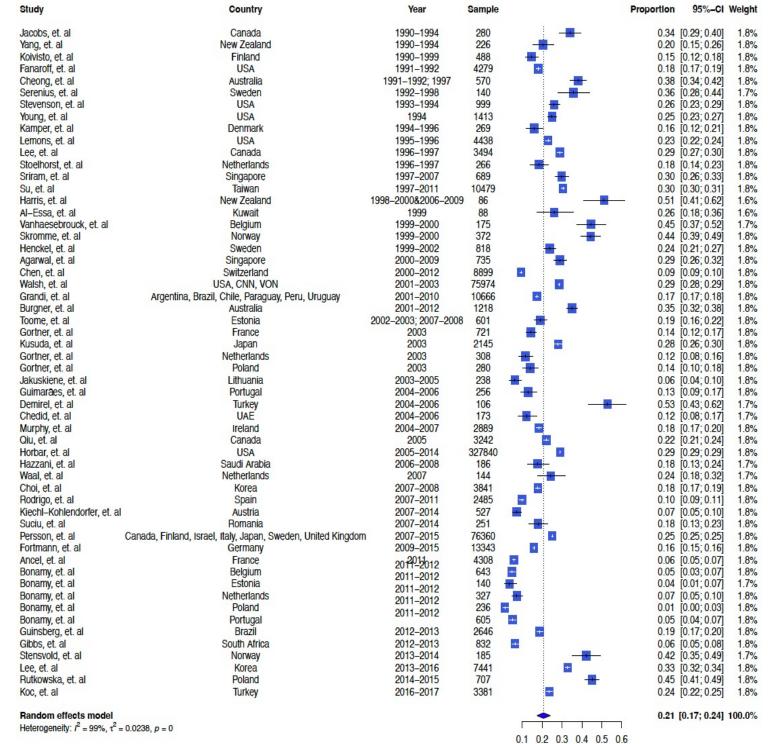


Figure 3. Pooled Prevalence for BPD36. Forest plot demonstrating pooled prevalence for BPD36 and 95% CI with a random-effects meta-analysis model. The pooled prevalence for BPD36 with 56 studies and 584,448 neonates was 21% (95% CI, 0.17-0.24).

Table 1. Global Prevalence of BPD28 and BPD36 Using Subgroup Meta-Analysis.

Variable	No. of Articles	No. of Cases	No. of Participants	Prevalence (95% CI)	 2	P Value
Subgroup Analysis for BPD28	8					
Birthweight						
501-750 grams	4	4327	6916	0.60 (0.42-0.77)	0.99	<0.01
751-1000 grams 1001-1250 grams	4 4	3263 1449	7379 7893	0.50 (0.41-0.59) 0.21 (0.16-0.28)	0.99 0.98	<0.01 <0.01
1251-1500 grams	4	570	9275	0.21 (0.16-0.28)	0.90	<0.01
<1000 grams	5	784	1481	0.40 (0.13-0.71)	0.99	<0.01
<1500 grams	6	10229	37795	0.25 (0.17-0.34)	1.00	<0.01
Overall	27	20622	70739	0.13 (0.11-0.14)	1.00	<0.01
Gestational age						
ELGA	2	160	247	0.53 (0.04-0.98)	0.99	<0.01
VLGA	10	13469	47484	0.18 (0.12-0.24)	1.00	<0.001
Overall	12	13629	47731	0.18 (0.13-0.25)	0.99	0.22
Year						
1990-1999	11	5118	16011	0.25 (0.15-0.36)	0.99	<0.01
2000-2009	3	6564	19776	0.25 (0.12-0.41)	0.97	<0.01
2010-2019	4	1219	4907	0.21 (0.11-0.32)	0.99	<0.01
Overall	18	12901	40694	0.23 (0.17-0.30)	0.99	0.83
Setting	10	198	1898	0.12 (0.07-0.18)	0.90	<0.01
Community Regional	2	145	734	0.12 (0.07-0.18)	0.90	0.01
National	16	25811	87884	0.21 (0.14-0.29)	1.00	<0.001
International	1	2768	11332	0.31 (0.22-0.41)	NA	NA
Overall	29	28922	101848	0.24 (0.23-0.25)	0.99	<0.01
Continent		20022	1010-70	0.24 (0.20 0.20)	1 0.03	-3.01
Africa	1	30	496	0.06 (0.04-0.09)	NA	NA
Asia	11	7,051	23,270	0.17 (0.11-0.25)	0.99	<0.01
Europe	10	9,068	34,391	0.26 (0.14-0.40)	1.00	<0.001
North America	6	10,005	32,359	0.34 (0.22-0.48)	0.99	<0.01
South America	1	2,768	11,332	0.24 (0.24-0.25)	NA	NA
Overall	29	28,922	101,848	0.23 (0.23-0.24)	0.99	<0.01
GDP						
1st quartile	5	99	814	0.17 (0.08-0.28)	0.93	<0.01
2nd quartile	2	1,295	8,088	0.47 (0.00-0.99)	1.00	<0.01
3rd quartile	4	1,149	3,861	0.22 (0.14-0.32)	0.98	<0.01
4th quartile Overall	8 19	18,602	62,709	0.19 (0.11-0.29)	1.00 0.99	<0.001 0.74
Subgroup Analysis for BPD36	_	21,145	75,472	0.20 (0.15-0.25)	0.99	0.74
Birthweight	1			T	1	
501-750 grams	5	1,406	3,549	0.45 (0.28-0.64)	0.99	<0.01
751-1000 grams	5	1,395	4,360	0.32 (0.28-0.36)	0.87	<0.01
1001-1250 grams	5	797	4,958	0.16 (0.14-0.18)	0.64	0.03
1251-1500 grams	5	468	5,879	0.08 (0.07-0.09)	0.22	0.28
<1000 grams	3	703	1,887	0.38 (0.30-0.47)	0.93	<0.01
<1500 grams	14	145,669	526,356	0.19 (0.15-0.23)	1.00	<0.01
Overall	37	150,438	546,989	0.12 (0.11-0.13)	0.99	<0.01
Gestational age						L
ELGA	16	401	338,497	0.06 (0.04-0.09)	0.99	<0.01
VLGA	28	519	104,930	0.03 (0.02-0.03)	0.98	<0.01
Overall Voor	44	920	443,427	0.03 (0.02-0.04)	0.98	<0.01
<u>Year</u> 1990-1999	13	4,011	16,950	0.24 (0.21-0.29)	0.95	<0.01
2000-2009	16	24,970	91,839	0.24 (0.21-0.29)	0.98	<0.01
2010-2019	12	4,532	21,451	0.20 (0.13-0.23)	1.00	<0.01
Overall	41	33,513	130,240	0.22 (0.19-0.25)	0.99	0.06
Setting		,	,			
Community	10	786	3,815	0.21 (0.13-0.31)	0.97	<0.01
Regional	9	1,419	5,429	0.24 (0.17-0.31)	0.97	<0.01
National	25	111,620	406,055	0.24 (0.20-0.29)	1.00	<0.001
International	12	43,556	169,149	0.11 (0.07-0.17)	0.99	<0.001
Overall	56	157,381	584,448	0.21 (0.18-0.24)	0.99	<0.01
Continent				1		_
Africa	1	53	832	0.06 (0.05-0.08)	NA 2.22	NA 2.21
	11 28	8,270	29,264	0.27 (0.21-0.33)	0.98	<0.01
Asia		5,585	40,621 421,959	0.16 (0.11-0.21)	0.98	<0.001
Europe		404 007		0.26 (0.23-0.29)	0.98	<0.01
Europe North America	9	121,227				∠n n₁
Europe North America Oceania	9 4	733	2,100	0.35 (0.24-0.48)	0.92	<0.01
Europe North America Oceania South America	9 4 2	733 2,358	2,100 13,312	0.35 (0.24-0.48) 0.18 (0.17-0.19)	0.92 0.61	0.11
Europe North America Oceania South America Overall	9 4	733	2,100	0.35 (0.24-0.48)	0.92	
Europe North America Oceania South America Overall GDP	9 4 2 55	733 2,358 138,226	2,100 13,312 508,088	0.35 (0.24-0.48) 0.18 (0.17-0.19) 0.17 (0.16-0.18)	0.92 0.61 0.99	0.11 <0.01
Europe North America Oceania South America Overall GDP 1st quartile	9 4 2 55	733 2,358 138,226 503	2,100 13,312 508,088 3,603	0.35 (0.24-0.48) 0.18 (0.17-0.19) 0.17 (0.16-0.18) 0.13 (0.07-0.20)	0.92 0.61 0.99	0.11 <0.01 <0.01
Europe North America Oceania South America Overall GDP 1st quartile 2nd quartile	9 4 2 55 9 7	733 2,358 138,226 503 877	2,100 13,312 508,088 3,603 5,013	0.35 (0.24-0.48) 0.18 (0.17-0.19) 0.17 (0.16-0.18) 0.13 (0.07-0.20) 0.18 (0.09-0.30)	0.92 0.61 0.99 0.97 0.98	0.11 <0.01 <0.01 <0.01
Europe North America Oceania South America Overall GDP 1st quartile	9 4 2 55	733 2,358 138,226 503	2,100 13,312 508,088 3,603	0.35 (0.24-0.48) 0.18 (0.17-0.19) 0.17 (0.16-0.18) 0.13 (0.07-0.20)	0.92 0.61 0.99	0.11 <0.01 <0.01

- A total of 82 articles and 696,881 patients were included in this review across 41 years and 44 countries.
- The highest incidences were found in those at the lowest birth weight. When stratified by setting, the highest prevalence were found at the national and regional levels across all definitions of BPD. The highest incidences based on continent were found in Oceania and North America.
- Across the definitions of BPD, there were no significant differences in prevalence across time and GDP.
- This study highlights global incidence across multiple subsets of the population and highlights the need for advancements in prediction and therapies going forward.

Acknowledgments

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