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Dana Patel

*University of Central Florida*



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THE FIGHTING JOURNEY OF THE PREMATURE BABY: A SYSTEMIC  
REVIEW OF THE DEVELOPMENTAL AND NEUROLOGICAL  
COMPLICATIONS OF THE PREMATURE BABY

BY: DANA PATEL

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## **Abstract**

Prematurity is a worldwide problem. Every year, 15 million babies are born prematurely, and 1 million of those babies die because of related complications. The surviving premature babies are struggling to hold on to their lives, and even when they do live, most of them end up having various complications to survive and get stronger. There are physical complications faced on their journey such as having underdeveloped lungs, pneumonia, obesity, sepsis, retinopathy of prematurity, respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), cerebral palsy, and motor impairment. They can also develop mental and behavioral health complications such as depression, seizures developmental delay, schizophrenia, autism spectrum disorder, psychological development disorders, behavioral problems, attention problems and attention deficit hyperactivity disorder (ADHD) later in life. The purpose of this systemic review is to understand the impact of long-term complications of premature birth on the individual life and society. We hypothesized that based on data from primary research, nearly one half of the infants will have either physical and/or cognitive/developmental health complications. We hypothesized that infants born premature have more physical complications than cognitive complications or infants born premature have more cognitive complications than physical complications. This research was carried out by finding cohort design studies through Medline, Academic Search Premier, and APA PsychINFO, where the studies were compiled from 2003 – 2020. It was concluded from this research that there were more cognitive complications than physical complications with the majority being behavioral problems.

Keywords: Prematurity, physical complications, respiratory illness, cognitive complications, mental illness, neurological impairment, cohort studies

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VLBW- Very Low Birth Weight Infant	WHO- World Health Organization
LBW- Low Birth Weight Infant	BPD- Bronchopulmonary Dysplasia
ELBW- Extremely Low Birth Weight Infant	NICU- Neonatal Intensive Care Unit
NIH- National Institute of Health	ROP- Retinopathy of Prematurity
RDS- Respiratory Distress Syndrome	IVH- Intraventricular Hemorrhage
BMI- Body Mass Index	ID- Intellectual Delays
DD- Developmental Delay	APA- American Psychological Association
ADHD- Attention Deficit Hyperactivity Disorder	ASD- Autism Spectrum Disorder
VAP- Ventilator Associated Pneumonia	NIH- National Institute of Health

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## **Introduction**

Prematurity is a worldwide problem. Every year, 15 million babies are born prematurely<sup>(1)</sup> and in 2015, it was recorded that one million of those babies died because of premature birth complications.<sup>(2)</sup> Premature births are becoming a significant issue in all parts of the world.

There are over 184 countries in which babies born premature were recorded. Out of the top ten countries with the greatest number of preterm births, the U.S. was number six.

There are certain criteria that define an infant as being premature. Prematurity is defined as “Live born infants born before 37 weeks from the first day of the last menstrual cycle”.<sup>(3)</sup> There are three different categories of prematurity: extremely low birth weight (ELBW), very low birth weight (VLBW), and low birth weight (LBW) infants. ELBW infants’ weigh less than 1,000 g, VLBW infants’ weigh between 1,000 g and 1,500 g, and LBW infants’ weigh between 1,500 g and 2,500 g.<sup>(3)</sup> If an infant is not born within both of these guidelines (i.e., gestational age, birth weight), they are not considered a premature baby.

The earlier the preterm labor occurs, the greater the health risks for the baby. The specific cause of preterm labor is often not clear. Certain risk factors might increase the chance of preterm labor. The National Institute of Health (NIH) states that there are many factors that make it a higher risk for women to go into preterm labor, especially women who have reproductive organ abnormalities or have had multiple gestations.<sup>(4)</sup> A mother who has certain medical conditions such as “urinary tract infections, sexually transmitted infections, diabetes, high blood pressure, certain vaginal infections, bleeding from the vagina, certain developmental abnormalities in the fetus, being underweight or obese before pregnancy, placenta previa, and blood clotting



problems may cause preterm labor.<sup>(4)</sup> However, preterm labor can also occur in pregnant women with no known risk factors.

There are problems that occur in preterm infants due to the preterm labor of the mom. Physical complications and cognitive complications are common in infants who were delivered preterm. Some of the physical complications that infants face due to being premature are underdeveloped lungs, pneumonia, obesity, sepsis, retinopathy of prematurity, respiratory distress syndrome, BPD, asthma, wheezing, bronchiolitis, and motor impairment. Cognitive complications include depression, anxiety, seizures, cerebral palsy, developmental delay, schizophrenia, autism spectrum disorder, psychological development disorders, behavioral problems, attention problems and ADHD. Each of these complications will be discussed.

## **Review of Literature**

### **Physical Complications**

There are many physical complications associated with premature infants. Most of the physical complications are related to the lungs.<sup>(5-16)</sup> Some of these complications include respiratory distress syndrome<sup>(5-8)</sup>, bronchopulmonary dysplasia, and pneumonia. There are other complications such as sepsis<sup>(17,18)</sup>, motor impairment<sup>(18,19)</sup>, obesity<sup>(20,21)</sup>, retinopathy of prematurity, and cerebral palsy<sup>(20,23)</sup> that also occur in preterm infants.

### **Respiratory Distress Syndrome**

Respiratory issues are the most common type of physical complication an infant born premature experiences. Respiratory distress syndrome (RDS) is one of the complications associated with immature lungs. RDS is common in premature newborns because their lungs cannot make

enough surfactant.<sup>(5)</sup> Surfactant helps the lungs fully expand so that newborns can breathe.<sup>(5)</sup> In one study that took place from 1998 – 2000 among a total of 97 infants who weighed less than 1,500 g and were born before 34 weeks of gestation, researchers found that 45/97 (46.4%) infants developed RDS, but 32/97 (33%) of the infants who developed RDS had a severe version of it.<sup>(6)</sup> In another study, researchers focused on the births of 19,334 infants who were born in the US between 2002 and 2008. They found that 3,700 infants were born at 34 weeks, 5,477 infants born at 35 weeks, and 10,157 infants born at 36 weeks.<sup>(7)</sup> They determined that 390/3700 (10.5%), 329/5,477 (6.0%), and 283/10,157 (2.7%) of infants who were born at 34, 35 and 36 weeks respectively developed RDS.<sup>(7)</sup> Both of these studies showed infants born between 34 and 36 weeks, developed RDS due to being premature.

### Bronchopulmonary Dysplasia

Bronchopulmonary dysplasia (BPD) is another complication due to premature infants having underdeveloped lungs. BPD is a breathing disorder where lungs do not develop normally and become irritated.<sup>(8)</sup> Research was conducted in Poland between November 2014 and December 2015 among 707 premature infants where researchers found that 276/707 infants had mild to moderate BPD and 43/707 infants had severe BPD.<sup>(9)</sup>

### Pneumonia

Pneumonia is an infection that occurs in either one or both of the lungs. It can cause the air sacs to fill up with fluid and can range for mild to severe based on different factors.<sup>(10)</sup> At the St. Louis Children's Hospital in Missouri from 2000 – 20001, a study was conducted for infants weighing  $\leq 2000$  g and born  $< 28$  weeks, in which a total of 229 infants were observed. Researchers found that 211 patients required intubation for greater than 48 hours. There were

24/229 (10.5%) infants who had 26 episodes of ventilator associated pneumonia (VAP) and 2/229 (<1%) infants had 2 episodes of VAP.<sup>(11)</sup> In the same study in which researchers examined RDS in infants born premature, they also investigated pneumonia in those 19,334 infants who were born in the United States between 2002 and 2008. There were 3,700 infants born at 34 weeks, 5,477 infants born at 35 weeks, and 10,157 infants born at 36 weeks.<sup>(7)</sup> In this study, researchers found that among infants born at 34 weeks, 35 weeks, and 36 weeks; 55 infants (1.48%), 65 (1.18%) infants, and 65 infants developed pneumonia respectively.<sup>(7)</sup>

### Other Physical Complications

Complications related to immature lungs are not the only physical complications that preterm infants experience. Some other complications include sepsis, motor impairment, obesity, retinopathy of prematurity, and cerebral palsy. Sepsis is the body's extreme response to an infection and can lead to tissue damage, organ failure, and death.<sup>(12)</sup> In one study in China, 1,133 infants born before 34 weeks and weighed between 750 g and 2,000 g who were admitted to the NICU were observed. The goal of this study was to find the risk factors associated with late-onset sepsis. Researchers found that there were 418/1,133 (36.9%) infants who had more than one episode of late onset sepsis, and two and three episodes of sepsis in 64 and 1 patient, respectively.<sup>(13)</sup>

Motor impairment is another physical complication that can occur in infants born premature. In Australia, from 1991 – 2005, 191 infants who were born ELBW were enrolled in this study at age 8 years to compare rates of motor impairment. Researchers found that 71/191 (37.2%) of the infants born premature had a motor impairment when they were 8 years old. It was concluded that motor impairment was more likely to occur in children born extremely preterm.<sup>(14)</sup>

Obesity is a common issue among infants who were born premature. The normal body mass index (BMI) for a person is between 18.5-24.9, but when an individual is obese they have a BMI of 30 and higher.<sup>(15)</sup> In one study among 388 children who were extremely preterm infants (born at <28 weeks of gestation), researchers concluded at the end of the study that there were 85/388 infants who were obese.<sup>(16)</sup>

Retinopathy of prematurity (ROP) is another complication that can occur due to infants being born premature. It is a potentially blinding eye disorder which occurs when abnormal blood vessels grow and spread throughout the retina.<sup>(17)</sup> In one study that was carried out in Turkey researchers observed 138 preterm infants, consisting of 78 males and 60 females. These infants were followed up in an outpatient premature clinic at 18 – 24 months. Hearing, vision, neurological, and developmental tests were performed by the researchers. Out of these 138 infants, the total number of infants who developed retinopathy of prematurity were 50/138 (36.2%).<sup>(18)</sup>

Cerebral palsy (CP) is another physical complication often attributed to infants being premature. CP affects a person's ability to move and maintain balance and posture.<sup>(19)</sup> It can be caused by abnormal brain development or any damage to the developing brain.<sup>(19)</sup> There were three studies in which researchers investigated infants who weighed between 800 g – 2,800 g. These studies took place in Denmark, California, and Norway, Denmark researchers had 39,420 infants born between 1997 and 2007 as well as between 32 and 36 weeks.<sup>(20)</sup> Researchers followed participants until they were diagnosed with CP. It was found that infants had an increased risk of developing CP with RDS than those without RDS. There were 2,255/39,420 (5.7%) infants who developed cerebral palsy when they had RDS.<sup>(20)</sup> Researchers in California between 2004 and

2005, wanted to find the risk of developing cerebral palsy in 10,262 infants born between 30-36 weeks and weighing between 1,500 g and 2,500 g.<sup>(21)</sup> They concluded that 357/10,262 (3.5%) infants had cerebral palsy.<sup>(25)</sup> Finally, another study which took place in Norway from 2010 – 2013 had 21,715 males and 17,750 females weighing between 855 and 2,785 g.<sup>(22)</sup> These infants were followed until adulthood and their medical disabilities were documented. It was found that 371/39465 (<1%) premature infants developed cerebral palsy.<sup>(22)</sup>

## **Cognitive Complications**

Infants born prematurely can also develop cognitive complications such as learning disabilities, behavioral problems, and even mental health disorders. These issues can begin at very young ages but can continue throughout their lifetime. Premature infants can also have an increased risk for developing intellectual problems, cognitive and language delays, psychiatric disorders, and emotional/behavioral problems. Cognitive problems like these are very common in premature infants and they can have a significant impact on their lives.

### **Intellectual Problems**

Infants who are born premature often have intellectual problems. One Finland study included infants born between 1990 – 2008 to establish whether there is an increased prevalence in intellectual disability (ID) in infants born moderately preterm and late preterm infants. This study defined ID as significant limitations in both intellectual and adaptive functioning and having an  $IQ \leq 70$ .<sup>(23)</sup> In this study, there were 53,053 participants which 6,329 infants born <32 weeks (very preterm), 6,796 infants born between 32 and 33 weeks (moderately preterm), and 39,928 born between 34 and 36 weeks (late preterm).<sup>(23)</sup> In total, 3,814/53,053 infants had intellectual disability.

Intellectual disability is not the only development problems that infants born premature can experience. They might develop problems in social-emotional skills, approaches to learning, communication skills, and cognitive skills. These are often associated with the five domains of development: cognitive, communication, motor, social- emotional and adaptive behavior. In one study which took place in Australia between July 2001 and May 2004 exactly those five domains were used to evaluate developmental performance among 195 infants who weighed <1250 g and were born <30 weeks.<sup>(24)</sup> After collecting the data from these five domains, it was found that 86/195 of very preterm infants were vulnerable in more than one of the categories of school readiness.<sup>(24)</sup> Another study which took place in Germany between 1985 and 1986, researchers examined the IQ in adults that were born <32 weeks and weighed <1500 g.<sup>(25)</sup> The total individuals who participated in this study was 217, in which 114 were males and 103 were females. There were six subtests used to assess ability: executive functioning, the Stroop test, visual search and attention test, Regensburg word fluency test, and the rapid automatized naming test. From these IQ tests, it was shown that 62/217 (28.6%) of the adults exhibited cognitive problems.<sup>(25)</sup> Another study took place in Europe between 2003 and 2006 to evaluate cognitive abilities in preterm babies. A total of 161 infants were born between 27 weeks and 31 weeks and weighed between 808.96 g – 1,643 g, with 88 males and 73 females.<sup>(26)</sup> The infants were followed up when they reached five years of age where an interview was done with the mothers and caregivers, physical and neurological examination was completed, and a cognitive development assessment administered using the Wechsler Preschool and Primary Scales of Intelligence. Six of the tests in the Wechsler Preschool and Primary Scales of Intelligence (WPPSI-III) were used for this study: block design, information, metric reasoning, vocabulary, symbol search, and coding.<sup>(26)</sup> From these, the child's verbal IQ score, performance IQ score,

processing speed quotient, and full IQ were calculated. After all the tests were done, it was found that 55/161 (34.1%) infants had reduced processing speed.<sup>(26)</sup>

### Neurodevelopmental Delays

Neurodevelopmental delays are another complication often present due to infants being premature. A study took place in Ohio from 2001 – 2003 involving 124 infants weighing between 700 g and 850 g and born <28 weeks of gestation.<sup>(27)</sup> Out of the 124 infants, 55 of the participants were males and 69 were females.<sup>(27)</sup> This study measured four different outcomes: spatial relations, spelling, visual matching, and letter-word identification. There were 84/124 (67.7%) infants who had spatial relation problems, 76/124 (61.3%) infants which had spelling problems, 79/124 (63.7%) infants which had visual matching problems, and 97/124 (78.2%) had letter-word identification problems.<sup>(27)</sup>

Some other neurodevelopmental impairments are seizures and developmental delay. One study that took place in California from 2004 – 2005 consisted of 141,321 premature infants born between 30 – 36 weeks and weighed between 1,500 g and 2,500 g.<sup>(21)</sup> Researchers in this study wanted to find the risks of developmental delay (DD) and seizures disorders in infants born premature. These infants were diagnosed with neurological disorders by using ICD-9 CM (International Classification of Diseases, Ninth Revision, Clinical Modification) codes.<sup>(21)</sup> After the infants were diagnosed using this system, they were identified with developmental delay and seizures. Seizures are bursts of uncontrolled electrical activity between brain cells and causes temporary abnormalities in muscle tone or movements, behaviors, sensations, or states of awareness.<sup>(28)</sup> This study had 1,340/141,321 (<1%) infants who had DD and 179/141,321 (<1%) had seizures due to being premature.<sup>(21)</sup>

Another study consisted of 120 participants which took place between 2010 – 2012 for infants born  $\leq 32$  weeks and weighed between 590 g – 2,000 g. Out of the 120 participants, there were 59 males & 61 females.<sup>(29)</sup> There were neurological and developmental assessments used to find the cognitive, language, and motor delay in infants born premature. In this study it was found that 90/120 (75%) infants had cognitive delays, 90/120 (75%) had language delays, and 88/120 had motor delays.<sup>(29)</sup> In another study, researchers investigated the risk of neurodevelopmental impairment among preterm infants. This study took place in Italy with infants born between 1990-2004 and consisted of 754 infants: 394 males and 360 females.<sup>(30)</sup> They were born between 24 and 33 weeks and weighed between 1,400 g – 1,500 g. Two tests were used to examine the neurological and cognitive function of the newborn infants: Ariel-Tison and Grenier for the neurological evaluation and The Bayley Scales of Infant Development for the cognitive evaluation. There were three categories for the follow ups at 3, 6, 12, and 24 months in which impairment was shown: unimpaired, mild impairment, or moderate to severe impairment.<sup>(30)</sup> It was concluded that 110/754 (14.6%) infants had mild impairment and 102/754 (13.5%) had moderate-to-severe impairment.<sup>(30)</sup> One study that took place in France in 1997 had 1,051 premature infants born between 24 weeks and 32 weeks of gestation.<sup>(31)</sup> Researchers aimed to evaluate the effect of fetal sex on the risk of neurodevelopmental impairment in infants born preterm.<sup>(31)</sup> There were 596 males and 505 females in this study. Researchers found that 140/1,101 (12.7%) infants had mild or moderate-to-severe impairment.<sup>(31)</sup>

Attention skills are another cognitive complication of infants born premature. This study took place in the Netherlands in 2010 – 2011 and consisted of 88 infants born between 32 and 36 weeks.<sup>(32)</sup> There were 51 males and 37 females that weighed between 1,420 g and 3,850 g. It was found that 55/88 (62.5%) of the moderately preterm infants had attention problems.<sup>(32)</sup>



Another study took place in New South Wales between 2007-2012 with 1,514 infants to find the neurodevelopmental outcomes in infants born between 23 and 28 weeks.<sup>(33)</sup> There were 720 males and 794 females. It was found that 130/1514 infants (8.6%) had mild developmental delay and 85/1514 (5.6%) had moderate-severe developmental delay.<sup>(33)</sup>

### Psychiatric disorders

Psychiatric disorders are other complications that premature infants may face. One study had a total of 40,826 infants born between 23 and 36 weeks in Norway from 1967 and then were following through 2003.<sup>(22)</sup> This study showed the number of infants who developed schizophrenia, autism spectrum disorder (ASD), and disorders of psychological development, behavior, and emotion for infants born from 23 weeks to 36 weeks. Schizophrenia is a mental illness that interferes with a person's ability to thinking clearly, manage emotions, and make decisions and can occur at any age.<sup>(34)</sup> ASD is a developmental condition where there are persistent challenges in social interaction, speech and nonverbal communication, and restricted/repetitive behaviors.<sup>(35)</sup> There were 80/40,826 (<1%) infants who developed schizophrenia, 22/40,826 (<1%) infants that developed ASD, and 152/40,826 which developed disorders of psychological development, behavior, and emotion.<sup>(22)</sup>

### Behavioral Problems

Infants born premature may also have problems with behavior. There were two studies conducted in which researchers wanted to find the prevalence of behavioral problems in very preterm children when they are three years old. One study took place in France and consisted of 1,228 infants in which 637 were males and 565 were females born between 24 weeks and 36 weeks.<sup>(36)</sup> The data were collected by following up the preterm infants and sending a

questionnaire to their parents. The categories that were looked at were hyperactivity, conduct problems, emotional problems, peer problems, and peer social behavior. Hyperactivity was found in 1205/1,228 (98%) of the participants.<sup>(36)</sup> Conduct disorder is a behavior disorder where the child has antisocial behavior and may even disregard basic social standards and rules.<sup>(37)</sup> There were 1,207/1,228 infants who were found to have conduct disorder, 1,207/1,228 were found to have emotional symptoms, and 1,205/1,228 were found to have prosocial behavior.<sup>(36)</sup>

### **Purpose of Present Study**

The purpose of this study is to find which type of complications, physical or cognitive, are more common among babies born premature. There are some systemic review studies that showed the specific complications such as periodontal disease linked to pre-term, low-birth-weight infants<sup>(38)</sup> or Circulating neutrophil concentration and respiratory distress in premature infants<sup>(39)</sup>. Unlike these two studies, this systemic review evaluated the overall complications that occurred in premature infants to assess which type of complications were the most common. Preterm birth has high medical costs especially during the neonatal period. In one article, it was found that premature infants born less than 2,500 grams had an average medical bill of \$76, 153, premature infants born less than 2,500 grams had an average medical bill of \$114, 427, and infants born less than 24 weeks had an average medical bill of \$603,778.<sup>(40)</sup> However, “the long-term medical, educational, productivity, and productivity costs borne by the individual, as well as by the family and society, are not well understood”.<sup>(40)</sup> This study will help to understand the impact of long-term complications of premature birth on the individual life and society. Specifically, there are many families that experience adverse impacts when having a premature baby, such as healthcare costs, educational issues, and productivity costs. The main purpose of this study is to

examine whether infants born premature have more physical complications or more cognitive complications.

### **Research Aim and Hypotheses**

**Research Question:** For babies born premature, what type of complications is more common: physical or cognitive?

**Hypothesis 1:** For babies born premature, physical complications are more common than cognitive complications.

**Hypothesis 2:** For babies born premature, cognitive complications are more common than physical complications

### **Methods**

#### **Search Procedure**

In this study, prematurity is defined as “Live born infants delivered before 37 weeks from the first day of the last menstrual period” by the World Health Organization (WHO).<sup>(1)</sup> According to WHO, there are three different categories of prematurity”: ELBW infants who weigh less than 1,000 g, VLBW infants who weigh between 1,000 g and 1,500 g, and LBW infants who weight between 1,500 and 2,500 g. An infant who is not born within the gestational age and birthweight guidelines are not considered premature babies.

Three different databases were used to conduct this research: APA PsychINFO, Academic Search Premier, and Medline. For the search strategy, specific keywords relating to prematurity were used to find the articles. The keywords that were entered into the search engine were:

premature birth, short term complications of prematurity, long-term complications of prematurity, physical complications, respiratory illness, cognitive complications, mental issues, neurological impairment, and cohort studies. The search included English and non-English language articles where the non-English articles were translated to English. The inclusion criteria for this study were cohort studies, premature infants born before 37 weeks, infants who weighed less than 2,500 g, and experienced either physical complications or, neurodevelopmental complications, articles published between 2003 – 2020, peer reviewed articles, and studies that found a correlation with premature babies and complications. The excluding criteria in this study were studies that were not cohort, infants born after 37 weeks, infants who weighed  $\geq 2,500$  g, articles published before 2003 and after 2020, non-peer reviewed articles, and studies that did not find a correlation with premature babies and complications. When entering study keywords into the search engine, there were a total of 4,629 articles. Articles were selected from this list.

DistillerSR removed all duplicate articles and then all articles from the primary search were reduced further using the above criteria. There were three levels utilized with in the software. Two independent reviewers completed the article screening using these three levels within DistillerSR. Level 1 was the title screening where if the title had the word premature infant it was included and moved to Level 2 for the abstract screening. The abstracts were read through and made sure that the study was met the criteria. If the abstract answered our inclusion criteria, it was moved to Level 3 which was the full text screening. In DistillerSR, the first level had a total of 108 articles, the second level had a total of 75 articles, and the third level had a total of 49 articles. From further analysis of the 49 articles, due to the articles not directly correlated with preterm birth, only 22 articles were used in the systemic review. (see Figure 1). One independent reviewer was added to increase reliability of screening. Any discrepancy and disagreements

were resolved with a discussion between the two reviewers to reach inter-observer agreement (IOA) of 100% and 0% disagreement across all three levels.

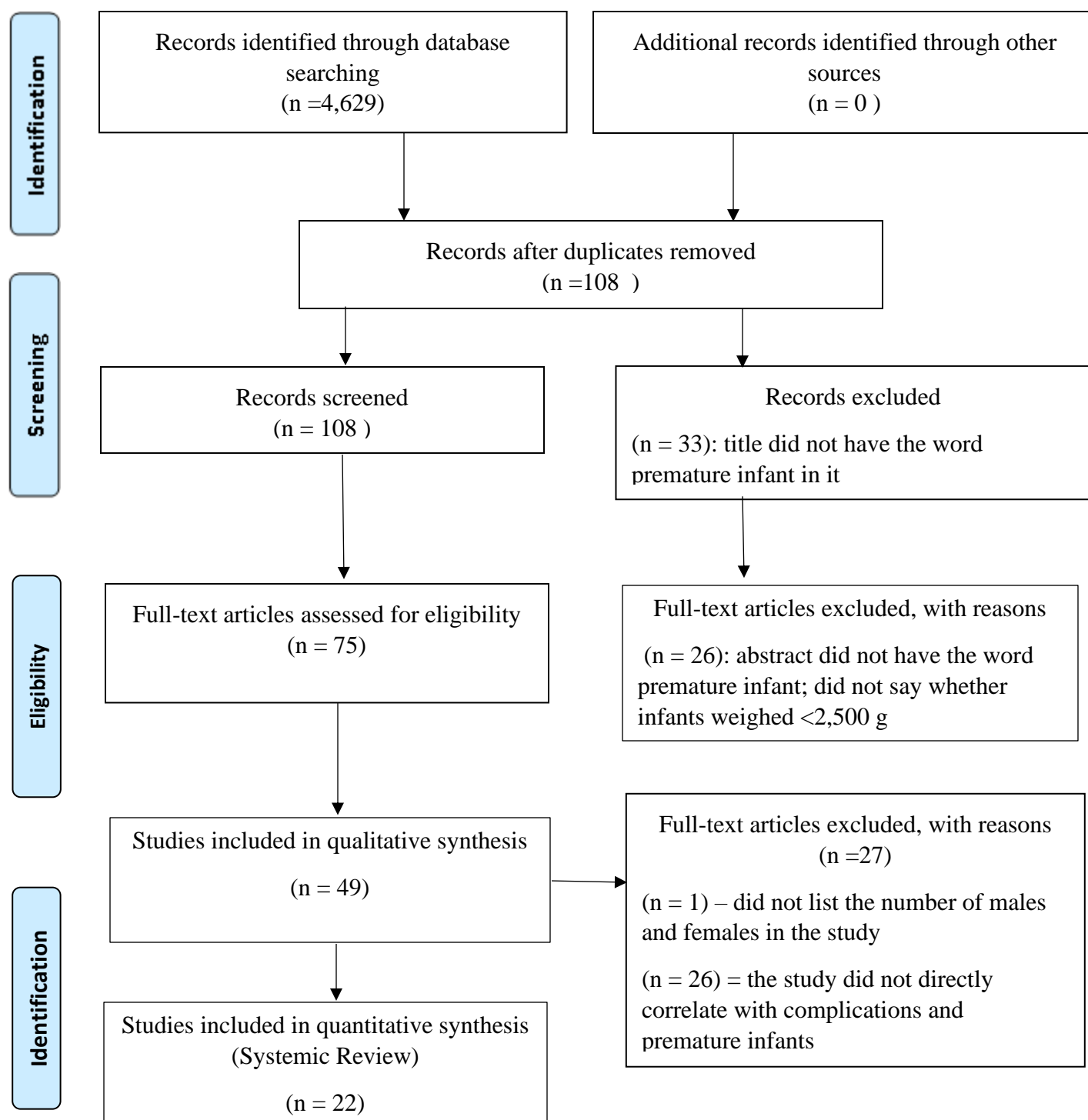


Figure 1: PRISMA Diagram of Studies (86 studies were excluded for not meeting inclusion criteria).

### Coding Procedures

Demographic data was extracted (i.e., the number and type of participants) from each of the final 22 articles by two independent reviewers. For each article, the following information was extracted: the authors' name(s), year of publication, the place where the study took place, number of males and females, the weeks of gestation, the infants' weight when they were born, the complications that occurred, whether neurological or physical, and the number of participants.

### Data Analysis

In order to explain the basic information and relationship between prematurity and different types of complications a graphical method of descriptive analysis was used. In an excel sheet, articles were sorted by the inclusion of physical complications and cognitive complications. Under each category there were the following subcategories: name of the article, the year the study took place, the weeks of gestation, the complications, the weight of the infant, where the study took place, percentage of complications, the number of participants, number of males and females in the study. Then, the data from the articles were analyzed based on how many of the total participants developed complications: type, number and percentage. The data were used to respond to the proposed research questions.

## **Results**

Based on the 22 articles that were used in this study, eleven articles included infants with physical complications and eleven with cognitive complications. For each category of complications, we examined the number of participants, the weeks of gestation/weight of the

infant, where the study took place, type of complications, the number of males and females in the study, what years the study took place, and the number of participants out of the total that had the complication. After the number of participants that had complications were calculated out of the total, the percentage was also calculated.

### Location of Studies

Out of the 22 studies six were conducted in the United States (27.3%), two in Australia (9.1%), one in South America (4.5%), ten in Europe (45.5%), and three in Asia (13.6%) (see Figure 2). There were 76,489 infants throughout the 22 studies that were males and 80,806 infants that were females (see Figure 3).

### Categories with Total Participants

Based on the total number of participants (169,805), there were more infants with cognitive complications 8,222/58,441 (74%) than physical complications, 5,249/111,364 (26%) (see Figure 4). In this study, the physical complications were subcategorized to six groups including: respiratory problems (RDS, BPD, and pneumonia), cerebral palsy, obesity, sepsis, motor impairment and retinopathy of prematurity. The cognitive complications were also subcategorized to four groups including: intellectual delay, neurological impairment, psychological disorders and behavioral problems to better determine the complications related to premature infant.



## **Physical Complications**

### **Respiratory Problems**

In this category there were 1,047/5,249 (19.95%) infants who developed RDS. BPD is another common issue that have to do with respiratory problems. It was found that 319/5,249 (6.08%) infants had some kind of BPD with 276/5,249 (5.26%) infants having mild to moderate BPD and 43/5,249 (.82%) infants had severe BPD. Additionally, there were 211/5,249 (4.02%) infants who had pneumonia. Overall, there were 1,577/5,249 (30.04%) infants who had respiratory problems.

### **Sepsis**

There was one study that evaluated sepsis in infants born before 34 weeks of gestation. Researchers found that 483/5,249 (9.2%) had episodes of sepsis.

### **Motor Impairment**

Motor impairment is a type of physical disability which includes muscle fatigue, weakness, spasticity, contracture, sensational impairment, and imbalance. Researchers found that a total of 71/5,249 (1.35%) infants had a motor impairment due to being premature.

### **Obesity**

There was a total of 85/5,249 (1.62%) infants that were either overweight or obese with 39/5,249 (.70%) being obese in their childhood.

### **Retinopathy of Prematurity**

One study evaluated ROP where it was found that 50/5,249 (.95%) those infants developed ROP.

### Cerebral Palsy

There were three studies that researched cerebral palsy and how many infants developed cerebral palsy due to being premature. It was found that 2,983/5,249 (56.82%) of those infants developed cerebral palsy due to being premature.

## **Cognitive Complications**

### Intellectual Delay

In this category, there were a total of three studies that examined intellectual delay (ID). It was found that premature infants where 4,017/8,222 (5.16%) had intellectual delays.

### Neurodevelopmental Delay

In this category, it was found that there were 2,745/8,222 (29.70%) who developed neurodevelopmental impairment due to being premature.

### Psychiatric Disorders

Psychiatric disorders are another problem with infants born premature. One study showed the number of infants who developed schizophrenia, autism spectrum disorder, and disorders of psychological development. It was found that 80/8,822 (1.03%) infants developed schizophrenia, 22/8,222 (.28%) infants developed autism spectrum, and 152/8,222 (1.95%) developed disorders of psychological development, behavior, and emotion due to being premature.

Behavioral Problems

Infants born premature may also have behavioral problems. There was a total of two studies that talked about behavioral problems. Overall, it was found that an average of 1206/8,222 (14.67%) infants developed some type of behavioral problem.

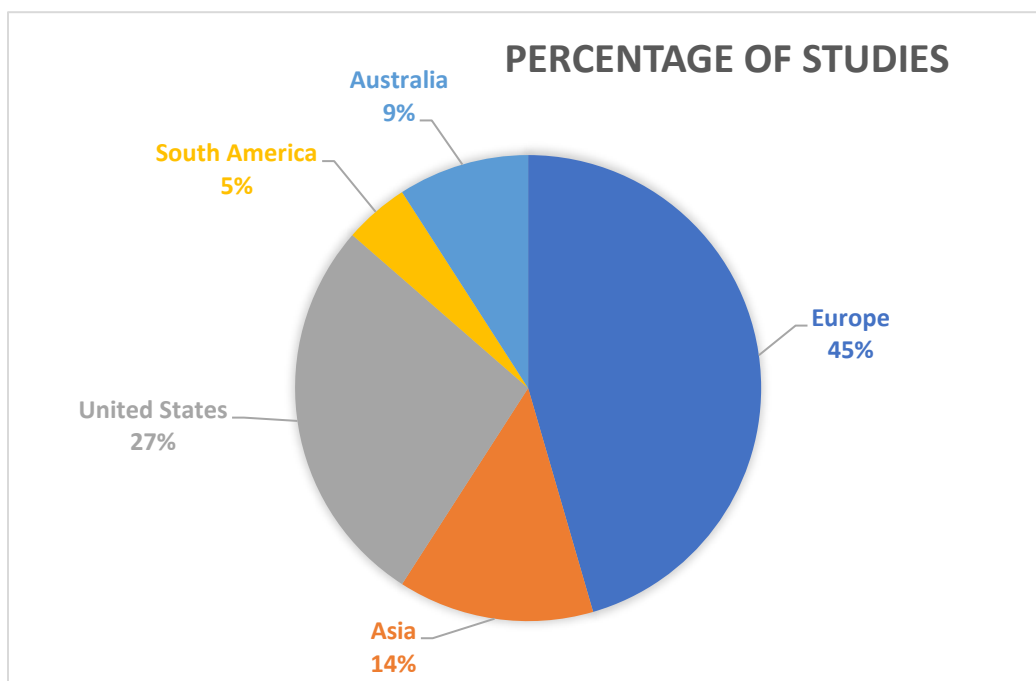


Figure 2: Locations of each of the 22 studies

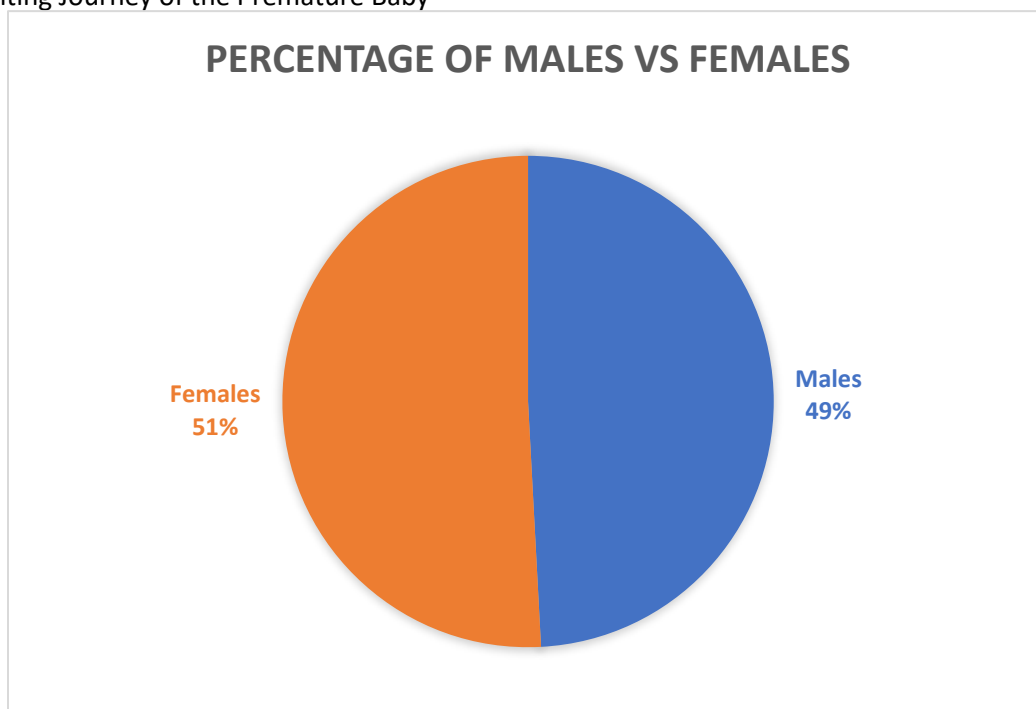


Figure 3: Percentage of males and females across reviewed studies (n = 22)

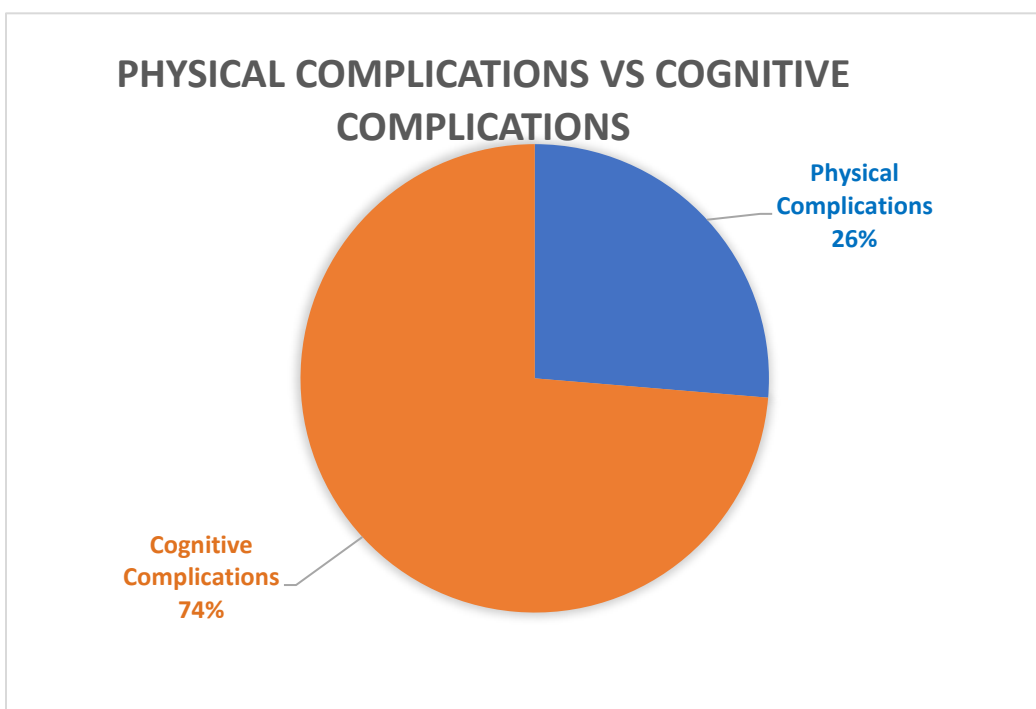


Figure 4: Percentage of physical and cognitive complications across reviewed studies (n = 22)

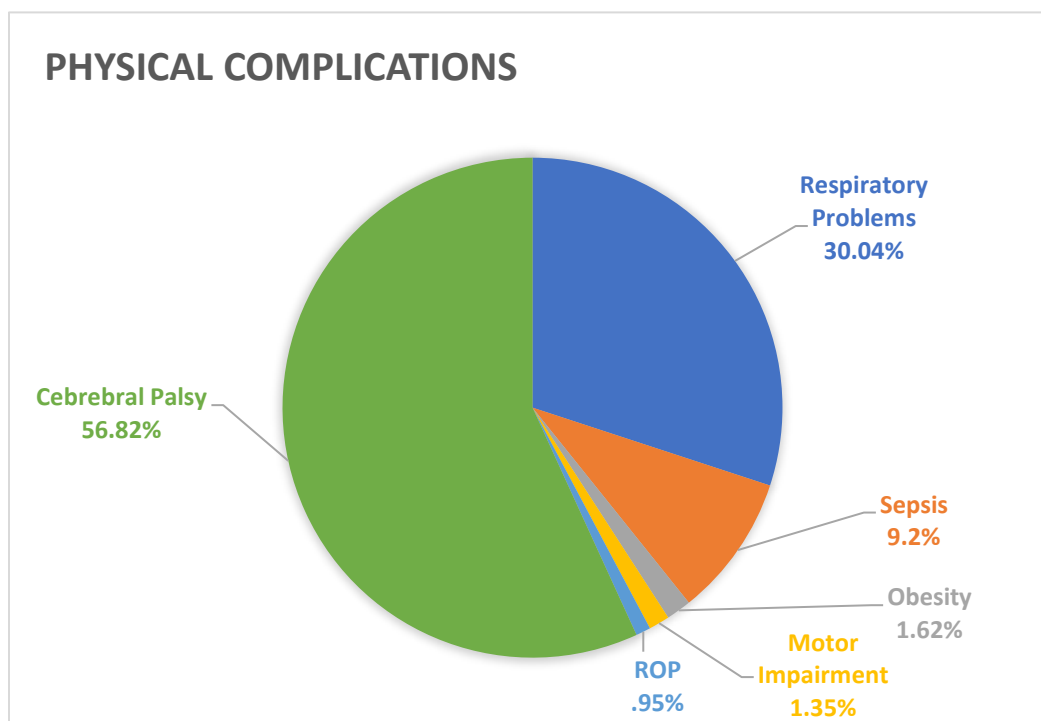


Figure 5: Breakdown of Physical Complications

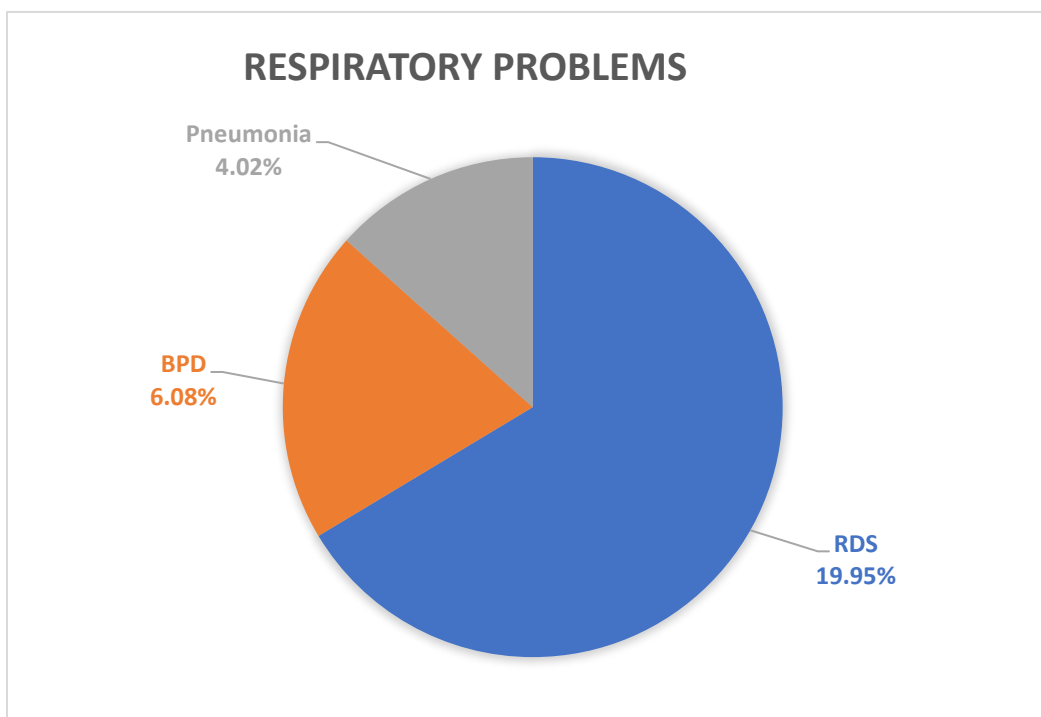


Figure 6: Breakdown of Respiratory Problems in the Physical Complication's Category

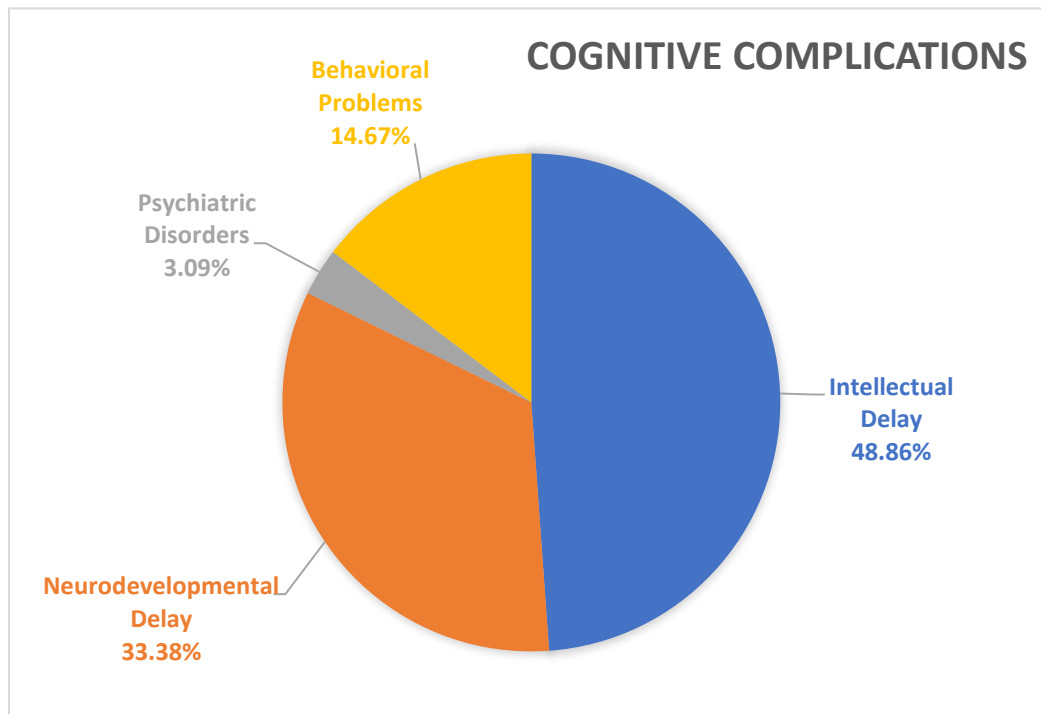


Figure 7: Breakdown of Cognitive Complications

## **Discussion**

Premature births are a worldwide problem with many infants facing both physical and cognitive complications. The aim of this study was to find which complication is more common among premature infants meeting the specified criteria: physical or cognitive.

In this study, we categorized physical complications in six subgroups. We expected that out of the six total categories, there would be more respiratory problems due to low amounts of surfactant in premature babies which causes their lungs to not be fully developed, therefore having respiratory problems in the future.<sup>(42)</sup> However, it was found that due to the higher number of participants, cerebral palsy was the most common physical complication and respiratory problems were the second most common. In the category of respiratory

complications, we had RDS, BPD, and pneumonia where we expected that RDS was more common because the lungs don't make enough surfactant which cause a majority of the respiratory issues.<sup>(43)</sup> The other physical complication categories were obesity, sepsis, motor impairment, retinopathy of prematurity, and cerebral palsy. The second most common in the physical complication's category was cerebral palsy due to the increased number of participants in that category. There were three studies that had similarities with the previous studies of BPD and severe retinopathy of prematurity (ROP). Schmidt, et al concluded that infants that development of BPD, serious brain injury, and severe ROP in premature babies predict the risk of disability or death where  $p < .001$ .<sup>(44)</sup> Vasylyeva TL, et al showed the impact of obesity due to being premature and found that they had a higher risk of gaining excessive weight in childhood with  $p = 0.001$ .<sup>(45)</sup> Vaidya B, et al showed that premature birth manifested in nonautoimmune hypothyroidism due to activating TSHR germline mutations with  $p = 0.004$ .<sup>(46)</sup> Through these three studies as well as a study on BPD, researchers found that through their studies, they did find a correlation between complications and prematurity.

In this study, we categorized cognitive complications in four groups: intellectual delays, neurodevelopmental delays, psychiatric disorders and behavioral problems. Of these four groups of cognitive complications, there were more intellectual problems. There were a total of ten studies out twenty-two studies that talked about intellectual problems such as low IQ, cognitive impairment, social-emotional skills, approaches to learning, communication skills, and cognitive skills. Additionally, other studies researched neurodevelopmental delays such as problems in spatial relations, spelling, visual matching, letter-word identification, cognitive, language, motor delay, and attention skills. One study concluded that infants born premature had a higher chance of having reading, math, or reading and math limitation.<sup>(47)</sup> Leviton A, et al showed that there are

limitations in school which correlated with cognitive complication studies. These studies reveal the different cognitive problems that infants face due to being premature. Overall, through researching these articles, there was a higher percentage of complications in the cognitive complications' category than the physical complications category.

Through the primary research, we found that infants born premature have more cognitive complications than physical complications. For the cognitive complications' category, there were more intellectual problems than intellectual problems, neurodevelopmental problems, and psychiatric disorders. In the physical complications' category, there were more complications with cerebral palsy with the respiratory complications being the second highest.

Through this systemic review, we aimed to see that physical complications were more common than cognitive complications. However, the opposite was found. We found that there were more cognitive complications than physical complications with the majority of them intellectual problems. We did not expect to see that there would be more cognitive complications than physical complications. It is commonly expected to see more physical complications, especially RDS as an earliest complication among premature infants.<sup>(3)</sup>

## **Conclusion**

This study is unique in that we reviewed both physical and cognitive complications in one systemic review. Through primary research we found that there are more cognitive complications than physical complications faced in infants born premature. Furthermore, it was found that in the cognitive complication's category, out of the four subcategories, infants born premature experienced more behavioral problems.



This research can help in future research and see how these complications affect the community as a whole by learning about the complications. It can be used to show the most common complications that are faced and research more into each complication and its effects on the community.

### **Limitations**

There were a few limitations to this study. One limitation was that this research only used 22 articles and due to this, there were a lower number of participants in the study. In total, there were only 169,919 participants. Another limitation was that there were only cohort studies used. In future, it will be better to include all different types of studies, and not just cohort studies to have a more variety of studies instead of only one study type. Additionally, the studies included in this review did not breakdown the gender of which participants developed each complication. For future research, it would be better to breakdown not only the complications that are faced by infants, physical and cognitive but what gender infants developed each complication due to being premature.

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