Structure and risk of Internalizing Problems in preschool boys and girls in São Paulo, Brazil

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Abstract

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(1) Problem: Research on internalizing problems in young children is scarce despite evidence that children can have problematic internalizing symptoms as early as preschool years[1-3]. In preschoolers, it is difficult to observe internalizing problems directly. While they are not overtly socially disruptive behaviors[4], they have negative consequences in their daily lives, can continue in adolescence, and potentially develop into disorders in later years [5-7]. Studying internalizing problems in preschoolers is of particular importance in Low- and Middle- Income Countries (LIMC) since there may be a higher prevalence of common risk factors (such as parental psychopathology, violence, and neglect) than in High-Income Countries. According to the World Health Organization, in 2015, Brazil (a LMIC) ranked first in the past-year prevalence of anxiety (9.3%) and fifth in the prevalence of depression (5.8%) [8,9] in people aged 15 years or older. Preschoolers in São Paulo, Brazil, have an estimated six-month prevalence of internalizing problems of 25.4%. There are few estimates in other regions of Brazil, partly due to the lack of validated scales to measure them. In addition, it is unknown if the disparate rates by sex (females have at least twice the rates of males) seen in adolescence and adulthood could be detected at an early age. This dissertation's primary goal is to advance our understanding of internalizing problems in preschoolers in Brazil, a LMIC that is highly affected by psychopathology and associated disability.

(2) Methods: First, a systematic literature review on the topic in LMIC was conducted. Second, data from the Preschool Mental Health Survey (the PreK Survey), with a representative sample (n=1,292) of preschoolers aged 4 to 5 years old and their caregivers in the city of Embu das Artes, São Paulo, was used to: (a) do Confirmatory Factor Analysis (CFA) of the internalizing section of a worldwide known assessment tool for problem behaviors in preschoolers (the Child Behavioral Checklist CBCL 1.5-5); and (b) conduct multigroup CFA to examine differences by sex in the structure of internalizing problems. Finally, Generalized Linear Models for complex data were used to assess the risk of internalizing syndromes by parental depression, severe physical or verbal violence, and low-quality time with parents differentially by sex of the preschoolers.

(3) Conclusions: From the literature review, a scarcity of research on internalizing problems of preschoolers was found in LMIC. Hence, (a) only a few risk factors, mainly parental psychopathology, have been explored in most LMIC; and (b) the large majority of studies in LMIC in the Americas use the CBCL 1.5-5 or other scales not validated for their study population. From the multigroup CFA, it was concluded that (a) the construct of internalizing problems in the CBCL 1.5-5 is valid in preschool boys and girls in São Paulo, Brazil, and in similar contexts, supporting previous and future studies on the topic; and (b) the main syndromes of internalization are "Anxiety/Depression" and "Emotionally Reactive." From the assessment of risk, it was concluded that (a) the main risk factor for internalizing problems in preschoolers in Brazil is parental depression; (b) externalizing problems are highly correlated with internalizing problems and are the main source of confounding; (c) there were no significant differences by sex in the prevalence of risky exposures, but they were all significantly associated with internalizing problems; (d) there were significant differences by sex in the mean scores of internalizing syndromes, and in the associations of risky exposures and internalizing problems, highlighting the need of a differential approach to primary prevention and treatment in preschool boys and girls.

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Dedication

A Jose Luis y a mis hijitos Martín y Andrés, mis grandes amores.

Chapter 1: Introduction

1.1 Background

The high prevalence of internalizing disorders worldwide (an estimated 322 million people suffer from depression and an estimated 264 million people suffer from anxiety[9]) is concerning due to the increased risk of mortality and the significant personal and financial burden caused[10-13]. In addition, internalizing disorders by themselves are among the leading causes of disability and suicide[9,14]. Moreover, internalizing disorders negatively affect several chronic diseases (gastric, respiratory, and cardiac problems, cancer, diabetes, among others [15-22]), leading to worsening of symptoms and adverse treatment outcomes.

Due to the adverse effects of internalizing disorders, there have been several studies on mechanisms of development and treatment approaches, with most of the research focused on adolescents or adults[23-27]. Research on internalizing problems in young children is scarce, despite evidence that children can have clinically significant internalizing (problematic) symptoms as early as preschool years[1-3]. These problems can continue in adolescence and can potentially develop into disorders in later years [5-7]. Internalizing problems are less understood than other psychopathology areas since they are difficult to observe directly (they have to be reported by a third person, such as a parent/caregiver), and they are not overtly socially disruptive behaviors[4].

Most of the studies on preschoolers' mental health focus on externalizing problems (aggressive behaviors/attention difficulties) because they involve conflicts with other people or normative behavior expectations are not met[28]. Externalizing problems can also have more direct negative consequences (e.g., having a poor relationship with teachers[29,30], being excluded from preschool or group activities[31,32]) than internalizing problems. However, internalizing problems are also associated with adverse

outcomes: higher school absenteeism rates, difficulty bonding with others, disinterest in everyday activities, and worse mental and general health in later years[30,33-36].

There is strong evidence that externalizing symptoms are highly comorbid with internalizing symptoms, and some authors have found that a single psychopathology dimension explains all psychopathology symptoms [37-39] in older children or adults. For example, a study in Brazilian children aged 6 to 12 years old in the cities of São Paulo and Porto Alegre[37] found that a general psychopathology factor ("P factor" [38]) accounted for most of the variance in a model including internalizing and externalizing symptoms. However, this could be different in preschoolers. A study on the Child Behavioral Checklist (CBCL 1.5-5)[28], the most widely used scale to examine behavioral problems in preschoolers, conducted Confirmatory Factor Analyses in data from 23 countries[40], confirming the seven-factor structure of behavioral problems. The seven-factor structure is two factors for externalizing problems, four factors for internalizing problems, and a single factor for sleep problems. The two first-order factors or syndromes of externalization are: "Aggressive Behaviors" and "Attention Problems." The four first-order or syndromes of internalization are: "Anxiety/Depression," "Somatic Complaints," "Withdrawn," and "Emotionally Reactive. If internalizing and externalizing problems are distinct constructs, their risks and effects should differ, and they should have different prevention and treatment approaches.

In addition to rarely being the main focus of attention, preschoolers' internalizing problems are usually considered only one outcome variable of the presence/absence of clinically significant (problematic) internalizing symptoms. Reducing internalizing problems to a single variable in studies hinders understanding the mechanisms of developing internalizing problems in preschoolers and decreases diagnostic and therapeutic accuracy. Just as internalizing disorders do not all stem from the same causes, it is expected that not all preschoolers' internalizing problems develop through the same pathways. Also, preschoolers could have different estimates of prevalence of internalizing problems

based on their characteristics, similar to what is seen at a later age. In adolescents and adults, there are estimates that females are at least twice as likely as males to develop psychiatric disorders [41-44]. The evidence also suggests that females develop internalizing disorders through different mechanisms than males. For example, a longitudinal study with measures of child behavior at ages 4, 6, 7, 8, 16, and 17.5 found that parental psychopathology has a direct effect on the symptoms of female children and an indirect effect on symptoms of male children mediated by parenting practices. If there are marked differences by sex in the pathways of development of internalizing symptoms in children, this would suggest that the treatment and prevention should be different in boys than in girls since preschool years (e.g., promoting specific communication skills).

Studying internalizing problems in preschoolers is of particular importance in Low- and Middle-Income Countries (LMIC) since there may be different patterns than in High-Income Countries (HIC) in the prevalence of known risk factors (violence, lack of emotional and financial support[13,45-48]), the possibility of additional risk factors, and their consequences. Worldwide, Brazil (an LMIC) ranks first in the prevalence of anxiety disorders (9.3% of the country's population) and fifth in the prevalence of depression (5.8% of the country's population) [8,9], and some of the highest estimates of the prevalence of disability from these disorders (8.3% from anxiety and 10.3% from depression, versus worldwide averages of 3.4% and 7.5%, respectively)[9]. Many other LMIC, in particular countries in Latin America, also have higher percentages of years lived with disability (YLD) from anxiety and depression than most HIC [9]. The high prevalence of internalizing disorders in adults and the resulting disability in Brazil and other LMIC implies a high prevalence of parental psychopathology. Parental psychopathology, summed to other widespread risk factors of internalizing problems (such as violence and other adverse childhood events [49-57]), indicates that millions of preschoolers in LMIC are at risk of suffering internalizing problems and their negative consequences.

A better understanding of the structure of internalizing problems and an assessment of the risk of the syndromes of internalization differentially by sex can help suggest novel targets of research, prevention, and treatment of internalizing psychopathology, improving the child's well-being during critical years of development, and reduce adverse outcomes in future years.

1.2 Dissertation Overview

This dissertation's primary goal is to advance our understanding of internalizing problems in preschoolers in an LMIC that is highly affected by psychopathology. Specifically, I evaluate the available evidence on internalizing problems in LMIC (Aim 1); examine the structure of internalizing problems in preschool boys and girls in São Paulo, Brazil (Aim 2); and examine the association of important risk factors with internalizing syndromes differentially by the sex of the preschoolers (Aim 3).

This dissertation contains five chapters. Following this introduction, **Chapter 2** presents a systematic review of the literature relevant to Aim 1.   The systematic literature review included studies written in English, Spanish, and Portuguese assessing prevalence, predictors, and the structure of internalizing problems in preschoolers in all LMIC.

Chapter 3 presents the analyses of the structure and characteristics of internalizing problems in the CBCL 1.5-5[28] differentially by sex in a representative sample of preschoolers in a region of Brazil, the Brazilian municipality of Embu das Artes, São Paulo. Data were obtained from The Preschool Mental Health Survey (The PreK survey[58,59]), a 2015 cross-sectional study on 1,292 preschool children (666 boys and 626 girls). This survey provided the opportunity to examine the construct of internalizing problems and its differentiation from the construct of externalizing problems in preschoolers in a LMIC.

Chapter 4 is based on the findings and the estimates obtained in **Chapter 3**, discussing results of the assessment of risks of internalizing syndromes in preschoolers in São Paulo by parental depression,

physical or verbal violence, and low quality-time with parents, examining differences by sex and confounding by child externalizing symptomatology, child sleep problems, age of the child, child food insecurity, parent substance use, neighborhood disadvantage, and parental social support.

Chapter 5 presents a discussion of the findings of this dissertation and future directions for research.

These findings will add to the evidence in public health and inform studies aiming to explore the mechanisms of development of internalizing problems in preschoolers in LMIC, leading to novel intervention and prevention targets to reduce their negative proximal and distal consequences.

Chapter 2: Internalizing Problems Of Preschool Children In Low And Middle-Income Countries: A Systematic Review

2.1 Introduction

An estimated 322 million people suffer from depressive disorders, and an estimated 264 million people suffer from anxiety disorders[9]. They are the leading causes of non-fatal loss of health and high rates of disability [12,60]. They are associated with developing chronic diseases, adverse treatment outcomes[15-22], substance use disorders [61,62], and increased mortality rates[11,20,63,64]. Due to their high prevalence and adverse effects, depressive and anxiety disorders are considered among the main threats to public health across the globe[9,12,60]. There is a growing body of research on their predictors, their effects, and their treatment in adolescents and adults.

Research on the predictors of internalizing problems in young children is scarce, despite evidence that children can have clinically significant (problematic) internalizing symptoms as early as preschool years[1-3]. Internalizing problems in preschoolers are commonly studied as predictors of adverse outcomes such as school absenteeism, inadequate adaptation skills, negative effects on children's general health and wellbeing[30,33-36], their potential continuation in adolescence, and their potential development into mental disorders[5-7]. The role of internalizing problems as outcomes is rarely explored, and they are commonly assessed as a dichotomous variable indicating the presence or absence of clinically significant problems [4,9,65,66]. The reduction to a single variable in studies of internalizing problems in preschoolers hinders the understanding of their characteristics and decreases diagnostic and therapeutic accuracy. We know more about the effects of internalizing problems in preschoolers than about their characteristics and predictors.

One of the main reasons why internalizing symptoms in preschoolers draw less attention than other areas of psychopathology is the difficulty in observing them (they have to be reported by a third person, such as a parent/caregiver). They are usually not overtly socially disruptive behaviors[4], unlike

externalizing problems. Externalizing problems (aggressive behavior/attention difficulties) involve

conflicts with others and not meeting normative behavior expectations. They can have more direct

negative consequences than internalizing problems, such as conflicts with family members[67], a poor

relationship with teachers and peers[29,30,68], and being excluded from preschool or group activities[31,32].

The characteristics and consequences of externalizing problems make them the focus of most young

child behavior studies, and internalizing problems play a secondary role. However, due to their high

comorbidity, externalizing and internalizing problems are not commonly studied separately. Some

authors have suggested that a single psychopathology dimension (also called the p-factor[38]) accounts for

the most variance in models with all behavioral problems or disorders[37-39]. They have conducted their

analyses in older children or adults, and it remains to be explored if their findings are also seen in

preschoolers.

The majority of the studies that focus on internalizing problems in preschoolers are conducted in

High-Income Countries (HIC) despite them being ubiquitous globally. In Low and Middle-Income

Countries (LMIC), health research frequently examines issues that directly threaten the lives of their

populations (infectious diseases, chronic diseases, drug use, access to essential health services[69]).

Compared to HIC or more developed economies, in LMIC, there have been fewer studies and lower

mental health treatment rates in adults[70,71], and even fewer studies on the examination of mental health

in young children. Due to the scarcity of research on mental health in young children in LMIC, studies

done with populations in HIC serve as the basis and sometimes as the only sources of evidence to make

decisions regarding health policies and treatment [72-74]. LMIC may have different patterns in the

prevalence of known risk factors (violence, lack of emotional and financial support[13,45-48]), the probability

of additional risk factors, their consequences, and the structure of the problems. Studies focused on

internalizing problems in preschoolers in LMIC are needed because knowing different patterns might

affect the prioritization of interventions for those risky or protective exposures that are modifiable and potentially prevent further psychopathology.

Worldwide, in people aged 15 years or older, Brazil (a LMIC) ranks first in the prevalence of anxiety disorders (9.3% of the country's population) and fifth in the prevalence of depression (5.8% of the country's population) [8,9], with some of the highest prevalence of disability resulting from these disorders (8.3% from anxiety and 10.3% from depression, versus worldwide averages of 3.4% and 7.5%, respectively)[9].

The World Health Organization (WHO) has quantified the losses in health and functioning with the Years Lived with Disability (YLD) estimate. In the YLD estimate, the prevalence of disorders is multiplied by the average level of disability associated with them[12,60]. Many LMIC (in particular, most of the countries in Latin America) have higher percentages of years lived with disability from anxiety and depression than most HIC [9]. The estimates refer to people aged 15 years or older, many of whom could be the parents of young children, suggesting high rates of parental psychopathology, one of the main risk factors of internalizing problems[75,76]. These estimates, along with the high prevalence of other known risk factors for anxiety and depression in LMIC (such as violence and other adverse childhood events [49-57]), imply that potentially millions of preschoolers in LMIC are at risk of suffering internalizing problems and their negative consequences.

To further understand the distinct characteristics of internalizing problems in preschoolers in LMIC, we conducted a systematic literature review of studies written in English, Spanish, and Portuguese. We included studies assessing prevalence, predictors, and structure of internalizing problems in preschoolers in all countries considered LMIC according to the Gross National Income (GNI) [77]. We defined preschoolers as all children who had not yet started primary school (from 1.5 to 6 years old).

2.2 Methods

A search was conducted for all studies up to February 16, 2020, written in English, Spanish, and Portuguese. Combinations of the keywords/terms for the searches were used: 1) internalizing disorders related terms: internalizing symptoms, internalizing problems, anxiety, depression, emotional symptoms, behavioral symptoms; 2) preschool related terms: nursery, kindergarten, playschool, pre-primary school, preschool-age; 3) low and middle-income countries, developing country, developing economy; 4) exclusion of high- income countries. The databases used were Pubmed, Embase, PsycINFO in EBSCOhost, SciELO, and Bireme. The search terms in Spanish and Portuguese did not yield any results; for that reason, the search in EBSCOhost was expanded to "all databases." In addition, in Spanish and Portuguese, the accents and special characters were eliminated to facilitate the search and avoid using "SmartSearch" in EBSCOhost, which leads to broader but mostly irrelevant results. For all keywords, filters, and expanders used, see Appendix A.

We were two independent reviewers, both with clinical and research experience in child psychiatry, psychology, and psychiatric epidemiology. We included studies examining predictors and mediators of internalizing symptomatology in preschoolers. We also included studies focused on the characterization of internalizing symptomatology. Additionally, we included studies examining internalizing and externalizing symptoms in preschoolers and older children if the estimates for internalizing symptoms in preschoolers could be isolated.

We excluded: 1) studies in countries not considered developing economies based on the GNI; 2) articles not published in peer-reviewed journals and other grey literature; 3) studies in children with developmental disabilities; 4)children with schizoaffective disorders; 5) specific samples (for example, samples that included only mistreated children, or only with chronic conditions with no comparisons with children in the community); 6) case studies, genetic studies, studies on effects of medication, and effects of treatment.

The list of results was exported from each database into EndNote to format references and exclude duplicates. The list without duplicates was imported in Covidence[78] to discard papers by title and abstract. After the two reviewers selected articles for full-text screening, the document of each selected paper was added to Covidence. Each reviewer screened the full text of the selected articles and described the reason for exclusion. Included papers were selected for extraction. The data for the selected studies were extracted using the following criteria: author and year, WHO region, country, language, aims of the study, type of study, sample, the definition of internalizing problems, main findings on internalizing problems, quality assessment. Each reviewer rated the quality of the studies using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies[79] and the PRISMA Checklist[80].

Our understanding of the internalizing problems and our interpretation of the findings is strongly based on the factor structure of the Child Behavioral Checklist (CBCL 1.5-5)[28], the most commonly used instrument to measure behavior problems in preschoolers worldwide. Data from five LMIC: China, Peru, Turkey, Kosovo[40], and Mexico[81] have supported the factor structure of the CBCL 1.5-5 v. Behavioral problems have three factors or dimensions: internalizing problems, externalizing problems, and sleep disturbance. The internalizing problems are composed of four syndromes: anxiety/depression, somatic complaints, withdrawn, and emotionally reactive. Each of the dimensions and syndromes has a score and cutoff points to determine if the problems are clinically significant, subclinical, or nonclinical.

The WHO grouped all countries in 6 regions: The Region of the Americas, the African region, the European region, the Eastern Mediterranean region, the South East Asia region, and the Western Pacific region[9]. These are groupings based on geographical terms, and they share strategies with particular focus and stages of development. There are different ways to classify countries into LMIC or HIC, such as using the Gross National Income (GNI)[77] by the World Bank. However, we decided to organize the

studies by WHO region since LMIC within each WHO region are in a similar stage of a global response to

the prevention and control of chronic, noncommunicable diseases such as internalizing problems.

For the full keywords, see Appendix A. From the search with English keywords, 507 titles were

obtained. From the search with Spanish keywords, 97 titles were obtained. From the search with

Portuguese keywords, 37 titles were obtained. All these together summed 641 references.

Of the 641 references located, 222 were excluded for being duplicates. One paper was added

from an external source. Of the 420 articles screened, based on title and abstract, 328 were excluded. Of

the 92 studies, 61 were excluded, and 31 were included and selected for extraction. The main reasons

for exclusion were: not an LMIC, unable to isolate effect in preschool age group, unable to extract

information on internalizing problems, written in a language other than English, Spanish, or Portuguese

(either Chinese Mandarin, Arabic, Persian, Russian or Turkish) (see figure 1).
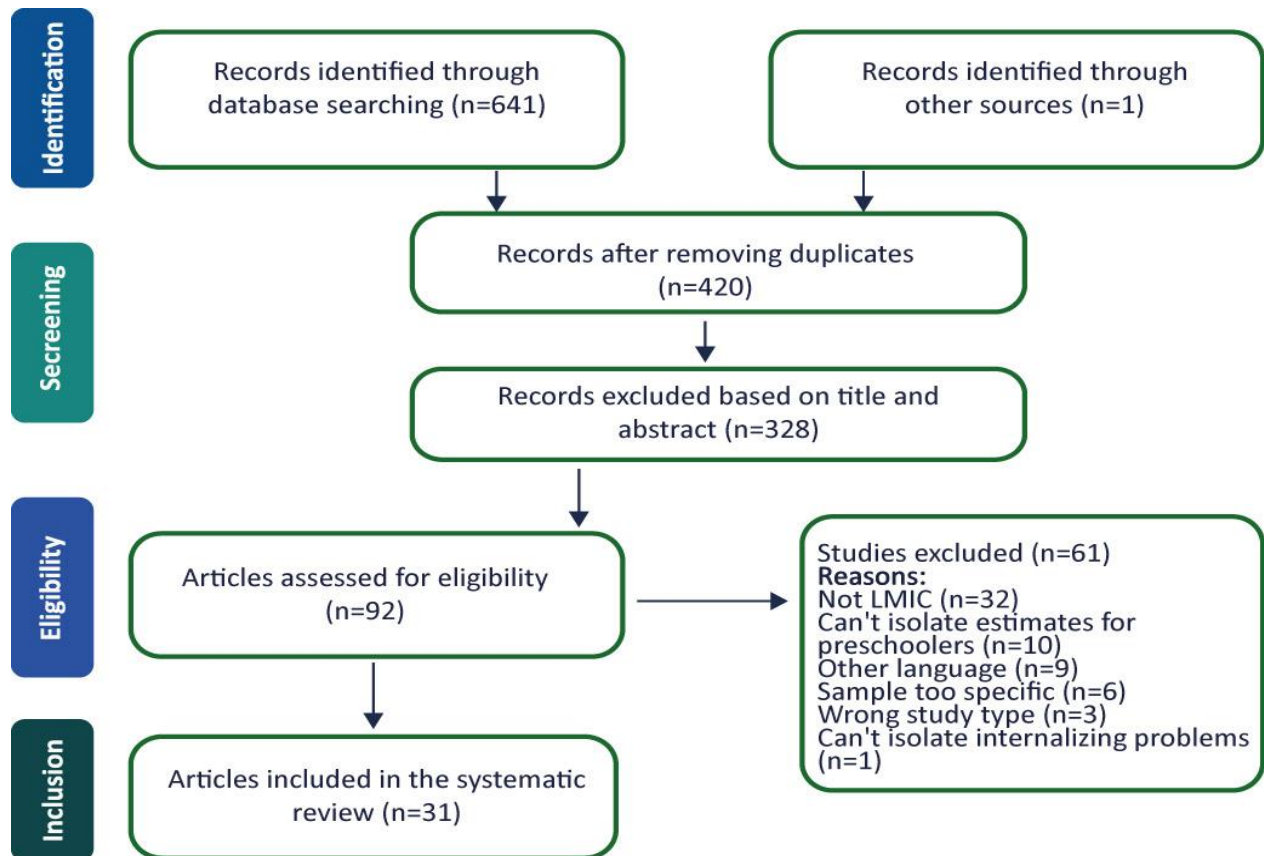
Figure 1. PRISMA Flowchart.

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2.3 Results

<u>General Characteristics of the Studies</u>

The 31 studies were classified according to their WHO region[9]: Region of the Americas, African region, European region, and the Western Pacific region. No studies from the Eastern Mediterranean region or the South East Asia region were eligible (see table 1).

Table 1. Distribution of studies by WHO region and languages.

Region of the Americas N=14	N	%	European Region N=10	N	%	Western Pacific Region N=5	N	%	Africa N=1	N	%	>1 region N=1	N	%
Brazil	6	43	Turkey	4	40	China	5	100	South Africa	1	100			100
Colombia	2	14	Romania	2	20									
Costa Rica	1	7	Russia	2	20									
Argentina	2	14	Serbia	1	10									
Mexico	2	14	>1 country	1	10									
Peru	1	7												
Languages														
English	5	36	English	10	100	English	5	100	English	1	100	English	1	100
Spanish	7	50												
Portuguese	2	14												

The majority of the studies selected (45%) were conducted in the Region of the Americas. The country with the most studies on the topic was Brazil (19% of the studies). This finding could be partly due to the use of additional keywords in Portuguese and Spanish. However, it shows that the alarmingly high rates of depression and anxiety in Latin America have led to a growing interest in the mental health of preschoolers and children of all ages. The topic of internalizing problems in preschoolers has drawn attention only recently in LMIC because the majority of the studies (74%) that met the inclusion criteria were published in the last decade. None of the articles included were published more than two decades ago. It is important to highlight that the number of studies conducted in China and Turkey (respectively,

five and four studies on the topic were included) would have been greater if articles written in Chinese Mandarin or Turkish were screened. There could be studies on the topic in other LMICs, but we could not include their official languages (for example, Arabic, French, Hindi). We also found that for articles written in English, the terms had to be more specific, and we needed to apply more filters because the search identified a large number of studies, mostly on irrelevant topics.

Another finding was that the majority (80%) of studies used versions of the CBCL, even if the instrument was not validated for use in their study population.

More than 30% of the studies had small samples with fewer than 100 people because they were recruited in a single preschool/institution or small areas. The small sample sizes may be representative of small areas, but they do not allow researchers to extend the findings to larger populations.

In a study examining internalizing problems in preschoolers in 24 countries[82] as reported by the CBCL 1.5-5, two of the six countries with the highest mean internalizing scores were LMIC in the European region (Romania and Turkey), and one (Iran) was an LMIC in the Eastern Mediterranean Region. Also, the authors reported that the estimated means of internalizing problem scores in the six countries (Singapore (a HIC), Iran, Romania, Lithuania (HIC), Turkey, and Chile (a HIC)) did not differ significantly from each other.

Findings by WHO Region

For the description of all the findings, see tables 2 to 5. We included studies for the region of the Americas, the European region, the Western Pacific region, the African region, and one for more than one region.

In this region, seven of the fourteen studies selected were written in Spanish, five articles were written in English, and two articles were written in Portuguese. Four of the five studies in English in this region were conducted in Brazil. With six included studies, Brazil was the country with the largest proportion of studies in this region (43%) and overall (19%).

Regarding study type, eleven studies were cross-sectional, and three were longitudinal. Regarding sample size, six studies (43% of the studies in this region) had small samples of fewer than 100 participants. The studies with larger samples were all conducted in Brazil.

The quality of the majority of studies was fair (57%) based on the Quality Assessment tool[79] and the PRISMA checklist.[80]

Prevalence of Internalizing problems and syndromes in the region of the Americas

Regarding the prevalence of internalizing problems in the region, only two studies[83,84], both conducted in Brazil, described the prevalence of internalizing problems in preschoolers. Their estimates were 7.8 %[84] and 9.7%[83]. Both studies worked with representative samples of two Brazilian cities, one in the city of Pelotas, Rio Grande in 2004 (n=3,750), and one in the city of Salvador, Bahía in 2001 (n=349), respectively. Other studies[85-87] described the prevalence of internalizing problems in their samples, but their samples had fewer than 100 participants, or they were not representative of their study population.

The study conducted in the city of Pelotas compared two cohorts and reported an increase of 10% in the scores of internalizing problems in eleven years (between 1993 and 2004) [84], but not a significant increase in the prevalence of clinically significant cases (from 5.6 to 7.8%). A study conducted in Mexico City[88] obtained scores of internalizing problems. This study, with 60 dyads of mothers and

their children, found that assuming a normal distribution, about 16% of the children could have been in the clinical range (≥64).

Three studies [83,84,89] described the most frequent internalizing syndromes in preschoolers: The two studies previously mentioned with representative samples of cities in Brazil found that the most frequent internalizing problem was "withdrawn." based on the CBCL. The other study[89], conducted in Colombia with a small sample (n=20), found that based on the report by the parents, the most common internalizing problem in preschoolers was somatization, and based on the report by the teachers, the most common internalizing problem was depression[89].

The remaining studies did not provide mean scores or prevalence of internalizing problems or syndromes in their samples. Their focus was to make comparisons and estimate associations, as described below.

Risk factors studied in the region of the Americas

The studies in this region focused on examining the risk by characteristics of the children and the home environment. The characteristics examined in the home environment were: maternal age, paternal age, number of siblings[85], mother psychopathology, absent father[83], socioeconomic status (SES)[84], early adversity[90], bed-sharing[91]. The child's characteristics examined were: a deficit in social skills[86], sleep disturbance[87], persistent child's ability to respond, child's involvement, child's general emotional availability, general emotional availability.[88]

Significant relationships were in the expected direction with all home environment variables, where risky exposures were associated with high internalizing problem scores (e.g., controlling criticism in the mothers, lower maternal education[85], absent father[83], dyadic emotional availability[88]). Persistent and early onset bed-sharing were both associated with increased odds of internalizing problems[91]. One study[83] found a significant association between maternal psychopathology and externalizing problems,

but not internalizing problems. Regarding specific syndromes, there were negative relationships between maternal age and somatic complaints[85], between maternal education and withdrawn[85], and between SES and anxious/depressed syndrome[84].

Significant relationships with the child's characteristics were also in the expected direction; internalizing problems were associated with a deficit in social skills[86], sleep disturbance[87], child's ability to respond, child's involvement, child's general emotional availability [88]. Regarding specific syndromes, there were negative relationships between anxiety/depression and the child's ability to respond, and between being withdrawn and the child's general emotional availability[88].

Assessment of Confounding

In the majority of the selected studies, there was no assessment of confounding, or it was not reported. Only four studies (29% of the studies in the region)[83,84,91,92], all conducted in Brazil, described the assessment or provided adjusted estimates. The confounders included in these four studies were family income[83,91,92], marital status[84,92], maternal age[83,92], child's age[84,91] schooling, skin color, parity, depressive symptoms and smoking during pregnancy, type of delivery[91], number of children under five in the home, number of persons per room, and level of mother-child interaction[83], other parental and socioeconomic characteristics, [92], age at the time of testing, family socioeconomic position, maternal parity, maternal smoking during pregnancy, child's low birth weight, multiple pregnancies, maternal employment, and maternal psychiatric problems.[84]

Mediators and Moderators

Two selected studies in Brazil examined mediators or moderators of the relationship between internalizing problems and their potential predictors. One study identified partial mediation by mother internalizing problems in the relationship between grandmother and child internalizing problems[92]. Another study examined the moderating role of verbal IQ in the relationship between early adversity

and internalizing problems in early childhood and early adolescence[90], finding that verbal IQ moderates this relationship in early adolescence but not in early childhood.

Differences by Sex and Age of Preschoolers

Differences by sex and age in scores of internalizing syndromes were explored in four studies. A study in Brazil[84] found that girls had higher scores of anxiety/depression than boys and an increase in mean somatic complaints over ten years. In Mexico, a study[81] found that the scores for somatic complaints have higher internal consistency for boys than for girls. Studies in Argentina and Peru found no significant differences by sex in behavioral inhibition[86] or anxiety/withdrawn[93].

Studies on the Measurement of Internalizing Problems

Three studies in the region examined the validity of the tests to measure internalizing problems. The study in Mexico[81] that examined the validity and internal consistency of the CBCL 1.5-5, concluded that anxiety and depression had better consistency when considered together. A study in Colombia[94] examined the criterion validity of the Early Childhood Screening Assessment, concluding that internalizing and externalizing symptoms load in more than one factor, unspecified. A study in Argentina[95] found that behavioral problems are explained by two factors: internalization and externalization. They examined the psychometric properties of the Preschool and Kindergarten Behavior Scales.

The European Region

In this region, all of the ten studies selected were written in English. In the search for articles in this region, only one study was discarded because it was written in Turkish. Turkey was the country with the highest number of studies (four, or 40% of the studies selected in this region).

Regarding study type, seven had cross-sectional measures, two had longitudinal measures, and one was a randomized control trial. None of the cross-sectional studies[96] had a sample of fewer than 100 people. The studies in this region with small samples had longitudinal measures.

The quality of the majority of studies was good (60%).

Prevalence of Internalizing Problems and Syndromes in the European region

Regarding the prevalence of internalizing problems in preschoolers in the region, only one study, conducted in Serbia[97], described the prevalence of clinically significant internalizing problems in a representative sample of preschoolers in a city, estimating it at 17%. One study in Turkey[98] estimated the prevalence of behavioral problems at 11.9%, but the estimate for internalizing problems could not be isolated. A study in Romania found that internalizing disorders are the most prevalent of the psychiatric disorders in preschool children[99].

On the prevalence of internalizing syndromes, only the study in Serbia described frequencies. They found that the most common internalizing syndrome was withdrawn (9.3%), and the least common (2.4%) was somatic complaints. One study in Turkey[100] estimated the mean score of internalizing problems in the CBCL 2-3 at 6.85. A study conducted in 24 societies[82] found that Turkey was the second highest-scoring society on the Anxious/Depressed syndrome and the fourth or fifth highest on the other three internalizing syndromes. Romania and Turkey were among the six societies with the highest mean scores on total internalizing problems in preschoolers.

Risk factors studied in the European region

In this region, the studies focused on the relationship of internalizing problems with characteristics of the environment and with adverse events, emphasizing on the effects of maternal psychopathology.

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The risk factors significantly associated with internalizing problems were: maternal psychological problems[96,101,102], alcohol use during pregnancy[101], prenatal smoking[103], early effortful control[104], lifetime lead exposure[103], family dysfunction[101], compromised postnatal condition of the child[101], effective emotion regulation strategies[105], attachment security[105], institutionalization[99], urban residence[98], mother's rejection of home-making role[102].

Known harmful exposures mentioned above (e.g., maternal psychopathology, low effective emotional reactivity strategies) all had an association in the expected direction with internalizing problems. There was one cross-sectional study that did not find a direct effect of attachment security on internalizing problems, only an indirect effect[105].

Regarding other exposures, one study[98] found that children from urban areas obtained significantly higher scores on internalization than children from suburban and rural residences. Another study[99] found that children removed from institutions and placed in foster families were less likely to have internalizing disorders than children who continued to be institutionalized (22.0% versus 44.2%).

Assessment of Confounding

Of the ten selected studies in the region, three reported an assessment of confounding and adjusted estimates. The confounders were: child's age[101,103,105], child's sex, ethnicity, language spoken at home, acceptance, and maternal education[103], SES[101].

Mediators and Moderators

A cross-sectional study in Russia[101] found that continued maternal and family dysfunction and compromised postnatal condition of the child, mediate the relationship between alcohol use during pregnancy and maternal psychopathology with internalizing symptoms. Another cross-sectional study in Romania[105] found that effective emotion regulation (problem-solving) in the child fully mediates the

relationship between attachment security and internalizing problems. Moderation by the sex of the child was examined, as discussed below.

Differences by Sex and Age of preschoolers

Half of the studies in this region examined differences in internalizing problems by sex. They found the following associations:

Two studies, one in Serbia[97] and another in Old Yugoslavia[103] (now Serbia, Kosovo, Albania, and others), examined differences in internalizing problems by sex. One of the studies[97] compared the mean scores of boys and girls on internalizing syndromes in Serbia with mean scores of boys and girls in the United States (US). They found that Serbian girls had significantly higher scores on total internalization than Serbian boys (2.2 vs. 1.8). Compared to the US, in the Caregiver Teacher Report Form (CTRF), both Serbian boys and girls had significantly higher mean in somatic complaints than boys and girls in the US (3.8 vs. 3.6, and 1.2 vs. 0.7)[97]. The study in old Yugoslavia[103], examined interaction by sex, finding that the only statistically significant interaction with sex was for Somatic Problems, where scores in boys' Somatic Problems do not differ across the maternal smoking status.

A study in Romania[99] examined children who were reared in institutions and never-institutionalized history. This study found that boys had a higher number of internalizing symptoms than girls regardless of institutionalization history. Also, unlike girls, the total psychiatric symptoms of the institutionalized boys did not reduce after being placed in foster care.

A study[100] in Turkey found that mean scores in the total internalizing scores of boys and girls are not significantly different. Regarding syndromes, another study in Turkey[98] found that girls have higher scores than boys in the anxious/depressed score.

These same two studies in Turkey examined differences in internalizing problems by age. One study[100] found no significant differences by age. The other study found among two and three-year-olds, younger children had more somatic complaints than older children.[98]

Studies on the Measurement of Internalizing Problems

Only one selected study[100], conducted in Turkey, assessed the validity and reliability of a scale to measure internalizing and externalizing problems in preschoolers (The Brief Infant-Toddler Social and Emotional Assessment[106]). The total score in this scale is correlated with internalizing and externalizing scores in the CBCL, but it does not differentiate between the two dimensions.

The Western Pacific Region

The Western Pacific Region, according to the WHO, includes some Asian countries. In the literature search, only five studies from China were included. Four studies additional studies from this country would have been eligible based on title and abstract but had to be excluded because they were written in Chinese mandarin. For more information.

The five studies selected were written in English, and they were rated as being of good quality. Four studies in China had longitudinal measures, and only one had cross-sectional data. One longitudinal study[107] had a sample of fewer than 100 people.

One study[108] estimated the prevalence of internalizing problem scores at 18%, obtained from a representative sample of preschoolers in the city of Jintan.

Risk factors studied in China

The risk factors were: Parenting stress[109], environmental tobacco smoke exposure during pregnancy (ETS)[108], micronutrient deficiency[110], blood lead concentration[111], infant temperamental withdrawal[107]. Except for parenting stress in fathers and ETS, the risky exposures had significant

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associations with internalizing problems in preschoolers. All the relationships were in the expected direction. For specific syndromes, an increase in blood lead concentration was associated with increased odds for anxious/depressed, and emotionally reactive, as well as with increased odds for DSM-oriented anxiety.[111]

Assessment of Confounding

Four of the five selected studies reported adjusted estimates or assessments of confounding. The confounders were: child's sex[108,110,111], parental education[108,110,111], occupation[108,109], school area, and psychopathologic problems; maternal age during pregnancy; father's current (postnatal) smoking status[108], family size, house size[111], residence, parents' marital status, single child, IQ[110], previous internalizing and externalizing problems[107].

Mediators and Moderators

Only one study[109] examined mediation. The study found that parental psychological aggression partially mediated the relationship between parenting stress and children's internalizing behaviors, but only in mothers. No significant direct effects or indirect effects on fathers were found.

One study examined interaction by maternal sensitivity (MSID) and toddler's ability to delay gratification in the relationship between infant temperamental withdrawal and internalizing problems, but the estimates were not significant.

Differences by Sex and Age

One study examined sex and age differences. In boys, there was a slight negative association between blood lead concentration and internalizing problems at age 4. At age 5, both boys and girls had a positive association between blood lead concentration and internalizing problems[110]. There were no studies on the measurement of Internalizing problems in China selected in this review.

The African Region

For the African region[112], only one study conducted in South Africa was included in this review since, in other studies with a relevant topic, the estimates for preschoolers could not be extracted. The study had good quality based on the PRISMA checklist.

The study was a randomized controlled trial to examine the effect of an intervention on maternal depression during pregnancy, and it also described the consequences of maternal depression in children's problem behaviors in the first three years of life. They examined differences in scores and differences in clinically significant scores. On the measure of internalizing scores, children of never depressed mothers had lower mean scores than the children of mothers who had been depressed postnatally, antenatally, or both. On the measure of internalizing score deviant, children of never depressed mothers had a higher probability of symptoms than children of mothers who had been depressed postnatally, antenatally, or both.

Confounders

The confounders in the study were maternal HIV status, alcohol use, food insecurity, and baseline education.

Other WHO regions

In the study on 24 countries[82], they included data from an unpublished study in Iran. They found that Iranian preschoolers had the fourth highest mean scores on internalizing problems (the six countries with the highest score were Singapore (a HIC), Iran, Romania, Lithuania (a HIC), Turkey, and Chile (a HIC)).

From the Eastern Mediterranean Region, we excluded two articles written in Persian and Arabic languages, which could have been included based on title and abstract. No studies from South East Asia

were included. Only two papers[113,114] from India published in 1995 and 1998 came up in the search, but they were excluded due to a difficulty in isolating and extracting estimates in the preschool age group.

2.4 Discussion

These findings provide further evidence that research on internalizing problems in preschoolers is scarce in LMIC. Despite the restrictive filters for the search, more than 250 studies in the search were conducted in HIC. Since English is not widely spoken in many LMIC, incorporating other languages such as Portuguese and Spanish includes other valuable research on preschoolers' internalizing problems worldwide. By extending our search to Portuguese and Spanish, we were able to better characterize the internalizing problems of preschoolers in LMIC in the Americas. Still, we fell short in all the other regions of the world, in particular the Eastern Mediterranean region and the South East Asian region, where we could not include any studies.

Our findings highlight the need for more studies on the validation of scales of behavioral problems of preschoolers and the examination of the structure of internalizing problems in LMIC. The lack of validated instruments in the studies that met search criteria raises questions on the accuracy of the measurements. A common limitation in LMIC is better described as a cycle: the lack of a valid scale that serves as a standard in a population complicates further validation efforts. Our search found four studies of at least fair quality on validation of behavioral problem scales in preschoolers (three in the region of the Americas[81,94,95], and one in Europe[100]). There are only four reports of studies in LMIC endorsing the seven-syndrome structure of the CBCL 1.5-5: China, Peru, Turkey, Kosovo[40], and one study supporting the criterion validity of the scale in Mexico[81]. We currently do not know if internalizing problems reported in any two given LMIC are comparable. We also do not know if they refer to different constructs (e.g., posttraumatic stress could be part of the internalizing problems), or if the syndromes could have a different meaning for different groups of preschoolers (e.g., boys and girls, rural and

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urban). Internalizing and externalizing problems should always be examined and reported in studies of child behavior in LMIC due to their high comorbidity and, in some cases, no differentiation of symptoms.

The studies with small samples or with poor quality may not provide the full background of the characteristics and predictors of internalizing symptoms in each country. However, they describe relevant variables to explore, such as sleep disturbance[87], mother and child emotional availability[88], or verbal IQ[90], and they provide plausible hypotheses that could be tested in larger samples measuring a larger number of variables. The region of the Americas was the region with the highest percentage of studies with small samples (43% had fewer than 100 participants). This high percentage could be due to the prioritization of more life-threatening conditions and fewer resources to fund studies at a larger scale than the European region or the Western Pacific region.

Brazil, the country with the most articles in our sample, was an outlier; most studies in this country were of good quality, had the largest samples and longitudinal measures. The increased attention to this topic in Brazil could be due to efforts to reduce the alarmingly elevated rates of anxiety and depression (first and fifth highest worldwide) and related disability in people aged 15 years and older[9]. One of the reasons for elevated rates of anxiety and depression could be stress [115]. There are reports of increased levels of stress among adults due to low income, job loss/unemployment, and other negative life events following the 2008 recession[116-118]. There is also evidence that the growing popularity of social media, especially among children and adolescents, is linked to increased depression in this age group[119]. The anonymity in social media reduces societal boundaries in human attitudes[120], leading to a lack of consequences for aggressive behavior and destructive criticism increasing the likelihood of being victims of cyberbullying[121,122].

Since the most reliable data that we found in the region of the Americas comes from Brazil, most of our results were extracted from Brazilian studies, and most of our conclusions on internalizing

problems could apply mainly to this country. To a lesser extent, they would apply to other LMIC in the

region. The estimate of the prevalence of internalizing problems in preschoolers (between 7.8% and

9.7%) was also obtained from Brazilian studies. However, we found common interests in this region in

terms of risk factors. This region focused on examining the risk by characteristics of the home

environment and the children. Maternal characteristics were the most common risk factor, but the

interest in parental psychopathology was not as marked as in studies in the European region.

The European region had a higher percentage of studies with good quality (60%) than the region

of the Americas. However, Turkey (the country with the highest number of articles selected in this

region) also has high rates of anxiety (four points above world average), depression, and related

disability, and it is probable that, like Brazil, this shows increasing efforts to reduce them[9].

Also, in the European studies, there was a larger focus on examining differences by sex of the

child than in other regions. In summary, boys and girls did not appear to have significantly different

scores on internalizing problems. They had significant differences in syndromes (e.g., girls have more

anxiety/depression than boys; boys have more somatic complaints than girls). This coincides with

findings in the region of the Americas. These results warrant further exploration in the examination of

the structure of internalizing problems of boys and girls, to identify the main problems and understand if

preschool boys and girls experience internalizing problems differently.

Another important finding in the region was that lead exposure was significantly and positively

associated with increased internalizing problems in preschoolers. This finding coincides with the ones

from a Chinese study[108], where blood lead was associated with higher scores on anxiety/depression,

emotional reactivity, and pervasive developmental problems. This study, along with two more studies in

China, shows that there is an interest in the effect that harmful substances or the lack of micronutrients

can have on internalizing problems. The direct effect of harmful substances should be further explored

in other regions to understand better all the risk factors that could lead to internalizing problems in preschoolers.

China was the only LMIC in the Western Pacific WHO region that was included in this study. The five studies in the sample were all of good quality, with large samples and longitudinal measures. In comparison with other regions, Chinese studies provided more mean estimates by syndrome (withdrawn, anxiety/depression, somatic complaints, emotional reactivity). There were mean estimates and more examinations of the relationships of each syndrome with the risk factors. This approach serves as a basis for more thorough explanations of the pathways of development of internalizing problems in preschoolers.

For the African region, the study that met eligibility criteria was conducted in South Africa[112]. Their findings were in agreement with several other studies that have found significant effects of maternal psychopathology in internalizing problems in their offspring[14,123,124]. One single study does not allow us to draw conclusions about the country and even less about the region. In this particular region, there could be several studies written in the official languages. We did not search for them or include other languages, which was an important limitation of this study.

In all the regions, there were few descriptions of the number of children with clinically significant internalizing problems. A suggestion to researchers on this topic is to describe further the clinically significant cases of internalizing and externalizing problems. Describing these would provide context to the results that an increase in mean scores does not. A significant increase in mean scores could still be clinically irrelevant. An increase in the number of clinically significant cases due to a particular risk factor, could warrant attention to these problems and help to identify targets of intervention.

Overall, all relationships between variables, significant or not, were in the expected direction. That is, exposures a priori considered as harmful had a positive association with increased internalizing problems, and beneficial exposures had a negative association with internalizing problems. Most of the studies in the European region and China focused on testing specific hypotheses of the association between potential predictors and internalizing variables. In contrast, studies in the region of the Americas had a more exploratory approach, mainly due to the small samples.

As previously mentioned, our study has the main limitation of not being able to include studies in different languages to have a broader picture of the internalizing problems in LMIC. Future research on the topic should aim to expand to other frequently widely spoken languages such as Chinese Mandarin, French, and Arabic.

We hope that this study provides the basis for future research on behavioral problems in preschoolers and helps to inform decisions on the mental health of young children in LMIC.

Table 2. Study in LMIC in the African Region.

Rotheram-Fuller et al. (2018) [112]	**Country**	South Africa
	Language	English
	Aims of Study	To examine the consequences of maternal depressed mood on children's growth, health, cognitive and language development over the first three years of life.
	Type of Study	Randomized controlled trial
	Sample	1,238 pregnant mothers and their children over the first three years of their lives.
	Internalizing Problems	Score for internalizing problems, classification into internalizing score deviant (yes/no)
	Associations, comparisons, or pathways examined	Comparisons of a standard of care intervention when pregnant or a home visit in depression of mothers. Associations of child internalizing problems with: maternal antenatal, postnatal, ante/post natal depression, and never depressed
	Instrument	CBCL 2-3
	Main Findings on Internalizing Problems	Patterns in the intervention groups were similar. On the Internalizing measure, children of never depressed mothers had lower scores compared to children of postnatally depressed mothers ($p < 0.01$; ES = 0.18) and antenatally/postnatally depressed mothers ($p < 0.01$; ES = 0.21). On the Internalizing deviant measure, children of never depressed mothers had lower probability of symptoms compared to children of postnatally depressed mothers ($p < 0.01$; ES = 0.15) and antenatally/postnatally depressed mothers ($p < 0.01$; ES = 0.23).
	Confounders	Maternal HIV status, alcohol use, food insecurity, and baseline education
	Quality Assessment	Good

Table 3. Studies in LMIC in the Region of the Americas.

Lacunza (2011)[86]	**Country**	Argentina
	Language	Spanish
	Aims of Study	To establish if the existence of social skills reduces the frequency of externalizing and internalizing problems.
	Type of Study	Cross-sectional study
	Sample	185 children aged 5 years old, of high or low SES and their parents
	Internalizing Problems	Total score for behavioral inhibition
	Associations, comparisons, or pathways examined	Correlations with social skills and comparisons based on Sex
	Instrument	Escala de Habilidades Sociales (Social skills scale)
	Main Findings on Internalizing Problems	40% of the children had behavioral inhibition. No significant differences by sex in behavioral inhibition. Children with behavioral inhibition have a deficit in social skills.
	Confounders	Not assessed
	Quality Assessment	Poor
Reyna and Brussino (2009)[95]	**Country**	Argentina
	Language	Spanish
	Aims of the Study	To analyze the psychometric properties of the Preschool and Kindergarten Behavior Scales in a sample of Argentinean children from 3 to 7 years old, and to obtain a reduced version of the scale with adequate psychometric properties for use as a screening tool
	Type of Study	Cross-sectional study
	Sample	Exploratory Factor Analysis and Confirmatory Factor Analysis, on responses of 208 and 184 children aged 3 to 7 years old, and their parents, respectively.
	Internalizing Problems	Score of Internalizing problems based on two scales: social isolation, anxiety/somatic problems.
	Associations, comparisons, or pathways examined	Exploratory and Confirmatory Factor Analyses of the Behavioral Problems Scale
	Instrument	Preschool and Kindergarten Behavior Scales
	Main Findings on Internalizing Problems	Behavioral problems are best explained by two factors: externalizing and internalizing problems. The level of internal consistency of the internalizing problems subscale was relatively low (Cronbach's alpha=0.67)
	Confounders	Not assessed
	Quality Assessment	Fair

El Rafihi et al. (2016)[87]	Country	Brazil
	Language	Portuguese
	Aims of the Study	To evaluate the relationship between internalizing and externalizing problems and sleep problems in children of pre-school age
	Type of Study	Cross-sectional study
	Sample	83 children between 2 and 5 years old, who attended a psychology service due to behavioral problems, and their mothers. Convenience sampling.
	Internalizing Problems	Internalizing Problems yes/no
	Associations, comparisons, or pathways examined	Correlations with all symptoms of sleep disturbance
	Instrument	CBCL 1.5-5
	Main Findings on Internalizing Problems	64 (77%) children had internalizing problems Children with sleep disturbance have a 40% higher risk of internalizing problems than those without child sleep disturbance (RP = 1.4; IC 95% = 1.14-1.67)
	Confounders	Not assessed
	Quality Assessment	Poor
Lins and Alvarenga (2015)[85]	Country	Brazil
	Language	Portuguese
	Aims of the Study	To investigate relations between maternal psychological control, behavior control, and internalizing problems of preschool children
	Type of Study	Cross-sectional study
	Sample	103 children aged 3 to 5 years old and their parents
	Internalizing Problems	Total score for internalizing problems and for each syndrome
	Associations, comparisons, or pathways examined	Associations with sociodemographic characteristics and maternal control
	Instrument	CBCL 1.5-5
	Main Findings on Internalizing Problems	Prevalence of clinically significant symptoms was 28.2% Total internalizing problems, emotional reactivity, and anxiety/depression are significantly and negatively correlated with maternal age, paternal age, and the number of siblings. Somatic complaints are significantly and negatively associated with maternal age. Withdrawn is significantly and negatively associated with maternal education. Anxiety/depression and withdrawn are significantly and negatively associated with controlling criticism in the mothers.
	Confounders	Not assessed
	Quality Assessment	Fair

Matijasevich et al. (2014)[84] cont.	Country	Brazil
	Language	English
	Aims of Study	To investigate changes in preschool behavioral/emotional problems in two birth cohorts from a middle-income country born 11 years apart.
	Type of Study	Cross-sectional study
	Sample	Mothers' reports of a randomly selected subsample of 4 year-olds from the 1993 cohort (634) and all 4-year olds from the 2004 cohort (3,750) from the Pelotas cohort studies.
	Internalizing Problems	Total score for internalizing problems, for each syndrome and classification into clinical or nonclinical range.
	Associations, comparisons, or pathways examined	Comparisons of prevalence in two cohorts.
	Instrument	CBCL 4-18
	Main Findings on Internalizing Problems	Substantial increases were detected in internalizing problems (10% approximately). Increases were also identified in mean somatic complaints, thought problems (only among girls). No significant differences in the withdrawn, anxious/depressed, social problems between the two cohorts. The CBCL total was identified to be affected by maternal schooling, marital status, maternal age, maternal smoking during pregnancy and maternal psychiatric problems, the internalizing problem score was additionally affected by parity. Girls were identified as having higher scores than boys in the anxious depressed syndrome but lower scores in the externalizing problems. SES was a confounder of the relationship between sex of child and the anxious/ depressed syndrome. Higher in 2004 than in 1993.
	Confounders	Age at time of testing; family socioeconomic position; maternal characteristics (marital status, maternal age, parity, maternal smoking during pregnancy); child characteristics (low birthweight and multiple pregnancy), maternal employment and maternal psychiatric problems.
	Quality Assessment	Good

Pearson et al. (2019)[92]	**Country**	Brazil
	Language	English
	Aims of Study	To examine the impact of grandmothers' emotional symptoms on internalizing and externalizing symptoms in grandchildren from a three-generation birth cohort study
	Type of Study	Cohort Study
	Sample	92 children aged 4 years old, parents and grandmothers
	Internalizing Problems	Total score for internalizing symptoms
	Associations, comparisons, or pathways examined	Mediation by mother internalizing problems
	Instrument	Self-reported questionnaire (SRQ) for internalization in grandmothers and parents. CBCL 1.5-5 for children internalization
	Main Findings on Internalizing Problems	The relationship between internalizing problems in grandmothers is partially mediated by internalizing problems in the mother.
	Confounders	Parental and socioeconomic characteristics identified in previous studies as potential confounding variables
	Quality Assessment	Fair
Santos et al. (2015)[83]	**Country**	Brazil
	Language	English
	Aims of Study	To identify the prevalence of internalizing and externalizing behavior problems among preschoolers and their associations with maternal mental health and family characteristics.
	Type of Study	Cross-sectional study
	Sample	349 children aged 49 to 72 months, and their mothers. Randomly selected to represent the city of Salvador de Bahía, Brazil.
	Internalizing Problems	Frequency of clinical/nonclinical syndromes, frequency of internalizing problems
	Associations, comparisons, or pathways examined	Associations between internalizing problems and maternal psychopathology and family characteristics (absent father, income, mother-child interaction, number of children under 5, number of people per room)

Santos et al. (2015)[83] cont.	**Instrument**	CBCL
	Main Findings on Internalizing Problems	The prevalence of internalizing problems was 9.7%. The most common internalizing syndrome was withdrawn (12.6%). Absent father was the only risk factor significantly associated with internalizing problems. Psychopathology in the mother was not significantly associated with child internalization, only with externalization.
	Confounders	Paternal absence, number of children under 5 in the home, maternal age, family income, number of persons per room, and level of mother-child interaction.
	Quality Assessment	Good
Santos et al. (2017)[91]	**Country**	Brazil
	Language	English
	Aims of Study	To study the effect of bed-sharing with the mother over the child mental health.
	Type of Study	Cohort Study
	Sample	3583 children followed from birth to 6 years of age, and their mothers
	Internalizing Problems	Internalizing Problems (anxiety and depression) yes/no
	Associations, comparisons, or pathways examined	Associations of internalizing problems with bed sharing: early-onset, late-onset, persistent
	Instrument	The Development and Well-Being Assessment (DAWBA)
	Main Findings on Internalizing Problems	In the adjusted analyses, persistent bed-sharers were at increased odds of presenting internalizing problems (OR=2.1; 1.4–3.1), as compared to non bed-sharers. Among the early-onset bed-sharers the OR for internalizing problems was 1.6 (1.2–2.1). Among the persistent bed-sharers, the OR for internalizing problems was 2.1(1.4-3.1)
	Confounders	Family income, schooling, age, marital status, skin color, parity, mood depression symptoms and smoking during pregnancy, and type of delivery.
	Quality Assessment	Fair
Cano, Acosta and Pulido (2018)[94]	**Country**	Colombia
	Language	Spanish
	Aims of Study	To identify, adapt, and establish evidence for the criterion validity of a screening tool for emotional and behavioral problems in children younger than 6 years old
	Type of Study	Cross-sectional study
	Sample	206 children 1.5-6 years old and their caregivers

Cano, Acosta and Pulido (2018)[94] cont.	Internalizing Problems	Validations of the Early Childhood Screening Assessment (ECSA)
	Associations, comparisons, or pathways examined	Contrast with variables of the CBCL 1.5-5
	Instrument	ECSA, CBCL 1.5-5
	Main Findings on Internalizing Problems	Three factors explain most of the variance. Common internalizing and externalizing symptoms loaded in more than one factor, not clearly distinguishing between them.
	Confounders	Not assessed
	Quality Assessment	Fair /Poor
Montoya et al. (2014)[89]	Country	Colombia
	Language	Spanish
	Aims of Study	To describe the cognitive, emotional, and behavioral characteristics, of a sample of 20 preschoolers.
	Type of Study	Cross-sectional study
	Sample	20 preschoolers between 3 and 5 years old, and their parents
	Internalizing Problems	Score for each dimension of internalization
	Associations, comparisons, or pathways examined	Description of the scores of internalizing problems as reported by parents and teachers
	Instrument	Behavior Assessment System for Children (BASC)
	Main Findings on Internalizing Problems	For parents, the main internalizing problem was somatization (mean=46.20). For teachers, the main internalizing problem was depression (mean=75.70). Mean scores were higher for teachers than for parents (no estimates)
	Confounders	Not assessed
	Quality Assessment	Poor
Corapci, Smith and Lozoff (2006)[90] .	Country	Costa Rica
	Language	English
	Aims of Study	To examine internalizing behavior problems (anxiety/depression) in early adolescence in relation to adversity in early childhood and child verbal competence
	Type of Study	Longitudinal
	Sample	191 Costa Rican children and their mothers, who were recruited in infancy from an urban community and assessed again at 5 and 11–14 years.
	Internalizing Problems	Total internalizing score
	Associations, comparisons, or pathways examined	Protective role of verbal competence in the relationship between adversity in childhood and internalizing problems in early childhood and early adolescence.

Corapci, Smith and Lozoff (2006)[90]	Instrument	CBCL
	Main Findings on Internalizing Problems	Verbal IQ was a moderator of early adversity on internalizing problems in early adolescence but not in early childhood, indicating that the same factor may act as either a protective or vulnerability factor in different periods of development.
	Confounders	Not assessed
	Quality Assessment	Poor
Albores et al. (2016)[81]	Country	Mexico
	Language	Spanish
	Aims of Study	To investigate the validity and internal consistency of the Mexican version of the CBCL/1.5 -5
	Type of Study	Cross-sectional study
	Sample	438 children (62 children suspected to be in the autistic spectrum, 376 not in the autistic spectrum) and their parents, aged 18 months to 6 years old
	Internalizing Problems	Total score for each internalizing problem and for each syndrome
	Associations, comparisons, or pathways examined	Comparisons of clinical vs. Community group
	Instrument	CBCL 1.5-5 and clinical interview
	Main Findings on Internalizing Problems	The internal consistency was high for internalizing problems (alpha=0.89). Test-retest using the interclass correlation coefficient (ICC) ≥0.95. Somatic complaints had higher reliability in boys than in girls. Anxiety and depression had better consistency when considered together. Report by mothers have higher internal consistency than report by fathers.
	Confounders	Not assessed
	Quality Assessment	Fair
Gil et al. (2018)[88]	Country	Mexico
	Language	Spanish
	Aims of Study	To analyze the association between emotional availability and children's problems; as well as the differences in the level of child externalizing and internalizing problems according to the interaction patterns.
	Type of Study	Cross-sectional study
	Sample	60 dyads of mothers and their children aged 4 to 5 years old in two preschools
	Internalizing Problems	Total score for internalizing problems and for each syndrome

Gil et al. (2018)[88] cont.	**Associations, comparisons, or pathways examined**	Variables of emotional availability of the mother and the child
	Instrument	CBCL 1.5-5
	Main Findings on Internalizing Problems	The mean score of internalizing problems was 56.38 (SD=9.08). Internalizing problems have significant inverse associations with child's ability to respond, child's involvement, child's general emotional availability, dyadic emotional avilability. Regarding symptoms, withdrawn is inversely associated with child's ability to respond, child's involvement and with child's general emotional availability. Anxiety/depression is inversely associated with ability to respond.
	Confounders	Not assessed
	Quality Assessment	Fair
Bárrig and Alarcón (2017)[93]	**Country**	Peru
	Language	Spanish
	Aims of Study	To determine the relationship between, social competence, and behavioral problems n preschoolers
	Type of Study	Cross-sectional study
	Sample	66 children between 2 and 6 years old, and their mothers in a preschool
	Internalizing Problems	Anxiety/ Withdrawn measured with a score
	Associations, comparisons, or pathways examined	Correlations with surgency, negative effect, intentional control
	Instrument	Social Competence and Behavioral Evaluation Scale (SCBE-30) adapted to Spanish
	Main Findings on Internalizing Problems	Surgency is correlated negatively with anxiety. There were no significant differences in the anxiety/withdrawn symptoms between boys and girls
	Confounders	Not assessed
	Quality Assessment	Fair

Table 4. Studies in LMIC in the European Region.

Wasserman et al. (2001)[103]	**Country**	Old Yugoslavia
	Language	English
	Aims of Study	To examine the contribution of maternal smoking during pregnancy and lead exposure to early child behavior problems
	Type of Study	Cohort Study
	Sample	Mothers with low lead exposure were enrolled since pregnancy, and their 191 children were assessed from 4 to 5 years old.
	Internalizing Problems	Total scores for internalizing problems and for each syndrome
	Associations, comparisons, or pathways examined	Associations between maternal smoking, cumulative lead exposure and child behavior problems
	Instrument	CBCL 1.5-5
	Main Findings on Internalizing Problems	With adjustment for both social factors and average lifetime BPb, prenatal smoking predicted significant increases in total score, in all subscales except for Somatic Complaints and Anxious/Depressed, and in both the Internalizing and Externalizing factors. The only statistically significant interaction with sex was for Somatic Problems [B= 0.18, S.E. = 0.08, P< .05]. Boys' level of Somatic Problems does not differ across maternal smoking status. With control for both social factors and smoking history, average lifetime BPb was significantly positively related to the Internalizing factor, The sex by lead exposure effect was not significant on the internalizing factors and none of the syndromes.
	Confounders	Child sex, ethnicity (language spoken at home: Albanian, Serbian, Other), home acceptance, and maternal education, age at assessment.
	Quality Assessment	Good
Ştefan and Avram (2017)[105]	**Country**	Romania
	Language	English
	Aims of Study	The purpose of this study was to investigate the relationship between attachment, emotion regulation(ER), and risk for internalizing/externalizing problems in typically developing children
	Type of Study	Cross-sectional study
	Sample	212 children aged 3 to 5 years old, through reports of their parents and teachers

Ştefan and Avram (2017)[105] cont.	**Internalizing Problems**	Total score of internalizing problems based on parent report, score based on teacher report, composite score
	Associations, comparisons, or pathways examined	Correlations of internalizng problems with age, attachment security, effective emotion regulation strategies, comforting, distraction, problem-solving. A mediation model in which the predictor was attachment security (X), the mediator was effective ER strategies (M). In another model, three mediators were simultaneously introduced in the statistical analyses. The predictor was attachment security (X), the mediators were comforting (M1), distraction (M2), and problem-solving (M3) (i.e., ER strategies which were initially included in the higher-order effective ER strategy to introduce two highly related outcome variables (internalizing and externalizing problems).
	Instrument	CBCL, C-TRF
	Main Findings on Internalizing Problems	Effective ER strategies were inversely associated with the combined teacher and parent ratings of internalizing problems. No significant direct effect was found between attachment security and internalizing problems. They found a significant indirect effect of attachment security on internalizing problems through effective ER) strategies (problem-solving).
	Confounders	Age
	Quality Assessment	Fair
Zeanah et al. (2009)[99]	**Country**	Romania
	Language	English
	Aims of Study	To determine whether removing young children from institutional care and placing them with foster families would reduce psychiatric morbidity at 54 months of age.
	Type of Study	Randomized controlled trial
	Sample	111 children living in institutions and 59 never institutionalized, and their caregivers or parents enrolled at 6-30 months and examined at about 54 months
	Internalizing Problems	Frequency of Internalizing disorders, depression disorders, anxiety disorders. Number of symptoms
	Associations, comparisons, or pathways examined	Prevalence comparisons between intitutionalized vs never institutionalized, and care as usual vs. foster care Comparisons in the number of symptoms of boys and girls
	Instrument	Preschool Age Psychiatric Assessment (PAPA)

Zeanah et al. (2009)	**Main Findings on Internalizing Problems**	Internalizing disorders are the most prevalent of the psychiatric disorders in all children. In children placed in care as usual, internalizing disorders are more common. In children placed in foster care, externalizing disorders are more common (32.4%). Children with any history of institutional rearing had more psychiatric disorders than children without such a history (53.2% versus 22.0%). Children removed from institutions and placed in foster families were less likely to have internalizing disorders than children who continued with care as usual (22.0% versus 44.2%). Boys were more symptomatic than girls regardless of their caregiving environment and, unlike girls, had no reduction in total psychiatric symptoms following foster placement
	Confounders	Not assessed
	Quality Assessment	Good
Kozlova, Slobodskaya, Gartstein (2019)[104]	**Country**	Russia
	Language	English
	Aims of Study	To examine the contribution of early temperament to mental health in preschool and school years
	Type of Study	Longitudinal
	Sample	96 children and their parents at age 7.1 months and 7.8 years in urban and rural areas
	Internalizing Problems	Emotional symptoms, peer problems, impact.
	Associations, comparisons, or pathways examined	Early effortful control as predictor of mental health in preschool and school age was. Negative affectivity as predictor of internalizing problems in later childhood. Sensitivity to slight stimuli from the external environment, as predictor of later internalizing problems. The lower-order trait of approach/positive anticipation, as a protective factor for internalizing problems.
	Instrument	Strengths and difficulties questionnaire (SDQ)
	Main Findings on Internalizing Problems	The strongest predictor of mental health in preschool and school age was early effortful control which contributed to both externalizing and internalizing problems
	Confounders	Not assessed
	Quality Assessment	Fair
Markóvic et al. (2016)[97]	**Country**	Serbia
	Language	English
	Aims of Study	To examine rates and distribution of emotional and behavioral problems among 4 to 6-year-old children. Comparisons with US children
	Type of Study	Cross-sectional study
	Sample	512 children aged 4 to 6 years old and their parents

Markóvic et al. (2016)[97] cont.	Internalizing Problems	Total score for internalizing problems and for each syndrome
	Associations, comparisons, or pathways examined	Differences by sex and comparisons with US children
	Instrument	CBCL 1.5-5 and the CTRF
	Main Findings on Internalizing Problems	17% of the children had clinically significant internalizing symptoms. The most common internalizing symptom is withdrawn (9.3%) and the least common is somatic complaints (2.4%). Serbian girls had significantly higher scores than Serbian boys. In the CRTF Serbian boys and girls had significantly higher mean scores in somatic complaints than boys and girls in the US. In the CBCL Serbian girls had significantly higher mean scores in somatic complaints than girls in the US In the CBCL Serbian boys and girls had significantly lower mean scores in emotional reactivity than boys and girls in the US.
	Confounders	Not assessed
	Quality Assessment	Fair/Good
Erol et al. (2005)[98]	Country	Turkey
	Language	English
	Aims of Study	Distribution and prevalence of parent-reported behavioral and emotional problems
	Type of Study	Cross-sectional study
	Sample	Final sample of 598 children aged 2 to 3 years old, and their parents. Nationally representative sample
	Internalizing Problems	Total score for internalizing problems and for each syndrome
	Associations, comparisons, or pathways examined	Differences by sex, age, race, urban residence, religion, employment
	Instrument	CBCL 1.5-5
	Main Findings on Internalizing Problems	Significant sex differences in the anxious/depressed score (multiple R=0.169), with girls having more problems than boys. Significant age differences in the somatic complaints(multiple R=0.169), with younger children having more problems than older children. Children from urban areas obtained significantly higher score on internalization than children from suburban and rural residence.
	Confounders	Not assessed
	Quality Assessment	Fair

Hesapciglou et al. (2017)[96]	**Country**	Turkey
	Language	English
	Aims of Study	To explore mother's whose psychiatric symptoms are related to child's internalizing and externalizing problems.
	Type of Study	Cross-sectional study
	Sample	Children aged 4-6 years old. 61 cases, 55 age-matched controls and their mothers.
	Internalizing Problems	Total score for internalizing problems, score for each symptom, and classification in terms of yes/no
	Associations, comparisons, or pathways examined	Association with mother's psychiatric problems
	Instrument	CBCL 4-18
	Main Findings on Internalizing Problems	Each symptom of internalization in children is significantly and positively associated with each psychiatric problem in mothers. Having child internalizing problems is significantly and positively associated with all psychiatric problems in mothers.
	Confounders	Not assessed
	Quality Assessment	Poor
Karabekiroglu (2009)[100]	**Country**	Turkey
	Language	English
	Aims of Study	To investigate the reliability and validity of the Turkish version of the brief infant–toddler social emotional assessment (BITSEA) in a community sample.
	Type of Study	Cross-sectional study
	Sample	462 children aged 12-42 months old, and their parents who applied for immunization in health centers
	Internalizing Problems	Total score for problems in BITSEA, total score for internalizing problems in CBCL and classification into clinical/subclinical problems
	Associations, comparisons, or pathways examined	Comparison with scores with the CBCL scores and clinical classification
	Instrument	The brief infant–toddler social and emotional assessment (BITSEA) and the CBCL 2-3
	Main Findings on Internalizing Problems	Mean score for the children in the sample was 6.85 ±4.54, with no significant differences by age or by sex. Total score in the BITSEA is correlated with internalizing problems, either reported by mothers or fathers
	Confounders	Not assessed
	Quality Assessment	Good

Yurdusen, Erol and Gencöz (2013)[102]	Country	Turkey
	Language	English
	Aims of Study	To examine the association between emotional and behavioral problems in preschool children and maternal attitudes
	Type of Study	Cross-sectional study
	Sample	204 preschool children aged between 18 and 71 months and their mothers
	Internalizing Problems	Total scores for internalizing problems
	Associations, comparisons, or pathways examined	Association between mother's parental attitudes, well-being measures and child behavior problems
	Instrument	CBCL 1.5-5
	Main Findings on Internalizing Problems	Mothers' rejection of their home- making roles and their level of anxiety were found to be significantly associated with their children's internalizing problems, and these two variables in total accounted for 29% of the variance for the internalizing problems of the children.
	Confounders	Not assessed
	Quality Assessment	Fair

Table 5. Study in LMIC in more than one region.

Rescorla et al. (2011)[82]	Country	More than 1 country
	Language	English
	Aims of Study	International comparisons were conducted of preschool children's behavioral and emotional problems as reported on the Child Behavior Checklist for Ages 1½–5 by parents in 24 societies.
	Type of Study	Ecological study
	Sample	24 countries. 6 LMIC: China, Kosovo, Iran, Peru, Taiwan and Turkey
	Internalizing Problems	Total scores for internalizing problems and for each syndrome
	Associations, comparisons, or pathways examined	Comparisons of mean scores in 24 societies
	Instrument	CBCL 1.5-5

Rescorla et al. (2011) (cont.)	**Main Findings on Internalizing Problems**	Turkey was the second highest-scoring society on Anxious/Depressed in this study and was fourth or fifth highest on the other three Internalizing syndromes. Internalizing, Externalizing, and the 13 narrow-band scales (seven syndrome scales, five DSM-oriented scales, and Stress Problems) all showed the same pattern of larger within society than between-society variation (i.e., their omnicultural standard deviations were much larger than the standard deviations of their omnicultural means) The six societies with the highest mean Internalizing scores (Singapore, Iran, Romania, Lithuania, Turkey, and Chile) did not differ significantly from each other
	Confounders	Not assessed
	Quality Assessment	Good

Table 6. Studies in LMIC in the Western Pacific Region.

Liang et al (2019)[107]	**Country**	China
	Language	English
	Aims of Study	To examine the associations between infant temperamental withdrawal and behavior problems during toddlerhood and to test the moderating effects of maternal sensitivity to infant distress (MSID), and toddlers' ability to delay gratification
	Type of Study	Longitudinal
	Sample	84 children and their mothers from two communities, two daycare centers, and two child healthcare networks, followed from 6 months to 2 years old
	Internalizing Problems	Total score for internalizing problems, classification into clinical/non-clinical concern
	Associations, comparisons, or pathways examined	Effect of Infant temperament withdrawal (fearful affect, shyness, social anxiety, and vigilance) on internalizing problems at 1 and 2 years old (T2 and T3) Moderating effect of MSID and toddler's ability to delay gratification
	Instrument	The Infant–Toddler Social and Emotional Assessment (ITSEA) ITSEA including three problem domains of internalization (26 items)
	Main Findings on Internalizing Problems	Infant temperamental withdrawal was positively associated with toddlers' internalizing problems at 1 year of age; however, when MSID was in the moderate range, the relation was negative, although not significantly.
	Confounders	Internalizing and externalizing problems at T1
	Quality Assessment	Good

Liu and Wang (2015)[109]	**Country**	China
	Language	English
	Aims of Study	To examine the mediating effect of parents' psychological aggression in the relationship between parenting stress and children's internalizing and externalizing problem behaviors 1 year later
	Type of Study	Cohort Study
	Sample	311 two-parent families with preschoolers ages 3-5 years old
	Internalizing Problems	total internalizing score, scores for each syndrome
	Associations, comparisons, or pathways examined	Predictive effects of both mothers' and fathers' parenting stress on children's internalizing and externalizing problem behaviors 1 year later testing the mediating role of mothers' and fathers' psychological aggression.
	Instrument	CBCL
	Main Findings on Internalizing Problems	The correlations among indicators of each latent variable were significant and in the expected direction. Psychological aggression partially mediated the relationship between parenting stress and children's internalizing and externalizing problem behaviors, only in mothers. For fathers, no significant direct or indirect effects of parenting stress in children's internalizing and externalizing problem behaviors were found.
	Confounders	Not assessed
	Quality Assessment	Good
Liu et al. (2013)[108]	**Country**	China
	Language	English
	Aims of Study	To examine the association between maternal environmental tobacco smoke (ETS) exposure during pregnancy and child behavior problems.
	Type of Study	Cross-sectional study
	Sample	646 dyads of mothers and children aged 5-6 years old
	Internalizing Problems	Total internalizing score, nonclinical/borderline/clinical range internalization
	Associations, comparisons, or pathways examined	Internalizing problems associated with child characteristics, and association between ETS exposure (yes vs. no)
	Instrument	CBCL 1.5-5
	Main Findings on Internalizing Problems	18% had internalizing problem scores in the borderline/clinical range. Internalizing problems in children of ETS exposed mothers were higher than those of children of unexposed mothers, but the difference was not statistically significant.

Liu et al. (2013)[108]	Confounders	Child sex and school area; parental education, occupation, and psychopathologic problems; maternal age during pregnancy; and father's current (postnatal) smoking status,
	Quality Assessment	Good
Liu et al. (2014a)[111]	Country	China
	Language	English
	Aims of Study	To investigate whether micronutrient deficiencies, specifically blood zinc and iron levels, will be associated with increased behavior problem scores, including internalizing and externalizing behaviors
	Type of Study	Cohort Study
	Sample	1,314 children ages 3-5 years old and their parents until their last months of preschool
	Internalizing Problems	Total internalizing score
	Associations, comparisons, or pathways examined	Behavioral outcomes regressed on low zinc and iron group
	Instrument	CBCL 1.5-5
	Main Findings on Internalizing Problems	Low zinc has a significant association with total behavioral problems. The model of internalizing score regressed on combined low zinc and iron showed living in the suburbs to be positively associated with internalizing problems.
	Confounders	Family size, sex, house size, mother's education
	Quality Assessment	Good
Liu et al. (2014b)[110]	Country	China
	Language	English
	Aims of Study	To examine the association between blood lead concentrations and behavioral problems in a community sample of Chinese preschool children.
	Type of Study	Prospective cohort study
	Sample	1,341 children at ages 3-5 years and their parents
	Internalizing Problems	Total internalizing score, scores for each syndrome, five DSM oriented scales
	Associations, comparisons, or pathways examined	Increase in score of internalizing problems with blood lead concentrations. Associations between blood lead and clinical behavioral problems.
	Instrument	CBCL 1.5-5/C-TRF (Caregiver- Teacher Report Form)

Liu et al. (2014b)[110] cont.	**Main Findings on Internalizing Problems**	Blood lead concentration had statistically significant harmful associations with scores on emotional, anxiety and pervasive developmental problems. One µg/dL increase of blood lead concentration resulted in a 0.32 and 0.25 increase of behavior scores on emotional reactivity, anxiety/depressed and pervasive developmental problems. Behavior scores for internalizing problems increased with blood lead concentration for girls at age 5 years (p=0.04) and age 4 years (p=0.048) Behavior scores for internalizing problems slightly increased with blood lead concentration for boys at age 5 years and slightly decreased for boys at age 4 years. Blood lead concentration was still significantly associated with increased odds for emotionally reactive (OR=1.10, 95%CI=1.02 – 1.19), anxious/depressed (OR=1.12, 95%CI=1.03 – 1.23), total internalizing problems (OR= 1.10, 95%CI= (1.03 – 1.18),as well as DSM-oriented anxiety (OR=1.10, 95%CI= 1.01 – 1.19) after adjusting by sex and other characteristics
	Confounders	Age at blood lead test, sex, residence, father's education, mother's education, father's occupation, parents' marital status, single child, and IQ
	Quality Assessment	Good

Chapter 3: Internalizing Problems in Preschool Boys and Girls in the City Of São Paulo, Brazil: Findings from the Child Behavioral Checklist 1.5-5 (CBCL 1.5-5)

3.1 Introduction

According to a 2017 WHO report[9], Brazil has the highest prevalence of anxiety worldwide (9.3%), the highest associated disability, and the fifth-highest prevalence of depression (5.8%). These estimates of internalizing problems refer to people aged 15 or older. Internalizing problems (clinically significant symptoms) in young children, such as preschoolers, are rarely the focus of attention[125], partly because they are largely unable to report their symptoms accurately. Internalizing problems in preschoolers have to be reported by a third person, such as a parent or caregiver[126]. They are also not overtly socially disruptive behaviors like externalizing problems (aggressive behaviors or attention problems)[4].

A systematic review of the literature was conducted up to February 2020 on internalizing problems in preschoolers (ages 1.5-6 years old) in Low and Middle-Income countries (LMIC). This review identified only six studies[8-11,15,16] in Brazil where estimates of prevalence (between 7.8 %[84] and 9.7%[83]) or examination of predictors of internalizing problems in non-specific samples could be isolated[83,84,91,92].

According to a study comparing data from two birth cohorts from 1993 and 2000 in the city of Pelotas[84], the prevalence of internalizing problems in preschoolers did not increase significantly in eleven years. However, they reported a 10% increase across time in the scores, meaning that internalizing problems increased in severity[84]. This increase is concerning due to their potential continuation in adolescence and their potential development into mental disorders in later years [5-7]. Unfortunately, not enough research is done on internalizing problems in preschoolers in Brazil; hence, more studies on the topic are required to inform prevention and treatment efforts for young children.

There were no studies on the factor structure of internalizing problems or validated scales of behavioral problems in preschoolers in Brazil in the review. However, the Child Behavioral Checklist (CBCL 1.5-5) [28], the most commonly used scale for behavioral problems in preschoolers worldwide, was used in three[85,87,92] of the six Brazilian studies included in the review. In addition, two studies used the CBCL 4-18 [83,84].

In the CBCL 1.5-5[28], behavioral problems in preschoolers are categorized by a seven-factor structure: there are two factors for externalizing problems, four factors for internalizing problems, and a single factor for sleep problems. The two first-order factors or syndromes of externalization are: "Aggressive Behaviors" and "Attention Problems." The four first-order or syndromes of internalization are: "Anxiety/Depression," "Somatic Complaints," "Withdrawn," and "Emotionally Reactive." A study tested the seven-factor model of the CBCL 1.5-5 with data from 23 countries in Asia, Australasia, Europe, the Middle East, and South America (not including Brazil) [40]. The seven-factor model was a good fit for the data in each of these countries. In Latin America, there were reports of the construct validity of the CBCL 1.5-5 in Chile[127](a High-Income country) and a report of criterion validity in Mexico[81].

It is currently unknown if the construct of internalizing problems measured by the CBCL 1.5-5 is valid in Brazilian preschoolers. It is also unknown if the four-factor model could be misspecified for this population (for example, incorrectly specifying the number of factors or omitting cross-loadings of items[128]). One study[37] provided evidence that in older children in Brazil, a general psychopathology factor ("P factor"[38]) accounts for most of the variance in the Development and Well-Being Assessment (DAWBA[129]). The DAWBA is a structured interview focused on current problems causing significant distress or social impairment. The study was conducted in children in São Paulo and Porto Alegre[37] in a community sample of 2,512 children aged 6 to 12 years old, randomly selected or at high risk, nested in a larger sample. Although they did not use the CBCL or included preschool children, having three specific factors (fear, distress, and externalizing problems) accounted for little residual variance than one factor,

similar to two studies in adolescents and adults in high income-countries[38,39]. Whether the model with a general P factor[17] for all behavioral problems or the hierarchical model of the CBCL is the best fit for Brazilian preschoolers remains unexamined. The structure of the CBCL 1.5-5 in Brazil could be similar to the structure of the CBCL 1.5-5 in other countries in Latin America. Brazilian studies of a previous version of the CBCL, the CBCL 4-18 (for children aged 4 to 18 years old)[130,131], validated a hierarchical model and supported the multicultural robustness of the CBCL 4-18 in Brazil[132].

Another unexplored aspect of internalizing problems in Brazil is the difference in internalizing problems by sex. In Brazil, as in several countries[41-44], adolescent and adult females have a significantly higher prevalence of internalizing disorders than adolescent and adult males, at least twice their prevalence. Adolescent and adult males are less likely than females to search for a treatment for internalizing disorders or discuss their symptoms[133] (being withdrawn). Females are more likely than males to develop conditions usually linked to internalizing disorders, such as Irritable Bowel Syndrome[134] (having somatic complaints). One likely explanation for the dissimilarities is the different gender roles and expectations in society[135-137], leading females and males to be exposed to different risk factors (such as males being the providers and women being the caregivers). An exploration of differences in the structure and characteristics of internalizing problems in females and males in preschool years, when children are still developing their gender identity[138], could help understand the mechanisms that lead to this disproportion in the prevalence estimates of internalizing disorders in adolescent and adult females versus males.

Considering that: a) research on internalizing problems in preschoolers in Brazil is scarce, b) internalizing problems are rarely the focus of research in this age group compared to externalizing problems, c) there is a lack of valid measures of internalizing problems in this population, d) there are potential differences by sex on internalizing problems at an early age, e) the CBCL 1.5-5 is the most widely used scale to measure internalizing problems, and f) understanding the construct of internalizing

problems in preschoolers could guide prevention and treatment efforts to reduce the incidence of internalizing disorders in Brazil; the present study focused on analyzing the structure and characteristics of internalizing problems in the CBCL 1.5-5 differentially by sex of a representative sample of preschoolers in the Brazilian city of Embu das Artes, São Paulo. Therefore, this study does not intend to validate the full CBCL 1.5-5 questionnaire for use in Brazil but to understand further preschoolers' internalizing problems in São Paulo, Brazil.

3.2 Methods

Data were obtained from the Preschool Mental health Study (PreK survey) [58,139], with previous authorization from the study's principal investigators.

The PreK Survey

The PreK survey[58,59,139] is a 2015 cross-sectional study on a sample of 1,292 preschool children (666 boys and 626 girls) aged 4-5 years old and their caregivers in Embu das Artes, a city in the metropolitan area of São Paulo, Brazil. The study was developed by researchers at the Psychiatry and Preventive Medicine departments of the *Universidade Federal de São Paulo* and collaborators at Columbia University Mailman School of Public Health and Johns Hopkins Bloomberg School of Public Health. Given that mental illness starts early in life and disproportionately affects children from LMIC, the main objective of the PreK survey was to assess the prevalence rates of internalizing and externalizing problems (clinically significant symptoms) and socio-emotional development delays among a representative sample of public preschool children aged 4-5 years in a poor urban region of Brazil[59].

Using an online database from the Brazilian National Institute of Educational Research, all public preschools in Embu das Artes were identified. The sample was a randomly recruited representative sample of the 4-5-year-old population using a stratified random sample of public preschools/ childcare centers, selected with a probability proportional to the number of 4-5-year-olds in each school within

census tracts. Trained health professionals from the Federal University of São Paulo collected data using face-to-face interviews in Portuguese within preschools. The study included the Brazilian Portuguese version of the CBCL 1.5-5[28]. Based on the CBCL scores, the six-month prevalence was 25.4% for internalizing problems, 12.1% for externalizing problems, and based on the Ages and Stages Questionnaires: Social-Emotional (ASQ:SE)[140], the prevalence of socioemotional development delays was 30.3%.

Instrument

The CBCL 1.5-5[28] is applied to primary caregivers of children aged 1.5 to 5 years old. It examines three dimensions of problematic behaviors in preschool children as observed by their parents: Internalizing, externalizing, and sleep problems. It consists of 99 items, each with three possible choices: not true, sometimes true, always true (0,1,2). The raw total score for each syndrome (first-order factors grouping behavioral problems) is calculated by summing the scores of 1 and 2 for all items. Each raw total score is then converted to a T score, which indicates the same degree of elevation on each scale relative to their peers. The T score indicates if the scores are in the normal, subclinical, or clinical range, which determines if the person who completed the CBCL reported enough problems to be of clinical concern.

The four syndromes of internalization (Somatic Complaints, Emotionally Reactive, Withdrawn, and Anxiety/Depression) and the corresponding symptoms are described in table 7. The terms "syndromes" and "first-order factors" are synonymous in the CBCL, and they will be used interchangeably throughout this text.

Table 7. Internalizing questions in the CBCL.

Internalizing questions in the CBCL (3-level responses: Never true, Sometimes true, Always true)			
Somatic Complaints	**Emotionally Reactive**	**Withdrawn**	**Anxiety/ Depression**
1. Aches	21. Disturbed by change	2. Acts too young	10. Clings
7. Can't stand things out of place	46. Twitches	4. Avoids eye contact	33. Feelings Hurt
12. Constipated	51. Panics	23. Doesn't answer	37. Upset by Separation
19. Diarrhea	79. Shifts Between Sad- Excited	62. Refuses active games	43. Looks Unhappy
24. Doesn't eat well	82. Moody	67. Unresponsive to affection	47. Nervous
39. Headaches	83. Sulks	70. Little afection	68. Self-conscious
45. Nausea	92. Upset by New	71. Little interest	87. Fearful
52. Painful bowel movements	97. Whining	98. Withdrawn	90. Sad
78. Stomach aches	99. Worries		
86. Too concerned with neatness or cleanliness			
93. Vomits			

Data Analysis

The analyses were conducted in four stages to examine the structure of internalization in the CBCL 1.5-5. Analyses were based on Confirmatory Factor Analyses (CFA). CFA postulates certain relationships among the observed and the latent variables, assuming a pre-specified pattern for the model parameters (factor loadings, structural parameters, residual variances)[141,142]. The number of latent variables and indicators that were used to measure each variable were shown in advance.

Findings in a stage guided the analyses in the following stages. The stages are summarized in figure 2. In stage 1, all 60 internalizing and externalizing questions of the CBCL were included to test if a two-factor model (internalization and externalization, model 2a) was a better fit for behavioral problems than a model with only one factor (model 1). The hypothesis for this first stage was: Based on the estimates of the Chi-Square difference test (at a 5% level of significance) and comparisons of other fit indices, Model 2a would have a significantly better fit than Model 1.

Externalizing questions were excluded in stage 2 since the focus of this study was internalizing problems, and Model 2a was a better fit than model 1. Therefore, only the 36 questions on internalization were included. The fit of two models (Model 2b and 3) were compared. Model 2b consisted of only one internalization factor, and model 3 was a hierarchical model of four first-order

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factors ("Anxiety/Depression," "Somatic Complaints," "Withdrawn," and "Emotionally Reactive") and one second-order factor for all internalizing problems. The hypothesis for this stage was: Based on the estimates of the Chi-Square difference test (at a 5% level of significance) and comparisons of other fit indices, Model 3 would have a significantly better fit than Model 2b.

Since Model 3 was a better fit than Model 2b, in stage 3, multigroup CFA was conducted to assess configural and metric invariance by the sex of preschoolers. Configural Invariance[143,144] means that the items measure the same construct in boys and girls (i.e., are best explained by the same model: four first-order factors and one-first order factor). Metric invariance[144] means that the factor loadings on the items are equivalent across groups. The hypotheses were that configural and metric invariance by sex would not be rejected based on non-significant Chi-Square tests (at the 5% level), and on the examination of model fit indices such as the comparative fit index (CFI), TLI, SRMR, and the Root Mean Square Error Approximation (RMSEA)[145].

Finally, in stage 4, despite not rejecting partial metric invariance, estimates for each syndrome were obtained separately for boys and girls based on factor loadings, followed by a description of the main factors and symptoms in boys and girls. For this stage of analysis, the hypothesis was that the main syndrome (the factor most endorsed factor and with the highest loadings) for both boys and girls would be "Anxiety/Depression." Other hypotheses were that in girls, the factor "Somatic Complaints" would have a greater correlation with the other factors than in boys, and, in boys, the factor "Withdrawn" would have a greater correlation with the other factors than in girls.

All CFA analyses were conducted in Mplus Version 8.3[145,146], which takes into account the survey's design effects (data were clustered by school), including parameter as well as standard error estimation and model fit calculations. The default estimator for the analyses was the variance-adjusted weighted least squares (WLSMV). This robust estimator does not assume normally distributed variables

and provides the best option for modeling categorical or ordered data. Standard indices such as Chi-square, comparative fit index (CFI), Root Mean Square Error Approximation (RMSEA), and SRMR were used to assess the goodness of fit in CFA. A CFI > 0.95 and SRMR <0.05 would indicate a good model fit, and an SRMR<0.08 would indicate an acceptable model fit[36]. The calculation of scores in stage 4 was done using SAS 9.4[147].

According to Kline (2015)[142], there should be at least ten people per item in CFA. Therefore, the sample size of 1,292 children (666 boys and 636 girls) was appropriate for the analyses. In stage 1, there were about 22 people per item (60 internalizing and externalizing questions). In stage 2, there were about 35 people per item (36 internalizing questions). In stages 3 and 4, there were about 18 people per item in the boy and girl groups. There was no missing data in these analyses. The CBCL 1.5-5 questionnaire was not validated as a whole due to the following reasons: a) In the multigroup analyses, the study's sample size was not large enough for the 99 total items (less than seven people per item); b) sleep problems are all symptoms related to one particular event and are therefore more specific than internalizing and externalizing symptoms, and c) this allowed to place greater emphasis on internalizing problems than on externalizing problems.
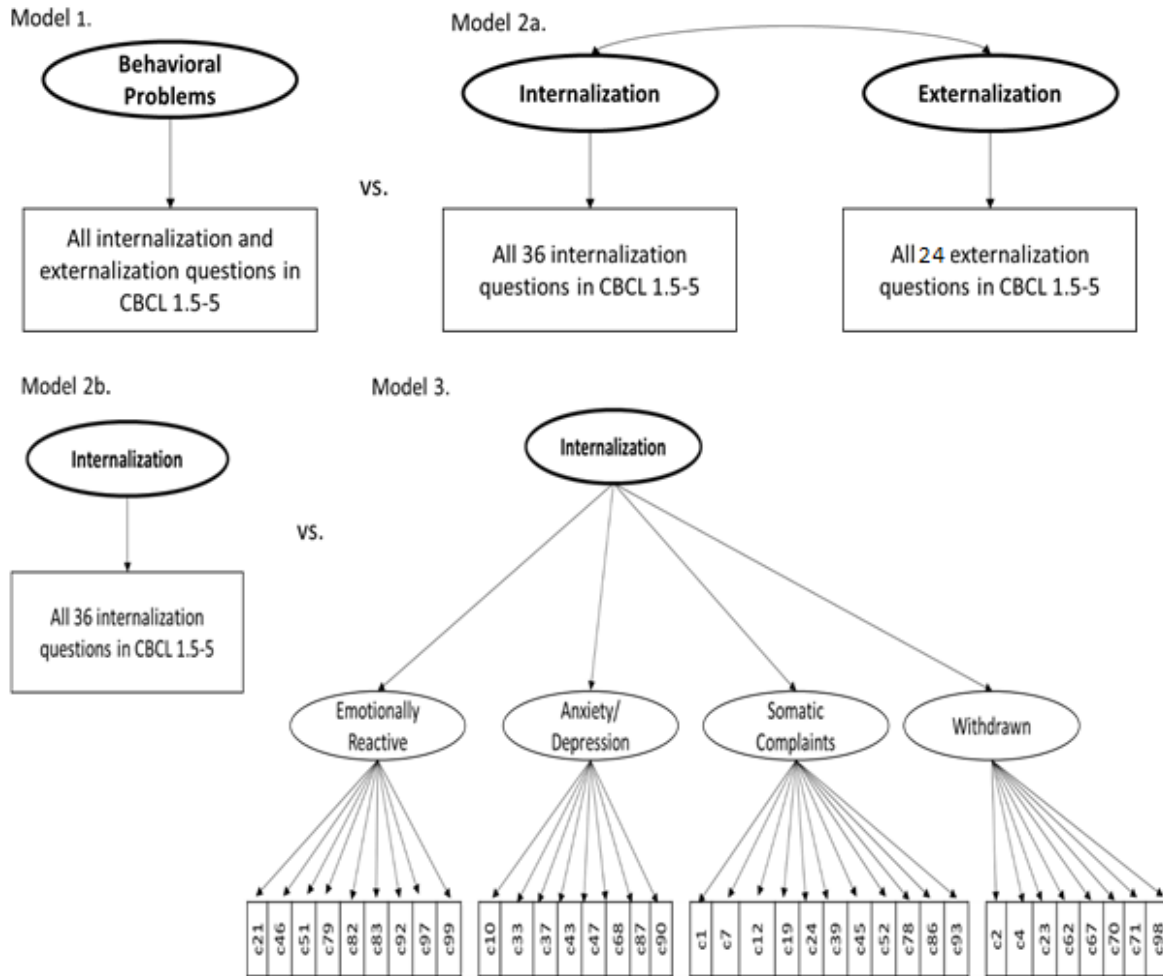
Stage 1: Model 1 vs. Model 2a

Stage 2: Model 2b vs. Model 3

Stage 3: Model 3 for boys vs. girls. Multigroup CFA.

**Stage 4:** Calculation of scores for Model 3 separately for boys and girls.

Figure 2. Models and Stages of the analyses.

3.3 Results

As previously stated, throughout the text, syndrome and factor will be used interchangeably.

Syndrome is the name that the authors give to the first-order factors in the CBCL 1.5-5[3].

Stage 1

As expected in large samples, Chi-square tests of model fit were significant for Model 1 (one factor for all items) and Model 2a (two factors)[144]. However, there was a significant decrease in the Chi-Square between Model 1 and 2a (Chi-Square difference test=147.052, df=1, p<0.001), indicating a better fit of Model 2a. Other fit indices, such as CFI/TLI, RMSEA, and SRMR, were considered to assess the fit of each model. Both models had an acceptable fit based on the CFI/TLI (>0.90) and the SRMR (<0.08), and a good fit based on the RMSEA (<0.06). Since Model 2a had better fit indices than Model 1 (see table 8), it was selected in this stage, indicating that internalizing problems is a correlated but different construct than externalizing problems.

Stage 2

Models 2b (one factor including all internalizing problems) and Model 3 (four first-order factors and one second-order factor) were compared. After an examination of the R-square, the item "Can't stand things out of place (item 7)" and the item "Too concerned with cleanliness and neatness (item 86)" explained little of the variance of the factor of internalization (each explained less than 7%). Hence, these two items were excluded from the analyses, improving the fit of Model 2b and Model 3. In Model 2b, SRMR went from 0.081 to 0.076, and in Model 3, the SRMR went from 0.077 to 0.062.

Models 2b and 3 were significantly different as per the Chi-Square difference test (420.149, df=4, p<0.001), and model 3 had better fit indices (see table 8), as such, model 3 (the hierarchical model) was selected. This finding indicates that there is one second-order factor of internalization that the four first-order factors can explain: "Anxiety/Depression, Emotionally Reactive, Withdrawn, and Somatic Complaints," endorsing the structure for internalizing problems in the CBCL 1.5-5.

Stage 3

Model 3 was assessed separately for boys and girls. When running the second-order factor model in boys, there was a warning about a correlation higher than 1.0 between the factor "Anxiety/Depression" and the other factors. Upon exploration of all the items of the "Anxiety/Depression" factor, the question "Is the child nervous or tense" (item 47) had a higher correlation with the factor "Emotionally Reactive" and a higher factor loading than with the factor "Anxiety/Depression" (r=0.754 vs. r=0.643, factor loadings: 0.748 v. 0.734). Since the question "Is nervous or tense" also had a higher correlation with the factor "Emotionally Reactive" (r=0.683 v. r=0.646) in girls, the question was moved to that factor, and the model ran without further problems.

Table 8. Fit indices of Models after CFA.

Fit índices	Internalizing and Externalizing		Only internalizing	
	Model 1	Model 2a	Model 2b	Model 3
CFI	0.917	0.928	0.925	0.962
TLI	0.914	0.926	0.92	0.959
RMSEA	0.021	0.02	0.025	0.018
AIC	114187.877	113622.208	60132.129	59510.94
BIC	115117.387	114556.883	60658.851	60058.318
SRMR	0.079	0.075	0.076	0.062
Chi-Square DifferenceTest	147.052, df=1, p<0.001		420.149, df=4, p<0.001	

Model 1: one factor for all, **Model 2a:** two factors (internalization and externalization), **Model 2b:** one factor for internalization, **Model 3:** four-first order factors, one second-order factor for internalization.

The item "Nausea, feels sick without a medical cause (item 45)" was endorsed by only 5% of the respondents (6% of boys and 4% of the girls). Therefore, the item was removed, improving model fit decreasing from an estimated SRMR of 0.062 to 0.060, as seen in table 9.

Table 9. Fit indices for Model 3 in Multigroup CFA.

Fit indices*	Both	Boys	Girls
CFI	0.0963	0.961	0.957
TLI	0.0961	0.958	0.954
RMSEA	0.018	0.018	0.019
AIC	59297.989	30921.846	28226.432
BIC	59829.876	31385.479	28683.685
SRMR	0.060	0.069	0.076

*Removing item 45 and changing item 47 from "Anxiety/Depression" to "Emotionally Reactive."

The multigroup analyses of configural and metric invariance led to the non-rejection of configural invariance and the non-rejection of metric invariance. Regarding configural invariance, despite a significant Chi-Square test, the model had a good fit, with good CFI (0.958) TLI (0.955), RMSEA(0.19), and an acceptable SRMR(0.072). Therefore, configural invariance was not rejected. The factor loadings of the model combining boys and girls can be seen in figure 3.

Regarding metric invariance, the assessment of the metric model against the configural model yielded a significant Chi-Square (44.045, df=29, p=0.0363) and an acceptable fit (SRMR=0.074). Despite the significant Chi-Square, upon exploring the factor loadings for each item in boys and girls, they were considerably similar (see table 10), and the metric invariance was not rejected. However, due to the removal of items throughout the analyses, only partial configural and metric invariance were attained[144]. Then, fit tests for the final model were estimated, and despite the non-significant differences in the factor loadings on boys and girls , the scores were calculated separately for boys and girls to have the most accurate results by sex .
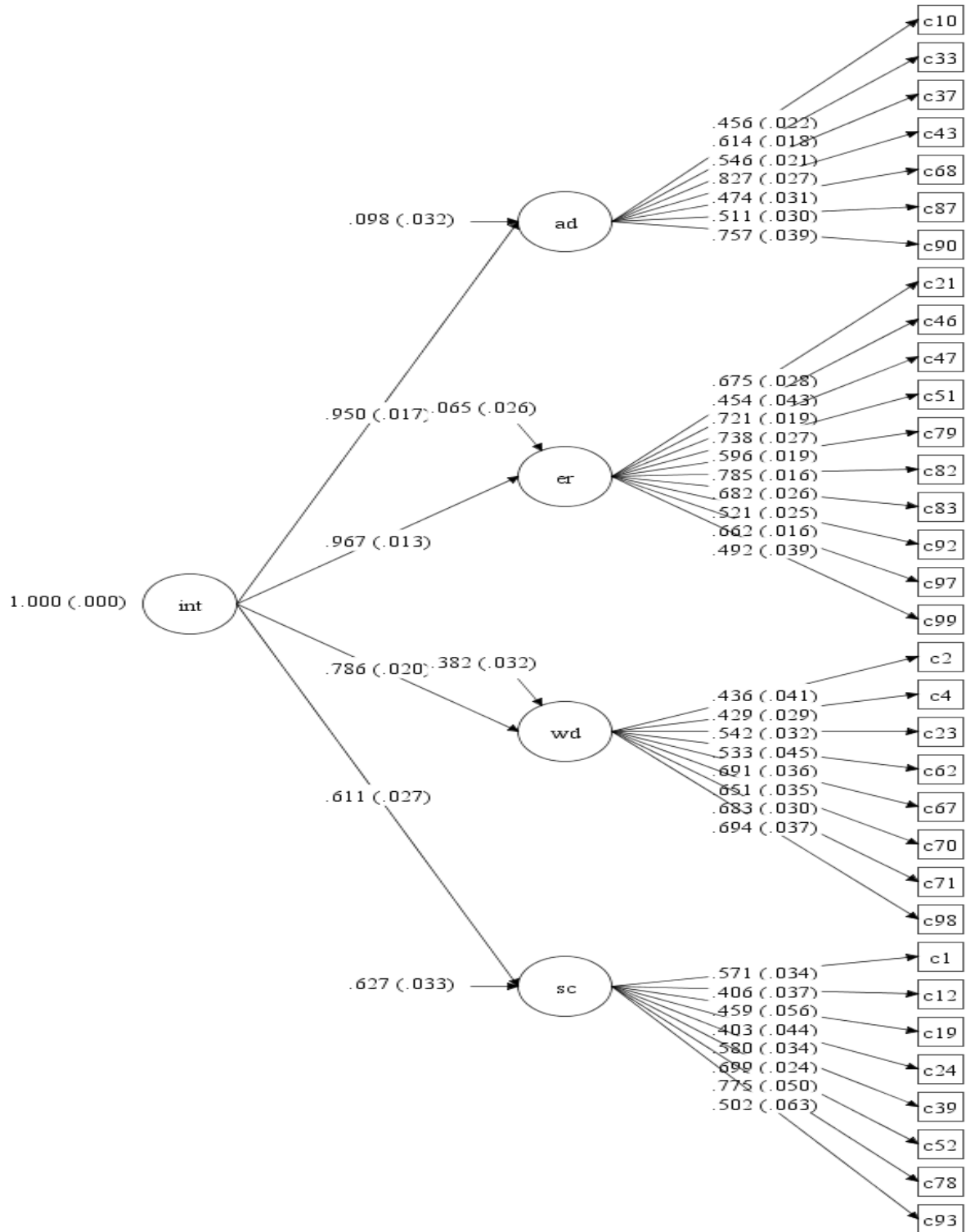
int: "Internalization," ad: "Anxiety/Depression," er: "Emotionally Reactive," wd: "Withdrawn," sc: "Somatic Complaints.Figure

Figure 3. Factor Loadings for the Selected Model Combining Boys and Girls.

Table 10. Factor Loadings for the Selected Model (Model 3) in Boys and Girls.

Syndrome	Item	Boys	Mean	Girls	Mean
"Anxiety/Depression"	CBCL10	0.413		0.491	
	CBCL33	0.572		0.675	
	CBCL37	0.589		0.491	
	CBCL43	0.857	0.588	0.801	0.603
	CBCL68	0.454		0.476	
	CBCL87	0.480		0.533	
	CBCL90	0.749		0.755	
"Emotionally Reactive"	CBCL21	0.686		0.668	
	CBCL46	0.526		0.377	
	CBCL47	0.748		0.685	
	CBCL51	0.698		0.785	
	CBCL79	0.561	0.6345	0.605	0.6267
	CBCL82	0.803		0.743	
	CBCL83	0.655		0.72	
	CBCL92	0.596		0.455	
	CBCL97	0.624		0.694	
	CBCL99	0.448		0.535	
"Withdrawn"	CBCL2	0.476		0.375	
	CBCL4	0.46		0.413	
	CBCL23	0.572		0.497	
	CBCL62	0.584	0.604375	0.465	0.54925
	CBCL67	0.687		0.716	
	CBCL70	0.659		0.624	
	CBCL71	0.732		0.616	
	CBCL98	0.665		0.688	
"Somatic Complaints"	CBCL1	0.480		0.633	
	CBCL12	0.331		0.454	
	CBCL19	0.462		0.495	
	CBCL24	0.402	0.508625	0.375	0.571875
	CBCL39	0.474		0.625	
	CBCL52	0.674		0.726	
	CBCL78	0.731		0.805	
	CBCL93	0.515		0.462	
Internalization	"Anxiety/Depression"	0.956		0.953	
	"Emotionally Reactive"	0.952		0.993	
	"Withdrawn"	0.802		0.794	
	"Somatic Complaints"	0.631		0.635	

It was hypothesized that the factor "Somatic Complaints" would have a higher correlation with the other factors in girls than in boys, and the factor "Withdrawn" would have a higher correlation with the other factors in boys than in girls. However, although the correlation estimate of "Somatic Complaints" with the factors was indeed higher in girls than in boys (r=0.635 vs.r=0.631), and the correlation estimate of "Withdrawn" with the factors was higher in boys than in girls(r=0.802 vs. r=0.794), the estimates were only marginally different. Thus, there is not sufficient evidence to support the hypotheses.

Regarding the frequency of the symptoms, in both boys and girls, the most frequently endorsed symptoms (answered with sometimes or always) were "Feelings are easily hurt" (74% of girls and 70% of boys), and "Sulks easily" (64% of boys and girls). The least endorsed symptom was "Is unhappy, sad or depressed" (4.5% of girls and 6.4% of boys). The most frequently endorsed factor in boys and girls was "Anxiety/Depression" (symptoms for this factor were endorsed on average by 43% of the girls and 42% of the boys).

In both boys and girls, the factors "Anxiety/Depression" and "Emotionally Reactive" were highly correlated (r=0.95). In girls, the syndrome "Emotionally Reactive" had the highest mean loadings (0.63), the highest mean correlation with all the factors (r=0.84), the highest correlation (r=0.99) with the second-order factor, and it explained the most variance in the model. In boys, the highest mean loadings were for "Emotionally Reactive" and for "Withdrawn"(see table 10), but correlation estimates with the other factors were higher for the syndrome "Anxiety/Depression."

The scores were calculated based on factor loadings separately for boys and girls to have the most accurate estimates by sex. If all symptoms were endorsed with "Always true," in girls, the maximum possible score would have been 33.30, and in boys, the maximum possible score would have been 32.84.

In order to have comparable scores for both boys and girls, percentages of the maximum possible scores were obtained. The average percentage points of internalizing problems in girls was 19.42 (Q1:10.3, median: 16.9, Q3:26.23), and in boys, the average was 19.22 (Q1:9.81, median: 15.70, Q3:25.09). Based on the third quartile (Q3) estimates, 26.2 points or higher were considered high scores for girls, and 25.1 points or higher were considered high scores for boys.

Table 11. Mean Scores of Internalization by Sex of Preschoolers.

Syndrome	Girls	Boys	t(df)	P
Anxiety/Depression	26.03	23.89	6.09(29)	0.001*
Emotionally Reactive	22.89	23.34	-1.31(29)	0.2002
Withdrawn	10.76	13.19	-10.94(29)	0.001*
Somatic Complaints	13.22	11.20	8.14(29)	0.001*
Total Internalizing Problems	19.42	19.18	0.97(29)	0.339

** Significant at the 1% level

As seen in Table 6, regarding each syndrome, girls had significantly higher estimates on "Somatic Complaints" (13.2 vs. 11.2) and "Anxiety/Depression" (26 vs. 23.9) than boys. Boys had significantly higher estimates on the "Withdrawn" (13.2 vs. 10.8) and the "Emotionally Reactive" (23.3 vs. 22.9) syndrome than girls.

Summary of Findings

The two-factor model (internalizing and externalizing problems) was a better fit than a one-factor model for all behavioral problems. This finding evidenced that internalizing and externalizing problems are correlated but distinct constructs.

Removing all externalizing questions, the hierarchical model (four first-order factors (syndromes) and one second-order factor) had a better fit than a one-factor model for all internalizing

problems. This finding evidenced that the internalizing problems in preschoolers in the population of Embu are explained by different syndromes.

In multigroup CFA, the non-rejection of configural invariance implies that the construct of internalizing problems is not different in preschool boys and girls. The non-rejection of metric invariance suggests that the factors do not have different loadings in boys and girls, meaning that boys and girls have the same syndromes.

The "Anxiety/Depression" and the "Emotionally Reactive" factors are strongly correlated with the other factors, and they are the most frequently endorsed. Both are the main syndromes in boys and girls.

Boys and girls have similar total scores for internalizing problems, as well as similar correlation estimates between the factors. However, it is relevant to note that preschool boys and girls have significant differences in the estimated mean scores for three out of four syndromes. The score for the syndrome "Emotionally Reactive" was not significantly different in boys and girls. The most notable differences are that the boys have higher "Withdrawn" scores than girls, and girls have higher "Somatic Complaints" scores than boys (see table 11).

3.4 Discussion

The selected model of the structure of internalizing problems in preschoolers in São Paulo, a hierarchical model with four first-order factors or syndromes ("Anxiety/Depression," "Somatic Complaints," "Withdrawn" and "Emotionally Reactive") and one second-order factor (internalizing problems), is in tune with previous findings[65] with the CBCL 1.5-5. It differs from p-factor proponents, who recommended that all behavioral problems be considered only one factor of psychopathology[38-4].

This finding suggests that using adapted versions of the CBCL 1.5-5 in São Paulo to measure internalizing problems in preschoolers would be appropriate despite the lack of studies on its validity. It also suggests that externalizing symptoms should always be measured when studying internalizing symptoms since they are distinct problems that are highly correlated.

Analyzing each syndrome rather than using a single score for internalizing problems leads to a better understanding of the construct of internalizing problems in these children. In this study, two highly correlated syndromes, "Anxiety/Depression" and "Emotionally Reactive," explain most of the variance of the internalizing problems in preschool children. Hence, the two syndromes are the core of internalizing problems in these children, and their prevention and treatment should be prioritized over the syndromes of "Withdrawn" and "Somatic Complaints" since they could very well be reduced when Anxiety/Depression are treated. Moreover, if, for example, a child tends to be withdrawn, it is essential first to identify if they could also have symptoms of Anxiety/Depression instead of trying to find several activities that could be more appealing to the child. Common recommendations for symptoms of "Anxiety/Depression," such as validating the child's emotions[148] and strengthening the bond with caregivers and teachers[149,150], could also result in the child being more engaged in activities and more affectionate toward others. However, since not all the symptoms arise from the same cause, it is suggested that future studies examine the potential predictors of internalizing problems in these children to plan for more effective preventive and treatment efforts.

The CFA was a useful method to identify items that did not explain much of the construct of internalizing problems. Upon a review of those items, it was clear that their inclusion in the analysis was not theoretically sound. The analyses showed that the items "Can't stand things out of place" and "Too concerned with cleanliness and neatness" explained less than 7% of the internalizing factor, and they led to worse fit estimates in all the models. These two symptoms seem to refer to obsessive thoughts or compulsions rather than "Somatic Complaints" as described in the ASEBA guidelines[28]. Studies on the

CBCL 4-18[151-153] include these questions in screenings for obsessive-compulsive disorder (OCD). It is recommended that for more accurate estimates of internalizing problems, these two questions be excluded from the analysis since they could be part of a separate construct. In addition, there could be low endorsement because the onset of problematic OCD-related symptoms usually occurs after 16 years old[154].

Despite a significant estimate in a Chi-square test, configural invariance was not rejected because other estimates showed that the hierarchical model is a good fit for internalizing problems for boys and girls. The model had better fit indices in boys than in girls; however, some high correlations were problematic in boys, and deleting or moving an item was necessary to ensure an appropriate fit of the model for both groups. For researchers interested in this topic, it is recommended to examine the correlation of the items in the "Anxiety/Depression" and the "Emotionally Reactive" syndromes. The two were only marginally distinguishable in the analyses, especially in boys.

Metric invariance was also not rejected because the model had appropriate fit indices in boys and girls, implying that the internalizing syndromes have the same structure in boys and girls. Since the focus of this study was to increase the understanding of the structure of internalizing problems by sex, it was decided to obtain the most accurate estimates possible accounting even for minimal differences, and the scores were calculated from factor loadings separately for boys and girls. However, since the differences in the estimates of boys and girls were negligible, it is recommended to continue calculating the scores as recommended in the CBCL 1.5-5 guidelines[28], not stratifying by sex. The calculated scores were standardized to make them comparable, and they were only marginally different in girls versus boys (19.42 vs.19.18). There is no evidence to suggest that the disparate rates of total internalizing problems between females and males seen in adolescents and adults are observed from an early age in this sample.

There is no sufficient evidence to suggest that the "Withdrawn" factor has a greater association with total internalizing problems in boys than in girls or that the "Somatic Complaints" factor has a greater association with total internalizing problems in girls than in boys. However, the mean scores in boys and girls in the two syndromes had a significant difference of more than two points. These findings suggest that there are more boys than girls with clinically significant "Withdrawn" syndrome and that there are more girls than boys with clinically significant "Somatic Complaints" syndrome. Interestingly, these findings, along with the differences in "Anxiety/Depression" (significantly higher in girls than in boys), indicate that boys and girls can have disparate estimates of specific internalizing syndromes even in preschool years, when there have been fewer exposures to gender norms than in adolescence and adulthood[155], and they have not yet been through puberty[156,157]. Thus, the differences in the prevalence of syndromes in earlier years may lead to different psychopathology risks and related conditions in later years through different pathways.

Since it was estimated that preschool girls have higher scores than boys in "Anxiety/Depression" and "Somatic Complaints," it is possible that the lack of focus on these problematic behaviors has led to their normalization in girls (it is usually expected that females be "more emotional" than males[158], even in childhood and adolescence). Females could consequently learn inappropriate coping skills when facing stressful situations[159], which summed to the expectation that they juggle several responsibilities at home and at work[160] may lead to higher rates than males in anxiety/depression and their related conditions (such as fibromialgya[161] and severe gastrointestinal symptoms[162,163]) in later years.

Since it was estimated that preschool boys have higher scores than girls in the "Withdrawn" syndrome, from an early age, boys can start learning to hide their feelings and seem stronger[158]. In adolescence and adulthood, males are less likely than females to seek treatment or analyze their emotions[133]. They are expected by society at large, particularly less gender-egalitarian societies, to be more competitive and successful than their female counterparts. Because of this, they could either be

more reactive when they underachieve[158] or disregard several problems until they become

unmanageable, potentially increasing their suicide risk compared to females[164-167].

The different prevalence of the internalizing syndromes in preschool years suggests that there

could also be different risk patterns between boys and girls. Exploring the effect of risky exposures on

internalizing syndromes by sex of preschoolers and assessing confounding in these associations is

needed. Analyzing confounding by variables such as child externalizing symptomatology, food insecurity,

parental substance use, neighborhood disadvantage, parental social support, and neighborhood

violence; is key to understanding what could have led to the difference in estimates between boys and

girls.

Like most studies in the field, the main limitations of this study arise from the use of a caregiver

report. Since the CBCL 1.5-5 scores are based on the report by a third person, potential recall problems

could have led to an overestimation or underestimation of the severity of the symptoms. The caregivers

could have overestimated the severity of the symptoms because they overprotect the child or because

they were depressed themselves. They can also underestimate the severity of symptoms or underreport

violent behaviors or neglect to avoid raising questions regarding their parenting skills. Moreover,

regarding differences in the syndromes by sex, parents or caregivers could have some gender

expectations that bias their perceptions of their behaviors, leading to an overestimation of these

differences.

Prospective studies where parents can register their children's behaviors, small clinical studies

with comprehensive assessments, or studies with reports by more than one caregiver are all potential

solutions to this limitation.

A central contribution of this study, based on the non-rejection of configural and metric

invariance between boys and girls, and the acceptable fit of the four-syndromes model of internalizing

problems before adjustments (SRMR=0.077), is the validation of the internalizing structure of the CBCL 1.5-5 and therefore that in future studies on the internalizing problems of preschoolers in São Paulo, the scoring guidelines of the CBCL 1.5-5 in the ASEBA manual[28] be followed. Thus, this study supports the use of CBCL 1.5-5 in previous and future studies in Brazil.

Regarding the strengths of this study, a major strength was the use of the PreK survey. Since it was a representative sample of children aged 4 to 5 years old attending public preschool in an urban region of Brazil, the findings are suggestive of a similar factor structure of internalizing problems in other cities in São Paulo and Brazil due to a common culture, language, and comparable health policies. The study had a large sample appropriate for CFA, and there was no missing data. The current study innovated in its approach by placing the focus on internalizing problems of preschoolers in São Paulo, examining in detail the construct of internalization, syndromes, and symptoms, and exploring differences by sex in order to aid in the understanding of these problems and inform treatment and prevention efforts in early childhood.

Chapter 4: Risk Of Internalizing Problems In Preschool Boys And Girls In São Paulo, Brazil.

4.1 Introduction

In a review of the literature in Low and Middle-Income Countries (LMIC) examining the structure, characteristics, and predictors of internalizing problems in preschoolers, LMIC in the region of the Americas had the largest proportion (45%) of studies. The review included studies written in English, Spanish, and Portuguese, the main languages spoken in the Americas, leading to an oversampling of studies in the region. Brazil had the largest number of studies included (six of the 31 studies) [83-85,87,91,92].

The review evidenced an increased interest in internalizing problems in Brazil since all the included studies were published in the last decade, perhaps due to a perceived increase in the prevalence of anxiety and depression disorders[8]. Among people aged 15 and older, Brazil has the highest estimated prevalence of internalizing disorders and associated disability worldwide[8,9], ranking first on anxiety disorders (9.3%)and fifth on depressive disorders (5.8%). Researchers have begun to explore characteristics of internalizing problems in young children, such as preschoolers, to identify potential antecedents of the high prevalence of internalizing disorders in adolescence and adulthood [5-7].

Although Brazil had the largest number (six) of studies on preschoolers' internalizing problems in any LMIC, six studies is a low number given the importance of the topic. According to the review, the prevalence of internalizing problems in preschoolers in Brazilian cities could be between 7.8 % and 9.7%, based on studies in the city of Pelotas in Rio Grande do Sul[84] and the city of Salvador in Bahía[83]. The study in the city of Pelotas[84] compared two cohorts and reported an increase of 10% in the mean scores of internalizing problems in eleven years (between 1993 and 2004). Internalizing problems are usually considered as predictors of other health problems in adolescence or adulthood [5-7]. More studies should assess the risks of internalizing problems in preschoolers, not only because preventing or treating them

could close the pathway to other health issues, but because it is estimated that they are increasing and have proximal consequences in the child's well-being. Consequences of internalizing problems, such as difficulty bonding with others, disinterest in everyday activities, school absenteeism [30,33-36] highly concern in a person's formative years.

The main risk factor for child internalizing problems described in the literature is parental internalizing psychopathology[83,84,96,101,102,108,112]. Other commonly described risk factors are violence and abandonment by parents[13,45-57,168]. The high rates of psychopathology[8,9] and violence[49,50] in Brazil and other LMIC underscore the importance of exploring the risk they may pose to child mental health. Exposures such as child externalizing symptomatology, child sleep problems[87], age of the child[105], child food insecurity[112], parent substance use[61], neighborhood disadvantage[111], and parental social support[13,45-48] could be confounding the associations between the risk factors and child internalizing problems.

No studies focusing on the factor structure of internalizing problems or validated scales of behavioral problems in Brazilian preschoolers were identified in the review. However, the Child Behavioral Checklist (CBCL)[28], the most used scale worldwide to identify clinically significant behavioral problems in preschoolers, was applied in five of the six studies included in the review[84,85,87,91,92]. The CBCL 1.5-5[28], designed for preschoolers aged 1.5 to 5 years old, categorizes behavioral problems in a seven-factor structure: four factors for internalizing problems, two factors for externalizing problems, and a single factor for sleep disturbance. The four first-order factors or syndromes of internalization are: "Anxiety/Depression," "Somatic Complaints," "Withdrawn," and "Emotionally Reactive." The two first-order factors or syndromes of externalization are: "Aggressive Behaviors" and "Attention Problems." The seven-factor structure for behavioral problems has been endorsed by Confirmatory Factor Analysis (CFA) of data in 23 countries[28], including Chile and Peru in the Region of the Americas.

Due to the lack of studies examining the structure of internalizing problems of preschoolers in Brazil, a CFA of the internalizing and externalizing problems of the CBCL 1.5-5[28] and a multigroup analysis by sex was conducted using data from the Preschool Mental health Study (The PreK survey). The PreK survey was implemented in 2015 on a sample of 1,292 preschoolers (4 to 5 years old) in the city of Embu das Artes, São Paulo. [58,139,169] In agreement with previous findings, the results showed highly correlated but distinct factors for internalizing and externalizing problems and endorsed the four-factor structure (four syndromes) for the internalizing problems. There were cross-loadings between the syndrome of "Anxiety/Depression" syndrome and the "Emotionally Reactive" syndrome, whereas the "Withdrawn" and "Somatic Complaints" syndromes had a more defined structure. Configural and metric invariance of the model in boys and girls were not rejected, concluding that the CBCL 1.5-5 measures the same construct of internalizing problems in both boys and girls. Based on the findings, the conclusion was to follow the manual's guidelines when assessing internalizing problems in preschoolers in São Paulo since the original model proposed in the CBCL 1.5-5 manual[28] had an adequate fit (SRMR <0.080). However, to have the most accurate estimates accounting for minimal differences by sex, the scores calculated from the factor loadings in multigroup CFA were used.

Upon exploring the differences by sex, the mean scores for "Somatic Complaints" and "Withdrawn," two distinct syndromes, were significantly different in boys and girls. Boys have higher scores in "Withdrawn," and girls have higher scores in "Somatic Complaints." Disparate estimates are seen in adolescence and adulthood, with females having almost twice the prevalence of internalizing problems than males[41,170,171]. It is worth exploring why there are significant differences in Brazilian boys' and girls' mean scores at such an early age when they have had fewer exposures than adolescents and adults to gender norms. Brazilian boys and girls could have experienced different exposure patterns that may have led to increased or decreased risk of preschool behavior problems.

The present study aims to reduce the gaps in knowledge on internalizing problems in preschoolers identified in the review and the multigroup analysis. It also aims to identify areas for research and intervention on internalizing problems according to the sex of the preschoolers. This study will assess the risk of internalizing problems differentially by sex of preschoolers in São Paulo, Brazil, and test for associations between internalizing problems and a) parental psychopathology, b) physical or verbal violence, and c) low quality-time spent with parental figures. A thorough assessment of confounding by child externalizing symptomatology, child sleep problems, age of the child, child food insecurity, parent substance use, neighborhood disadvantage, and parental social support will be conducted.

4.2 Methods

Data were obtained from the Preschool Mental health Study (PreK Survey) [58,139], with authorization and support from the study's principal investigators.

Sample

The sample consisted of 1,292 preschool children (weighted frequency: 665 boys and 627 girls) aged 4-5 years old and their parents in Embu das Artes, a city in the metropolitan area of São Paulo Brazil. A parent or parental figure reported on their child's information, and the parental variables were self-reported. The large majority of the survey respondents were biological mothers (weighted frequency: 1,045. 80.9%).

The PreK Survey

The PreK survey[58,139] is a 2015 cross-sectional study. The study was developed by researchers at the Departments of Psychiatry and Preventive Medicine of the *Universidade Federal de São Paulo* and collaborators at Columbia University Mailman School of Public Health and Johns Hopkins Bloomberg

School of Public Health. The PreK survey's main objective was to assess the prevalence rates of internalizing and externalizing problems (clinically significant symptoms) and socio-developmental delays among a representative sample of public preschool children aged 4-5 years in a poor urban region in Brazil.

Using an online database from the Brazilian National Institute of Educational Research, all public preschools in Embu das Artes were identified. The sample was a randomly recruited representative sample of the 4-5-year-old population using a stratified random sample of public preschools/ childcare centers, selected with a probability proportional to the number of 4-5-year-olds in each school within designated census tracts[58,139]. Trained health professionals from the Federal University of São Paulo collected data using face-to-face interviews in Portuguese within preschools. The study included the Brazilian Portuguese version of the CBCL 1.5-5[28]. Based on the CBCL scores, the six-month prevalence was 25.4% for internalizing problems, 12.1% for externalizing problems, and the prevalence of socioemotional development delays was 30.3%, based on the Ages and Stages Questionnaires: Social-Emotional (ASQ:SE)[140],

Measures

The internalizing problems score was first calculated based on each item's factor loadings in a Confirmatory Factor Analysis of the internalizing section in the CBCL 1.5-5[28]. Since the scores for boys and girls were calculated based on different loadings, for each child, a percentage of the maximum possible score was obtained for each syndrome (factor) and for the total score to make them comparable. After that, a t-test was done to compare the mean scores in boys and girls per syndrome, and the syndromes with more significant and noticeable differences in estimates were selected. Hence, the outcomes explored in this study were a) the calculated score for Total Internalizing Problems, b) the

calculated score for the Withdrawn Syndrome, and c) the calculated score for the Somatic Complaints Syndrome, all with a minimum score of 0 and a maximum score of 100.

Based on a literature review, parental psychopathology, severe physical or verbal violence, and low-quality time spent with parents are among the most common predictors of child internalizing problems. They were selected as the exposures for this aim, with parental psychopathology being the most important. The process of creation of the variables in this study was as follows:

Parental Psychopathology

In the PreK survey, there were measures of the severity in the last two weeks of three parental internalizing problems; depression, as measured by the Patient Health Questionnaire (PHQ-9) [172]; anxiety, measured by the Generalized Anxiety Disorder 7-item scale (GAD-7)[173]; and Posttraumatic Stress Disorder (PTSD), measured with the PTSD Checklist-Civilian Version (PCL-C). The PCL-C (the measure of PTSD) was answered by only 209 participants (16.5% of the total) because 1,024 participants were not exposed to a traumatic event, and there were 59 missing observations; therefore, the variable for PTSD was discarded from the risk assessments.

Then, five models were used to decide the best measure of parental psychopathology. The variable for total internalizing problems score was regressed on: 1) a calculated variable indicating presence or absence of depression or anxiety; 2) a calculated variable coded from 0 to 2 indicating no anxiety or depression, anxiety or depression, or both; 3) the two variables for the scores of depression (PHQ-9) and anxiety (GAD-7); 4) only the PHQ-9 score variable, and 5) only the GAD-7 score variable.

The best fit was the model with the two variables for the scores of depression and anxiety (Adjusted R square: 0.1812, with 74/1,292 missing observations), followed by the model with only the PHQ-9 score (Adjusted R-square: 0.1651, with 70/1,292) missing observations), and the model with only the GAD score (Adjusted R-square: 0.1486, with 50/1,292 missing observations). There were no

significant differences in missingness by sex. The variable for the PHQ-9 score (parental depression) was selected as the measure of parental psychopathology considering the need for a parsimonious model to conduct all risk assessments, the significant correlation between anxiety and depression scores (r=0.74 p<0.01), and the interest in having comparable results with other studies in LMIC that mainly assess the risk of internalizing problems from parental depression.

Severe Physical or Verbal Violence

The variable for physical or verbal violence was created based on Section B of the Brazilian version of the World Studies of Abuse in Family Environments Core Questionnaire (WorldSAFE) [174,175], which measures the severity of verbal and physical punishment of the child by the parents in the past 12 months. Any severe punishment, verbal or physical, was coded as 1, no severe punishment was coded as 0. The preliminary analyses that led to this coding can be seen in Appendix B.

Low-quality time with parents

This variable was created from a question in the PreK survey from the Protective Factors Survey (PFS)[176]. The question was, "What is the time quality each parent spends with the child (good/medium/bad)?" The variable was calculated for different combinations of both parents, with 5 indicating the lowest quality: 5 both bad, 4 bad-medium, 3 medium-medium, 2 bad-good, 1 medium-good, 0 both good. Children without a mother or a father figure (3 and 88 children, respectively) were coded as missing since this variable refers to both parents. However, additional analyses comparing the low-quality time with the mother figure in all children versus only those who have both parental figures were conducted (see Appendix C). This variable was also dichotomized as presence/absence of low-quality time, where any score above 3 (no good time quality with either of the parental figures) was considered low-quality time.

Hypothesized confounders were: Child externalizing problems (from the CBCL 1.5-5[28]), Child

sleep problems (CBCL 1.5-5[28]), child's age, child food insecurity (based on the Escala Brasileira de

Insegurança Alimentar EBIA), parent substance use (from the ASSIST questionnaire[177-179]), parent

support score (from the Social Support Survey Instrument[180-184]), and neighborhood vulnerability(from

instruments of the Project on Human Development in Chicago Neighborhoods[185,186]). The definition of

these variables can be seen in Table 12.

Table 12. Hypothesized Confounders.

Potential confounders: Child externalizing symptomatology, food insecurity, caregiver substance use, sleep problems, caregiver social support, neighborhood disadvantage, and child's age.	
Child externalizing symptomatology	This is the main confounder, as child externalizing problems can co-occur with internalizing problems, affect the experience of internalizing problems, and potentially explain some of the effects. Although they are less frequent than internalizing problems, most of the studies on mental health in young children examine externalizing problems since they are easier to observe and considered more problematic, taking away the focus from internalizing symptoms. In the PreK study, externalizing symptoms are measured with a subscale of the CBCL 1.5-5[28]. Externalizing symptoms refer to conflicts with other people and with their expectations for children's behavior, and they are classified into behaviors and attention problems. Each of the 24 items on externalizing symptoms is scored 0 to 2 (not true, sometimes true, often true), and a total score was calculated to identify the normal range, subclinical range, or clinical range.
Food insecurity	Based on the Escala Brasileira de Insegurança Alimentar (EBIA) Validated for its use in Brazil. Two questions were selected for this variable: 1) the question referring to the number of months when there has been enough money to buy sufficient food or balanced meals. Any number of months indicates a lack of food security. 2) The question: "Do you think your child is underweight, normal weight or overweight?" was considered if the answer to question 1 indicated lack of food security. Therefore, the variable in this study had three categories: food security (coded as 0), lack of food security and normal weight (coded as 1), and lack of food security and abnormal weight (either underweight or overweight- coded as 2).
Caregiver substance use problems	In the PreK study, The Brazilian Portuguese version of the 8-item Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST)[177-179] was used to detect substance use-related problems. According to the WHO, the ASSIST has undergone significant testing in three sequential phases (I, II and III) to ensure that it is feasible, reliable, valid, flexible, comprehensive and cross-culturally relevant[177,187]. The PreK study examined alcohol, tobacco, cocaine, and marijuana use. For each substance, there are eight questions related to use of substances and the frequency. Each answer is assigned a different score. A total score of 6 for each substance is calculated. The score determines if there is a low (0-10 for alcohol, 0-3 other substances), moderate (11-26 for alcohol, 4-26 for other substances), or high risk of substance use problems (more than 27 for alcohol and other substances). The variable used in this study was binary (presence of any moderate or high risk of substance use problem other than tobacco/ low risk for all).

Child Sleep problems	It is a subscale of the CBCL 1.5-5. It assesses aspects of sleep, such as quality and time of sleep. Each of the seven items on sleep disturbance was scored 0 to 2 (not true, sometimes true, often true), and a total score was calculated to determine the normal range, subclinical range, or clinical range.
Caregiver Social support and social networks	A validated Brazilian version of the Medical Outcomes Study was used to measure social support [180-184]. The social support questions ask about emotional, informational, financial, and appraisal support, including questions regarding whether or not participants have support persons to whom they can turn for help, from whom they can borrow money, etc. Social network questions were about the number of close friends and relatives respondents have and the frequency with which respondents see these friends and relatives. In a previous validation study in Rio de Janeiro, Cronbach's alpha for social support measures was >0.83 in all domains [183].
Neighborhood Disadvantage	Data from the Brazilian Institute of Geography and Statistics (IBGE: http://www.ibge.gov.br) was used to assess area-level disadvantage, through measures such as social stratification, percent of residents in the lowest social class, and the proportion of residents eligible for public assistance. Stratification was made for each block face, based upon housing conditions (e.g., type of door, size of front lawn), urban surroundings (types of roadways and streets), and zone where the block is located. In addition, the SEADE, a São Paulo state governmental agency has created, based upon Census data from the IBGE, a São Paulo neighborhood vulnerability index- the IPVS (which measures social vulnerability and poverty- from very high vulnerability to low vulnerability neighborhoods- see: http://www.seade.gov.br/projetos/ipvs) as well as a similar neighborhood index focusing only on youth using the juvenile vulnerability index- the IJV (see: http://www.seade.gov.br/produtos/ivj) to calculate area-level disadvantage.
Child's age.	It was calculated from the child's date of birth and response date. It measures whole and partial years.

Data Analysis

This study used complex data analyses since probability weights were calculated based on the class, and data could be clustered by the school (30 schools) or by class within each school (144 classes). Calculations for Intra Class Correlation Coefficients (ICC) were performed using empty mixed models, as seen in Appendix D. The school explained 0.3% of the variance in internalizing problems, and the class

explained 0.2%. Although the ICC was very low, clustering by the school was included in all the models to account for any potential similarities in the children's backgrounds.

The variable low-quality time with parents excluded children without a mother (0.20%) or a father figure (6.81%), because the reasons for having a completely absent parental figure could not be determined based on the available information. In addition, those who did not answer or answered "I don't know" were also excluded, leading to a total of 176 missing observations (13.6%) for this variable. There were few missing observations in all the other variables, and there were no missing observations for the outcomes (see table 1). The difference in missingness by child's sex in this variable was not significant (Chi-Square= 1.01, df=1, p=0.33).

Depending on the level of measurement of the variables, t-test of means or Chi-Square tests were performed to examine differences by sex of all outcomes, exposures, and confounders. The estimates are compared in table 1.

The normality of the outcome variables (Total Internalizing Problems, Withdrawn Syndrome, and Somatic Complaints Syndrome) was examined graphically. All three variables were right-skewed; hence they were log-transformed to have a more normal shape.

A thorough assessment of confounding with each exposure and outcome was performed. The following three criteria: a) being significantly associated at p<0.05 with exposure, b) being significantly associated with outcome in unexposed, c) leading to a change of 10% or more of the adjusted estimates versus the crude estimates of the association between exposure and outcome. These analyses permitted identifying the minimal set of confounders to adjust. However, since all statistical associations detected in the data are not enough to characterize confounding[188] all the hypothesized confounders associated with the exposures and the outcomes in unexposed were included in the models even if the adjusted and crude models were not appreciably different because they were theoretically relevant [38].

Parent substance use was excluded from the analyses of confounding because the majority of the parents did not answer the ASSIST questionnaire (49% reported not drinking alcohol, 72% reported not smoking, 94% reported not using marijuana, 97% do not use crack).

The regression models used to assess risk were Generalized Linear Models (GLM)[189], accounting for clustering by the school, probability weights, and a finite population correction (fcp). The selected models were later run in GEE[190] to compare, resulting in near-exact estimates. SAS 9.4[147] was used to perform all analyses.

Interaction between sex and the exposures was examined in all models. In addition, the interaction with parental depression was examined in the models with severe physical or verbal violence and low-quality time with parents.

When the interaction terms were significant at $p < 0.05$, the models' estimates were reported using the third variable's strata. All estimates were exponentiated.

4.3 Results

Almost 27% of the girls in the study had clinically significant internalizing problems, compared to 25% percent of the boys. Girls also had a significantly higher mean score than boys in the Somatic Complaints Syndrome ($p < 0.01$) and in the Anxiety/Depression Syndrome ($p < 0.05$). Boys had a significantly higher mean score than girls in the Withdrawn Syndrome ($p < 0.01$). The Withdrawn Syndrome and the Somatic Complaints Syndrome had the most significant differences between boys and girls; hence they were selected along with Total Internalizing Problems as the outcomes in this study.

Table 13 shows the differences in outcomes, exposures, and confounders by sex of the preschoolers. For further information on estimates, see Appendix E.

Table 13. Differences in outcomes, exposures, and confounders by sex of the preschoolers.

	Girls (n=626)	Boys (n=666)	P		Missing
Internalizing Problems					
% of Clinically Significant Internalizing problems	26.63	25.11	0.503		.
Mean Scores of CBCL 1.5-5 based on CFA					
Anxiety/Depression	26.03	23.89	0.001	**	.
Emotional Reactivity	22.89	23.34	0.200		.
Somatic Complaints	13.22	11.2	0.001	**	.
Withdrawn	10.76	13.19	0.001	**	.
Total Internalizing Problems	19.42	19.18	0.339		.
Parental Psychopathology					
% of parents with 1 or more problems	28.74	29.36	0.827		74
% parents with high scores for depression[1]	18.66	20.06	0.463		70
% of parents with high scores for anxiety[2]	20.94	22.52	0.516		50
% of parents with high scores for PTSD[3]	3.16	3.15	0.954		59
Physical or verbal Violence					
% of children exposed to severe verbal or physical punishment	54.9	54.1	0.830		11
Low quality-time with Parents					
% of children with low quality-time	8.02	6.7	0.467		176
% of children with clinically significant externalizing problems	9.73	13.8	0.004	**	.
% of children with clinically significant sleep problems	3.35	2.86	0.560		.
% of children with food insecurity	3.04	1.81	0.195		4
% parents substance use	5.9	5.2	0.725		.
Mean parent social support score	50.64	51.54	0.064		16
Mean score neighborhood violence	16.75	16.91	0.574		17

**significant at p<0.01
[1] Score is 9 or greater in the PHQ- 9
[2] Score is 10 or greater in the GAD-7
[3] Score is 44 or greater in the PCL-C

Parental Psychopathology (Parental Depression)

None of the estimates of parental psychopathology differed significantly by sex. As seen in table 1, percentages of parents with high depression, anxiety, and PCL-C were similar in boys and girls. Parental psychopathology is a highly frequent exposure since about 29% of the parents of boys and girls had at least one of the three. The most common internalizing problem was anxiety reported by about 21.5% of the parents, followed by depression, reported by about 20%.

Based on preliminary analyses previously described, the score in the PHQ-9, a monitoring tool for the severity of depression, was selected as the variable for parental psychopathology and renamed parental depression.

A thorough assessment of confounding between parental depression and child internalizing problems was conducted, as well as an assessment of its relationship with other exposures. The examined variables were externalizing problems, sleep problems, child's age, food insecurity, social support score, and neighborhood violence. All potential confounders were significantly associated with exposure and outcome in unexposed. Only adjusted estimates for externalizing and sleep problems were appreciably different than crude (unadjusted) estimates in all the models. However, all confounders that were theoretically relevant were included. Among potential confounders examined, food insecurity predicted the highest scores of parental depression (2.242 point increase in parental depression per unit increase in food insecurity). For the assessment of confounding, see Appendix F.

Table 14 shows the crude and adjusted estimated mean changes for the models and the models' fit based on the Adjusted R-square. The adjusted models with parental depression as the main exposure explained 48.9% of the variance in Total Internalizing Problems, 21.4% in the Withdrawn Syndrome, and 15.9% in the Somatic Complaints Syndrome. In addition, the Adjusted R-Square increased greatly in the

adjusted models, particularly with the inclusion of the externalizing problems score, the variable that

had the strongest association with internalizing problems.

Table 14. Crude and Adjusted Estimated Mean Increase of Internalizing problems scores by Parental Depression, Physical or verbal Violence, and Low quality-time between Parents and Child.

Outcome	Exposure	N	Model	Estimate	95% CI		Adj R[2]
Total internalizing	Parental Depression	1,218	Crude	0.057	(0.055 ,	0.060)	0.165
			Adjusted[a]	0.019	(0.017 ,	0.021)	0.489
	Physical or verbal Violence	1,275	Crude	0.319	(0.289 ,	0.350)	0.036
			Adjusted[a]	0.043	(0.025 ,	0.060)	0.476
	Low quality-time	1,102	Crude	0.125	(0.109 ,	0.141)	0.020
			Adjusted[a]	0.028	(0.017 ,	0.039)	0.469
Withdrawn	Parental Depression	1,218	Crude	0.064	(0.061 ,	0.067)	0.067
			Adjusted[a]	0.017	(0.140 ,	0.021)	0.214
	Physical or verbal Violence	1,275	Crude	0.365	(0.324 ,	0.408)	0.014
			Adjusted[a]	0.034[c]	(0.000 ,	0.070)	0.209
	Low quality-time	1,102	Crude	0.167	(0.129 ,	0.206)	0.011
			Adjusted[a]	0.046	(0.020 ,	0.073)	0.197
Somatic Complaints	Parental Depression	1,218	Crude	0.067	(0.063 ,	0.071)	0.073
			Adjusted[ab]	0.030	(0.025 ,	0.036)	0.159
	Physical or verbal Violence	1,275	Crude	0.462	(0.333 ,	0.426)	0.020
			Adjusted[ab]	0.153	(0.099 ,	0.211)	0.156
	Low quality-time	1,102	Crude	0.193	(0.160 ,	0.226)	0.014
			Adjusted[a]	0.092	(0.060 ,	0.126)	0.159

a Models were adjusted for externalizing problems, sleep problems, food insecurity, social support score, and neighborhood violence.
ab Also adjusted for child's age
c Not significant at p<0.05

Since the sex of the preschoolers could potentially modify the effect of parental depression on

internalizing problems in preschoolers, there was an assessment of the interaction between parental

depression and the sex of the preschoolers. Table 15 includes the estimates stratified by sex of

preschoolers and parental depression if the interaction terms were significant.

In summary, parental depression was the primary exposure. It explained the most variance in Total Internalizing Problems, the Withdrawn Syndrome, and the Somatic Complaints Syndrome. After adjusting for confounders, the models with parental depression explained greater proportions of the variance than the models with severe violence and low-quality time. As seen in Table 15, the effect of parental depression on Total Internalizing Problems is greater in boys than in girls (0.009 estimated difference). Their confidence intervals do not overlap. The estimates for parental depression and the other outcomes were not stratified because the interaction term was not significant at p<0.05.

Table 15. Adjusted Estimated Mean change for Internalizing problems stratified by Sex of the Preschoolers and Levels of Parental Depression.

	Total Internalizing Problems			Withdrawn Syndrome	Somatic Complaints Syndrome	
	Parental depression	*Physical or Verbal Violence*	*Low Quality-Time*	*Low Quality-Time*	*Physical or verbal violence*	*Low Quality-Time*
Girls	**0.014**	**0.091**		0.011	0.052	
	(0.010, 0.017)	(0.066,0.117)		(-0.023, 0.047)	(-0.022, 0.132)	
Boys	**0.023**	0.009		**0.087**	**0.242**	
	(0.020, 0.025)	(-0.034, 0.016)		(0.052, 0.123)	(0.166, 0.323)	
Parental Depression		**0.030**	**0.040**		**0.375**	**0.136**
		(0.010, 0.050)	(0.025, 0.054)		(0.216, 0.554)	(0.095, 0.178)
No Parental Depression		0.015	-0.009		**0.067**	-0.037
		(-0.025, 0.057)	(-0.023, 0.005)		(0.015, 0.123)	(-0.09,0.019)

Estimates in bold are significant at p<0.05.

Physical or verbal Violence

It was estimated that 30.5% of preschool boys and girls had suffered from severe punishment, physical or verbal, by one or both of their parents. The estimates for physical or verbal violence were similar for both boys and girls, as seen in table 13. There are no significant differences by sex in the kind of severe violence.

In table 14, the crude model regressing internalizing problems on severe physical or verbal violence explained 3.6% of the variance. The criteria for confounding were met by child sleep problems

and parent social support in the models for total problems, Withdrawn Syndrome, and the Somatic

Complaints Syndrome, but the model was adjusted for all the hypothesized confounders. The beta for

physical or verbal violence and the Withdrawn Syndrome was the only adjusted estimate that was not

significant.

Assessments of the interaction between severe physical or verbal violence and sex of

preschoolers and between severe physical or verbal violence and parental depression were conducted.

In the crude estimates, the associations were significant in boys and girls. After adjusting for

confounders, the interaction term for sex of preschoolers and physical or verbal violence was significant

at $p<0.01$ for Total Internalizing Problems and the Somatic Complaints Syndrome. The estimates are

reported accordingly in Table 15. Based on the adjusted models, severe physical or verbal violence was

significantly associated with Total Internalizing Problems in girls, but not in boys. Conversely, severe

physical or verbal violence was significantly associated with the Somatic Complaints Syndrome in boys

but not in girls.

The interaction term with parental depression was significant at $p<0.01$ for the Total

Internalizing Problems and the Somatic Complaints Syndrome. In children of a parent with depression,

there was a significant association between physical or verbal violence with Total Internalizing Problems.

In children of a parent without depression, the association was not significant.

In children of a parent with depression, the estimate between physical or verbal violence and

the score of the Somatic Complaints Syndrome was 0.309 points higher than in those children whose

parent did not have depression.

The effect of physical or verbal violence on Total Internalizing Problems was greater in children

whose parent has depression than in those children whose parent does not have depression (0.309

estimated difference). Their confidence intervals did not overlap. The estimates for physical or verbal

violence and the Withdrawn Syndrome were not stratified because the interaction term was not significant at $p < 0.05$.

Low quality-time between Parents and Child

It was reported that 8.0% of the girls and 6.7% of the boys do not spend good quality time with their parental figures. These estimates were not significantly different, and the estimates suggested that most preschool children in Embu spent good time quality with their parental figures. There were seventeen children (1.36%) who had a deceased biological father excluded from the analyses of this variable.

In table 14, the crude model regressing the Total Internalizing Problems score on the low-quality time with parents had a good fit, explaining 2% of the variance. Externalizing problems, sleep problems, and social support were the main confounders, but all hypothesized confounders were included in the model. The adjusted model explained 47% of the variance.

An assessment of the interaction between low quality-time with parents and sex of preschoolers was conducted, and between low quality-time with parents and parental depression. The interaction term between low quality-time and sex of the preschoolers was significant at the 1% for the Withdrawn Syndrome. Low quality-time with parents had a significant association with the Withdrawn Syndrome in boys but not in girls.

The interaction term between low quality-time and parental depression was significant at $p < 0.05$ for Total Internalizing Problems and the Somatic Complaints Syndrome. Low quality-time had a significant association with Total Internalizing Problems and the Somatic Complaints Syndrome in children of a parent with depression, but not in children of a parent without depression.

Children with both parental figures and no missing information (n=1,116) were included in the analyses of low quality time. Additional analyses comparing the estimates of the association of quality time with the mother and the outcomes in all children versus those with both parent figures showed appreciable differences only in the Withdrawn Syndrome. See Appendix C for more information.

4.4 Discussion

This study is the first of its kind in a Latin American population of preschool children and their parents, with a detailed assessment of the risk of preschool boys' and girls' internalizing problems. The assessment results suggest that the disparate rates between females versus males in internalizing psychopathology in adolescence and adulthood may be seen early. Common exposures such as parental psychopathology, physical or verbal violence, and low quality-time spent with parents all had different effects on preschool boys' and girls' mental health in São Paulo.

Once it was established through CFA that internalizing and externalizing problems in children are correlated but distinct constructs, externalizing problems were controlled for in the models instead of being made the focus of attention. Externalizing problems could be either a confounder or a mediator of the relationship between several risk factors and internalizing problems. This study could not discriminate between the two due to the use of cross-sectional data. If externalizing problems are mediators, adjusting for them removed some of the effects of the explored exposures, but it also isolated the effects of the exposures on internalizing problems, even if they were low. By itself, externalizing problems explained most of the variance in internalizing problems. The relationship between exposures and outcome was much weaker but still significant when externalizing problems were controlled. Due to their high correlation, both internalizing and externalizing problems should always be considered in studies aiming to understand the risks and consequences of problematic child behavior. Temporality between sleep problems and the exposures was also not discernible, but, similar

to externalizing problems, estimates were significant in both the crude models and the models adjusted

by sleep problems. Based on this, it was estimated that parental psychopathology, physical or verbal

violence, and low quality-time spent with parents all have a harmful and significant association with

child internalizing problems, adjusting for externalizing problems, sleep problems, food insecurity, social

support score, neighborhood violence, and child's age.

All exposures studied are parental variables that, in the literature[83,87,90], have frequently been

shown to precede young children's behavioral problems. Food insecurity, lack of social support,

substance use, and neighborhood vulnerability could increase the risk of parental depression, anxiety,

and PTSD. They could also affect physical or verbal violence and low quality-time spent between parents

and children. These variables were explored as confounders in this study and had significant and strong

associations. Parent substance use, which would be theoretically relevant, was excluded from the

analyses of confounding because, as previously stated, the ASSIST questionnaire did not apply to most

parents, and they did not provide answers to it.

Parental depression was the measure of parental psychopathology because it was the variable

that explained the most variance in the outcomes, as seen in table 2. It is important to highlight that the

three variables that indicated parental psychopathology in the PreK survey (depression, anxiety, and

PTSD) were scores for screening scales and do not constitute a clinician's formal diagnosis. They

identified if a parent was more likely to have a disorder. Hence, throughout the text, depression,

anxiety, and PTSD are referred to as problems and not as disorders. Depression and anxiety are highly

correlated [191]. Maintained anxiety can lead to depression, and several of the symptoms overlap. In

consequence, high scores in PHQ-9 are likely to account for some anxiety in the parents.

Parental depression was also the most critical exposure overall because it was the exposure that

consistently explained the most variance in all the models; the association with child behavioral

problems has been widely tested and confirmed[14,75,83,96,101,102,112,123,192-196]; and it is also an internalizing

problem, with behavioral symptoms that can be learned and replicated by the child. Being depressed

can make parents more aware of their own adversities or could alter their perceived vulnerability. It

could also make them more likely to identify problematic symptoms in their children, or perceive them

as more severe, which could lead to an overestimation of exposures and outcomes, and in turn, to an

overestimation of their association. For this reason, the interaction of parental depression with the

other exposures (physical or verbal violence and low quality-time with parents) was assessed. Parental

depression modified the estimated associations of violence and low quality-time on Total Internalizing

Problems and Somatic Complaints. As expected, the estimated associations were only significant or

higher in children of a parent with depression than in those children of a parent without depression.

Parental psychopathology should always be considered in studies on child behavior. However, since the

main focus has been parental depression, future studies could emphasize the specific risk increase by

parental anxiety, which is less disabling but more prevalent than depression in Brazil and LMIC in the

Region of the Americas[9].

Regarding physical or verbal violence, the association was significant with Total Internalizing

Problems and the Somatic Complaints Syndrome, and not significant with the Withdrawn Syndrome.

One reason why not all estimates were significant could be that the variable in the study did not

fully reflect physical or verbal violence experienced or witnessed by these children. There was no

information on whether the parent was also a victim of domestic violence, and most importantly, it was

highly likely that parents underreported and therefore underestimated the effects of harsh physical and

verbal violence to avoid being judged. The parents were more likely (not significantly) to report harsh

discipline from their partners toward the children than from themselves. Since there is sufficient

evidence of an association between physical or verbal violence and behavioral problems in children

[45,49,55,197], this study aimed to explore if the girls and boys experience this association differently. Based on the estimates, it appears that they do. After adjusting for confounders, it was estimated that physical or verbal violence had a significant association with Total Internalizing Problems in girls but not in boys, and a significant association with Somatic Complaints in boys but not in girls. The findings suggest that violence affects boys' and girls' behaviors through different mechanisms, and other variables should be assessed to understand them better. One of the variables that could significantly impact the association between physical or verbal violence and internalizing problems in the child could be intimate partner violence (IPV), determining the child's response when facing violence.

The large majority of the survey respondents were biological mothers (80.9%). All the children without a mother or a father figure (91 children, 7%) or missing observations were excluded from the analyses. The father figure could be absent by choice; the mother could have been a single mother by choice, there could be more than one maternal figure, a parent could be incarcerated, the mother could have cut ties with the father due to conflicting relationships, all of which could have added uncontrolled confounding. Again, there is a high likelihood that parents overestimated the quality of the time spent with their children since only about 7.4% reported low quality-time in general.

A significant association between low quality-time and the three outcomes (Total Internalizing problems, Withdrawn, and the Somatic Complaints syndrome) was estimated in this study, despite the limitations of measuring the quality of time between parent and child based only on a parent's self-report. Parent-perceived social support score was an important confounder of these relationships. A parent with low social support could have less time to spend with the child, and the child could have more behavioral problems if he/she has a weak support network [197].

The relationship of low quality-time with the Withdrawn Syndrome is experienced differently by boys and girls. The estimated association was significant in boys and not in girls. One of the reasons for

this is that parents could have different expectations in boys' and girls' communicative behavior. Girls are usually slightly ahead of boys in early communicative gestures, productive vocabulary, and combining words[198]; hence, boys could be perceived as more withdrawn. Some studies have affirmed that boys are expected to be less shy than girls[173]. Also, based on additional analyses, the negative effect of lower time quality with the mothers added to the absence of a father figure was more significant in boys, adding to the evidence that boys and girls have different mechanisms of developing internalizing problems[199]. Besides measuring the parents' perceptions and expectations of boys' and girls' behavior, it is recommended that future studies inquire about the boys' and girls' perceptions and expectations of the relationship with their parents to explain the disparate risks of syndromes.

These differences in estimates provide evidence that even from an early age, such as preschool years, males and females in São Paulo experience exposures differently. They may follow different pathways leading to the near-ubiquitous significant disproportion in the rates of anxiety, depression[41,170,171], related conditions such as Irritable Bowel Syndrome (higher in females than in males[134]), and other severe internalizing problems (such as isolation and suicide higher in males[165,200]) in adolescence and adulthood. Studies with longitudinal measures could explore the mediating or confounding roles of the bond between the parent and the child, parenting skills, functioning, and the stress related to parenting. Not having self-reported measures is a significant limitation of this study. The child's perception of the quality of the time spent with the parents could also be taken into consideration, as it may be different from the parent's perception, positively or negatively.

This study's attention to detail led to identifying disparate estimates of boys and girls in the Withdrawn and Somatic Complaints Syndromes in São Paulo, Brazil, from an early age, even before adolescence and adulthood, when gender roles and expectations become more pronounced and internalized. Exploring the risks and interaction by sex and parental depression led to identifying that even if there were similarities in the prevalence of exposures, boys and girls experience the exposures

differently. Therefore, there could be different approaches to treating internalizing problems for boys and girls. There could be a greater focus on implementing strategies to be more open about their emotions in boys. More strategies could be implemented to identify toxic environments or aggressions in girls since their Total Internalizing Problems are significantly associated with being exposed to severe physical or verbal violence. Both boys and girls need to be provided with a safe space with no biased judgments. However, it is essential to highlight that the focus should be on the parents/caregivers to prevent and treat child internalizing problems. This study provides further evidence that parental depression, severe physical or verbal violence toward the child, and low quality-time between parents and children negatively impact the children's behavior. If a child has clinically significant internalizing problems, this could be a strong indicator of the parents' need for mental health care.

This study's main limitations are the lack of a report by the children and the use of cross-sectional data. The report by parents of their own psychopathology and harmful behaviors could have led to biased estimates. However, this is a limitation in all studies with preschoolers since they cannot respond to most of the questions. Future studies in LMIC could consider adding another family member and teachers to examine the agreement in parental variables and child behaviors[89,105,110]. Also, the children's perception of their relationship with their parents could be taken into account for more accurate estimates of the quality of the time they spend together.

The use of cross-sectional data limited the study to risk assessments and the suggestion of different potential pathways that need to be investigated longitudinally. To explain what could have led to the disparate estimates between boys and girls, an assessment on mediation with longitudinal measures would enrich the discussion and identify more effective ways of preventing and treating internalizing problems.

This study's most important strength was exploring the risks of specific syndromes of internalizing problems instead of comprising them in a single variable. This research leads to a better understanding of child behavior and the different experiences that they can have since a young age based on their sex. The PreK survey was essential to assess the risk of internalizing problems in preschoolers in São Paulo. The percentage of missing observations was low, and there were measures at all levels: the macro, the microsystem, and the mesosystem. Few studies have focused on this topic in preschoolers in LMIC in the Americas, and none have considered the variety of risks in this study permitted by using the PreK Survey.

This study is relevant to public health because it brings light to a problem that affects preschoolers' health and relationships in São Paulo and may explain some of the high psychopathology and disability rates in later years[5-7]. The findings suggest that treating parental psychopathology could lead to a significant decrease in the risk of child internalizing problems. Another essential finding is that the child's sex should always be taken into account in the research and treatment of behavioral problems, even at a young age. Investigating different approaches by sex could lead to more accurate treatments to reduce the high prevalence of emotional disorders and related disabilities that we currently witness.

Chapter 5: Conclusions

One reason for the scarcity of research on internalizing problems in preschoolers in Low and Middle-Income Countries (LMIC) is that they are considered less challenging than externalizing behaviors (aggressive behaviors and attention problems) since they cause fewer disruptions in school and are not as easily observed by a third party. Also, information on the risk of preschoolers' internalizing problems is limited because they are usually analyzed as a single variable (presence/absence) without considering specific syndromes (such as anxiety/depression, emotionally reactive, withdrawn, and somatic complaints) and potential differences in the risk of boys and girls.

With this dissertation, I intended to further the understanding of preschoolers' internalizing problems in LMIC. *First,* I reviewed the literature to examine the definition of internalizing problems in preschoolers in LMIC, the prevalence, and predictors in each world region. *Second,* I analyzed the construct of internalizing problems in a sample of 1,292 preschoolers in São Paulo, Brazil, by examining the distinction between internalizing and externalizing problems and the differences between boys and girls. *Third*, I assessed the association of total internalizing problems and syndromes with parental depression and other common exposures differentially by sex in the same sample of preschoolers. The results of these studies are summarized and discussed below.

The low number of studies in LMIC (31 studies) that met the inclusion criteria for the systematic review **(Chapter 2)** of literature on predictors of internalizing symptomatology in preschoolers and their structure and characterization highlighted the scarcity of research on this topic. The review provided five main findings that I outline in the paragraphs below.

Analyzing the characteristics of the studies in LMIC, I identified an increased interest on the topic in Brazil and Turkey, both with a high prevalence of internalizing disorders. The studies in all regions were of mixed quality, except for China, where all included studies were of good quality. More than 30% of the studies included samples of fewer than 100 participants. The scarcity of studies on the validation

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of scales to assess behavioral problems raised questions on the accuracy of the measurements and highlighted the need for more studies examining the construct of internalizing problems in LIMC.

I found that the structure of internalizing problems in the Child Behavioral Checklist (CBCL 1.5-5 [28] and other versions) was the most accepted in LMIC. It is the most used scale to assess behavioral problems in preschoolers worldwide, and it was applied in 80% of the studies in the review. The hierarchical structure of behavioral problems consisted of two second-order factors (internalizing and externalizing problems) and seven first-order factors (the six syndromes previously mentioned plus sleep problems). Studies aiming to examine the construct of internalizing problems in preschoolers and having comparable variables to other countries or regions should consider using the CBCL 1.5-5.

Regarding potential predictors examined in the literature in LMIC, I found that they included the characteristics of the child's home environment and maternal psychopathology in all world regions, but each region had different exposures of interest. In the region of the Americas, there was an interest in examining risk by the characteristics of the children, such as social skills and emotional availability. In the European region, there was an interest in examining the effect of adverse events, and in China, there was an interest in the effect of harmful substances and nutrients. All the associations with internalizing problems were in the expected direction. Exposures a priori considered harmful had a positive association with internalizing problems scores or frequencies, and beneficial exposures were negatively associated. These findings led me to conclude that the focus on internalizing problems should not be the assessment of the harmful effect of an adverse exposure but under which conditions these events have a more negative effect and through which pathways are they leading to an increased risk of internalizing problems.

Another important finding was that although there are no significant differences in mean scores or frequency of total internalizing problems between boys and girls, there are significant differences in the mean scores of syndromes. Only one study in the European Region examined interaction with sex

for each syndrome of internalizing problems, finding some significant estimates. Analyzing syndromes individually and not as a whole could provide more information on the risk and suggest potential development pathways.

Finally, all the included studies examined the risks or the characteristics of internalizing and externalizing problems. It is mostly unexplored if internalizing and externalizing problems could be distinct constructs or if they could be understood as a single psychopathology factor in LMIC. These findings corroborate the importance of always taking externalizing problems into account.

The study had the strength of including articles written in English, Spanish in Portuguese, leading to an inclusion of a larger number of studies. However, this likely led to an oversampling of studies in the Region of the Americas. There is the need to include more languages in systematic reviews to have a clearer picture of the research currently conducted in LMIC was identified. No studies in the Eastern Mediterranean region and the South East Asian region were included. We excluded studies written in Turkish and Mandarin Chinese, and, likely, several studies did not show in the search.

In **Chapter 3**, I conducted a Confirmatory Factor Analysis (CFA) of the internalizing and externalizing problems sections of the CBCL 1.5-5 and a multigroup CFA by sex to address some of the gaps identified in the systematic literature review. I analyzed data from the Preschool Mental Health Survey applied in Embu das Artes, São Paulo. The study provided three main findings, described in the paragraphs below.

In this population, the hierarchical structure of internalizing and externalizing problems in the CBCL 1.5-5 was confirmed with the CFA. This study supports its use following the authors' guidelines. I obtained estimates suggesting that internalizing and externalizing problems are highly correlated but distinct factors with different syndromes. Since internalizing and externalizing problems are different constructs and the main interest was understanding the structure of internalizing problems, I only examined the structure of the internalizing section of the CBCL in the remaining analyses. By focusing on

internalizing problems, I was able to explore the differences by sex in the multigroup analyses with a larger number of people per item.

In the multigroup analyses, the model was a good fit for boys and girls, with a better fit in girls than in boys. Despite significant estimates, the specific differences between items were minimal. These findings led to the decision to continue considering that the construct of internalizing problems is the same for boys and girls, with the four syndromes of internalization (anxiety/depression, emotionally reactive, withdrawn, and somatic complaints).

Although the study concludes that the structure of internalizing problems proposed in the CBCL guidelines is valid in this population of preschool children, there were differences in some of the items, which could be accounted for to obtain more precise estimates. Future studies with internalizing problems as a variable of interest in preschool. children in São Paulo and in Brazil could consider the factor loadings obtained in this study to calculate the scores for the CBCL 1.5-5.

I calculated the new scores based on the factor loadings separately for boys and girls to have more accurate and precise measurements. Also, I obtained percentages of the maximum scores for each group in order to make comparisons. The comparison of these scores showed that preschool boys and girls had significant differences in the scores in the withdrawn and somatic complaints syndromes and the anxiety/depression syndrome, which warranted further exploration of the reasons for these differences.

The study's limitations arose from using a scale based on the reports by caregivers who could introduce information bias due to social desirability and their own history of psychopathology.

The study's main strengths were examining the structure of internalizing problems in a Brazilian sample, which provided support for previous and future studies using the CBCL 1.5-5 to assess internalizing problems in preschoolers. Also, the exploration of differences by sex led to identifying

relevant outcomes to examine, which could shed light on potential pathways of development of internalizing problems.

Using the calculated scores from Chapter 3, in **Chapter 4,** I examined the risks of total internalizing problems and the syndromes of withdrawn and somatic complaints in boys and girls, by relevant exposures identified in the systematic review: parental internalizing psychopathology, physical or verbal violence, and low quality-time with parents, adjusting by externalizing problems and common confounders.

The main risk factor for total internalizing problems and syndromes was parental depression. All other exposures did not explain the same amount of variance alone or did not lead to a greater increase in the scores. Except for physical or verbal violence and the withdrawn syndrome score, all the exposures (parental depression, physical or verbal violence, and low quality-time with parents) were significantly associated with the outcomes at the 5% level and in the expected direction. A careful assessment of confounding was conducted, and the main confounders identified were: externalizing problems, sleep problems, social support, and food insecurity. This study provided further evidence of the negative effects of parental depression, physical or verbal violence, low quality of time between parents and children, and parental psychopathology.

I found no significant differences by sex in means or the frequencies of the exposures of interest. An assessment of the interaction between sex and each exposure for each of the outcomes, showed that some associations were only significant in boys (low quality-time with the withdrawn syndrome and physical or verbal violence with the somatic complaints syndrome), or higher in boys than in girls (parental depression with total internalizing problems). The estimates suggest that boys and girls experience the exposures differently and develop internalizing problems through different pathways. These findings could inform future studies in São Paulo intending to explore potential mechanisms for internalizing problems in preschoolers.

Analyzing the risks per syndrome provided a more thorough picture and suggestions of potential mechanisms that could lead to the disparate estimates in females and males seen in later years. It has been estimated that in adolescence and adulthood, females have a higher prevalence of anxiety, depression, and associated conditions, and males tend to be more withdrawn and with higher rates of suicide or untreated mental health problems.

Analyses were conducted and compared in children of parents with depression and without depression. The association between Total Internalizing problems with physical or verbal violence and with low quality-time was only significant in children of parents with depression. The association between Somatic Complaints and low quality-time was only significant in those children of parents with depression.

The findings indicate that the sex of the child and the history of parental psychopathology should be considered in the assessment of internalizing problems, symptoms, and treatment approaches since they modify the effects of exposures on the outcomes.

This study's main limitations were using a parental report for all the variables and the cross-sectional nature of the data. The parental report may have led to information bias, where the parents could have underreported negative behaviors, such as violent punishments. Due to the study's cross-sectional nature, there was a lack of sufficient information to establish temporality between exposure and outcomes, which did not permit assessing pathways of development of internalizing problems. Although the theory suggests that they could be predictors, we cannot completely rule out that depression in a parent was not partly due to stress derived from caring for a child with internalizing problems.

In conclusion, the results from the three studies in this dissertation provide evidence that differences by sex in internalizing problems can be seen from an early age, in preschoolers, and an examination of the risk for different syndromes of internalization instead of comprising all in a single

variable could further the understanding of the pathways that lead to the disparate estimates in males and females. Preschool boys and girls in São Paulo have a similar exposure history, but the way they experience those exposures may be different.

The literature review provided a critical analysis of available data from studies in LMIC. The analysis led to identifying gaps in the knowledge of child behavioral problems. There was a scarcity of research on the structure of internalizing problems in preschoolers in LMIC, their differentiation from externalizing problems, and the differences in risk of boys and girls. The review also helped to identify exposures of interest in different world regions.

This dissertation also presented evidence from two analytical approaches that attempted to address limitations observed in previous studies. Findings from the first analytical study provided evidence on the distinction between internalizing problems and externalizing problems and supported using the CBCL 1.5-5 by past and future studies interested in examining behavioral problems in preschoolers in São Paulo. The second analytical study provided a novel approach by considering the risk of syndromes of internalization differentially by sex. Overall, the two analytical studies advanced our understanding of internalizing problems in LMIC and proposed future research directions.

5.1 Implications and Future Directions

The findings from this dissertation support the use of the CBCL 1.5-5 in previous and future studies on the internalizing problems in preschoolers in Brazil and similar LMIC. A valid measure of internalizing problems in preschoolers used worldwide provides comparable estimates with studies in HIC and other regions, promoting the translation of knowledge into novel research, treatment, and school and family-based prevention approaches of internalizing problems in preschools in LMIC. The analyses confirmed the harmful effect of violence, parental depression, and low quality of time with parents in child mental health in the preschool years. They emphasized the need to involve parents in preventive or treatment approaches to reduce the prevalence and further incidence of internalizing

problems and associated problems. Future studies aiming to assess the risks and the mechanisms of development for internalizing problems should focus more on the parents' experiences since they are the ones who provide the information, and their behaviors greatly affect children. Further research should explore differences by sex of the parent, violence that parents have experienced, the child's input regarding his/her perceived quality of time with the parents, and in general questions about the dynamic between the parents. Future studies should also consider using longitudinal data to improve the assessment of the temporal relationship between these exposures and outcomes and examine the different mechanisms of development of disorders and related conditions. A better understanding of these mechanisms could lead to the identification of other potential targets for future prevention of child internalizing problems and treatment efforts.

Notably, these results highlight several aspects to be explored in behavioral problems in LMIC, where anxiety, depression, and associated disability are highly prevalent. Understanding the development of mental health problems in LMIC is exceedingly relevant for public health to prevent and mitigate the negative impact of internalizing problems in the well-being of people of all ages.

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Appendix A

Literature Review Search Strategy

Search Terms (English)

(internalizing OR internalization) AND ("mental health" OR "psychopathologies" OR "mental illness" OR anxiety OR depression) AND (preschool OR "pre kinder" OR kinder) AND ("africa" OR "asia" OR "caribbean" OR "west indies" OR "south america" OR "latin america" OR "central america" OR "afghanistan" OR "albania" OR "algeria" OR "angola" OR "argentina" OR "armenia" OR "armenian" OR "azerbaijan" OR "bangladesh" OR "benin" OR "byelarus" OR "byelorussian" OR "belarus" OR "belorussian" OR "belorussia" OR "belize" OR "bhutan" OR "bolivia" OR "bosnia" OR "herzegovina" OR "hercegovina" OR "botswana" OR "brasil" OR "brazil" OR "bulgaria" OR "burkina faso" OR "burkina fasso" OR "upper volta" OR "burundi" OR "urundi" OR "cambodia" OR "khmer republic" OR "kampuchea" OR "cameroon" OR "cameroons" OR "cameron" OR "camerons" OR "cape verde" OR "cabo verde" OR "central african republic" OR "chad" OR "china" OR "colombia" OR "comoros" OR "comoro islands" OR "comores" OR "mayotte" OR "congo" OR "zaire" OR "costa rica" OR "cote divoire" OR "ivory coast" OR "cuba" OR "djibouti" OR "french somaliland" OR "dominica" OR "dominican republic" OR "east timor" OR "east timur" OR "timor leste" OR "ecuador" OR "egypt" OR "united arab republic" OR "el salvador" OR "eritrea" OR ethiopia OR fiji OR gabon OR (gabonese AND republic) OR gambia OR gaza OR "georgia republic" OR (georgia* AND republic) OR "georgian republic" OR ghana OR "gold coast" OR grenada OR guatemala OR guinea OR "guinea-bissau" OR guiana OR guyana OR haiti OR honduras OR india OR maldives OR nauru OR "papua new guinea" OR indonesia OR iran OR iraq OR "jamaica" OR "jordan" OR "kazakhstan" OR "kazakh" OR kenya OR kiribati OR "north korea" OR "peoples republic of korea" OR kosovo OR kyrgyzstan OR kirghizia OR (kyrgyz AND republic) OR kirghiz OR "lao pdr" OR laos OR lebanon OR lesotho OR basutoland OR liberia OR libya OR "north macedonia" OR macedonia OR madagascar OR "malagasy republic" OR malaysia OR malaya OR malay OR sabah OR sarawak OR malawi OR nyasaland OR mali OR "marshall islands" OR mauritania OR mauritius OR "agalega islands" OR mexico OR micronesia OR moldova OR moldova OR mongolia OR morocco OR ifni OR mozambique OR myanmar OR burma OR namibia OR nepal OR "netherlands antilles" OR nicaragua OR niger OR nigeria OR pakistan OR palestine OR paraguay OR peru OR philippines OR romania OR rumania OR roumania OR russia OR "russian federation" OR rwanda OR ruanda OR "saint lucia" OR "st lucia" OR "saint vincent" OR "st vincent" OR grenadines OR samoa OR "samoan islands" OR "navigator island" OR "navigator islands" OR "sao tome" OR "senegal" OR serbia OR montenegro OR "sierra leone" OR "sri lanka" OR ceylon OR "solomon islands" OR somalia OR "south africa" OR "south sudan" OR sudan OR suriname OR surinam OR swaziland OR syria OR "syrian arab republic" OR tajikistan OR tadzhikistan OR tadjikistan OR tadzhik OR tanzania OR thailand OR togo OR "togolese republic" OR tonga OR tunisia OR turkey OR turkmenistan OR turkmen OR tuvalu OR uganda OR ukraine OR ussr OR "soviet union" OR "union of soviet socialist republics" OR uzbekistan OR uzbek OR vanuatu OR venezuela OR vietnam OR "viet nam" OR "west bank" OR yemen OR yugoslavia OR zambia OR zimbabwe OR rhodesia OR ((developing OR

"less developed" OR "under developed" OR underdeveloped OR "middle income" OR "low income" OR "underserved" OR "under served" OR poor) AND (country OR countries OR nation OR nations OR population OR world OR economy OR economics)) OR ("low" AND ("gdp" OR gnp OR "gross domestic" OR "gross national")) OR ("low and middle income" AND (country OR countries)) OR lmic OR lmics OR "third world" OR "transitional country" OR "global south")

Last search: February 15, 2020

Pubmed: 92 results

Filter: none

PsycINFO: 160 results

Filters (Limiters): Peer reviewed, exclude dissertations

Expanders: apply related words, also search within the full text of the articles, apply equivalent subjects

Bireme (Virtual Health Library): 127 results

No filters. Search in title, abstract, subject

Embase: 116 results

Filters: All fields, publication type: article.

SciELO: 12 results

No filters

By including all terms, there were 2 papers. All the countries had to be removed. These were the search terms for SciELO:

(internalizing OR internalization) AND ("mental health" OR "psychopathologies" OR "mental illness" OR anxiety OR depression) AND (preschool OR "pre kinder" OR kinder)

Total of search with English keywords: 507 references.

Keywords in Portuguese and Spanish were added without accents to facilitate searches and avoid the use of SmartSearch, which yields a large number of irrelevant references.

Search Terms (Spanish)

 (internalizacion OR internalizante) AND ("salud mental" OR "psicopatologia" OR "enfermedad mental" OR "trastorno mental" OR ansiedad OR depresion OR problema de comportamiento) AND (preescolar OR primera infancia OR prekinder OR kinder OR jardin)

Psycinfo: 83 results but there were errors and only 58 were exportable

Search in "All databases" in EBSCO Host in order to expand the search because PubMed and EMBASE did not yield any results for words in Spanish.

Expanders: Apply equivalent subjects, Apply related words, Also search within the full text of the articles

Limiters: Scholarly (Peer Reviewed) Journals, exclude dissertations

Bireme(VHL): 36 results.

No filters

Scielo: 3 results

I removed the keyword: problema de comportamiento because including it led to fewer results (3)

No filters

Total of search with Spanish keywords: 97 references.

<u>Search Terms (Portuguese)</u>

(Internalizacao OR internalizante) AND (saude mental OR "psicopatologia" OR doenca mental OR transtorno mental OR ansiedade OR depressao OR transtorno conduta OR perturbacao conduta) AND (pre-escola OR primeira infancia OR pre-K OR educacao infantil OR jardim infancia)

Psycinfo: 23 results

Search in All databases in EBSCO Host because PubMed and EMBASE did not work for words in Portuguese.

Expanders: Apply equivalent subjects, Apply related words, Also search within the full text of the articles

Limiters Scholarly (Peer Reviewed) Journals, exclude dissertations

Bireme (VHL): 11 results

For **Bireme**, the initial combination just got 1 article. The terms were adjusted.These were the terms

(Internalizacao OR internalizante) AND (ansiedade OR depressao) AND (pre-escola OR pre-K OR primeira infancia OR pre-K OR educacao infantil OR jardim infancia)

No filters

SciELO: 3 results

For SciELO, the terms were adjusted: (Internalizacao OR internalizante) AND (pre-escola OR pre-K)

No filters.

Total of the search with Portuguese keywords: 37

Total eng+spa+por: 641 total

Duplicates removed: 222

Total to screen: 419 articles.

Appendix B

Coding of the Violence variable

The variable violence is based on Section B of the World SAFE questionnaire[201,202]. The Worlds SAFE inquires about levels of punishment from the caregiver and the partner, based on the caregiver's self-report. In the PreK survey, the levels of punishment for physical and verbal violence are coded as follows:
Non-violent punishment (yes/no)
Verbal: moderate (yes/no) or severe (yes/no)
Physical: moderate (yes/no) or severe (yes/no) (coded separately for caregiver and partner)

Upon analyses of the contingency tables, the levels of severity of the punishment were not mutually exclusive. For example, a child could be exposed to severe physical punishment and moderate physical punishment by the caregiver. Since in this study violence is defined as being exposed to severe forms of punishment by any of the parental figures (either physical or verbal), initially, a variable for violence was coded as follows:
0: No exposure
1: Exposure to severe physical OR verbal punishment.
2: Exposure to severe physical AND verbal punishment.

However, this variable, when included in the analyses, was not linearly associated with the outcomes. It showed that being exposed to severe verbal AND physical punishment led to implausible estimates, such as a protective association with internalizing problems, compared to no exposure, as seen in Table B1.

Table B1. Estimated Regression Coefficients with Violence coded as a 3-level variable.

Parameter	Estimate	Standard Error	t Value	Pr > |t|	95% Confidence Interval	
Intercept	2.2391005	0.02597163	86.21	<.0001	2.1859826	2.2922185
dviolencer 1	0.1195409	0.01125589	10.62	<.0001	0.0965201	0.1425618
dviolencer 2	-0.0221749	0.00886812	-2.50	0.0183	-0.0403122	-0.0040375
dviolencer 0	0.0000000	0.00000000	.	.	0.0000000	0.0000000

It was then decided to use binary coding for Physical or Verbal Violence:
0: No exposure

1: Exposure to any severe punishment.

The explanatory power of this variable is reduced with the binary coding. Studies intending to go beyond the scope of this study to explore the association of different forms of violence against the child and child behavioral problems, would require less parsimonious models. The models should include different kinds of violence, explore levels of severity, and consider other variables from the caregiver, such as sex and kind of parental figure.

Appendix C

Effects of Quality-Time spent with the Mother

The effects of quality-time spent with the mother in all children versus those with both parental figures were examined. All models were adjusted by externalizing problems score, sleep problems score, food insecurity, social support score, and neighborhood vulnerability score.

Table C1 shows the mean change in each of the outcomes: total internalizing problems, the Withdrawn Syndrome, and the Somatic Complaints Syndrome.

Table C1. Mean change in the outcomes in all children and those with both parent figures

Outcome	All the children	Those with both parent figures
Total Internalizing Problems	-0.015 (95% CI: -0.036, 0.005)	-0.01593 (CI: -0.039, 0.008)
Withdrawn	-0.046 (95% CI: -0.112, 0.024)	-0.089* (95% CI: -0.152, -0.022)
Somatic Complaints	-0.071* (95% CI: -0.128, -0.010)	-0.108* (95% CI:-0.176, -0.035)

*Significant at the 5% level

Since there were differences between all and those with both parent figures in the withdrawn syndrome, interaction by sex of preschoolers and by parental depression was examined. See table 2.

Table C2. Assessment of interaction between quality-time spent with the mother by sex and by parental depression.

Interaction term	All Children	Those with both parent figures
Mother time quality* Sex	Significant*	Not significant
Mother time quality* parent depression	Not significant	Not significant

Since the interaction term with sex was significant in all the children, the model was ran stratifying by sex to compare.

In girls, the null was not rejected at the 5% level of significance.

It is estimated that, on average, boys who spend lower time quality with their mother have a score 0.102 points greater than those who spend higher time quality with their mother figure.

Appendix D

Calculation of the Intra Class Correlation Coefficient

The data in the PreK survey could be clustered by the school (30 schools) or by class within each school (144 classes). Calculations for Intra Class Correlation Coefficients (ICC) were performed using empty mixed models with total internalizing problems score as the outcome.

Ignoring grouping by school, the estimates of the empty model were the following:

Variance between: 0.000077

Variance within: 0.01638

$$\text{ICC} = \frac{0.000077}{0.01638 + 0.000077} = 0.0047$$

The class explained 0.47% of the variance. A three-level model was specified to take school into account, providing three variance components.

Variance between school: 0.000053

Variance between class nested in school: 0.000032

Variance within group: 0.01637

$$\text{ICC for school} = \frac{0.000053}{0.01637 + 0.000053 + 0.000032} = 0.0032$$

$$\text{ICC for class} = \frac{0.000032}{0.01637 + 0.000053 + 0.000032} = 0.0019$$

Grouping by school explained 0.3% of the variance in internalizing problems, and grouping by class explained 0.2% of the variance. Although the ICC was very low (below 1%), clustering by the school was included in all the models to account for any potential similarities in the children's backgrounds.

Appendix E

Table E1. Mean scores estimates on Outcomes, Exposures, and Confounders

	Girls	Boys	P	Missing
Mean Scores of CBCL 1.5-5 based on ASEBA guidelines				
Anxiety/Depression	4.61	4.51	0.514	.
Emotionally Reactive	3.78	3.91	0.469	.
Somatic Complaints	3.20	2.77	0.002**	.
Withdrawn	1.92	2.26	0.004**	.
Parental Psychopathology				
Depression (PHQ-9 score)	4.80	5.05	0.415	70
Anxiety (GAD-7 score)	6.04	6.18	0.641	50
PTSD (PCL-C score)	5.64	5.26	0.633	59
Intrafamilial Violence				
% of children with severe forms of violence	28.90	31.96	0.224	11
Low time Quality with Parents				
Mean quality of time (score 0 to 5)	4.57	4.61	0.384	176
Mean score externalizing problems	13.08	14.80	0.000**	.
Mean score Sleep problems	2.71	2.70	0.938	.
% Children without food security	3.04	1.81	0.195	4
% parents substance use (including tobacco)	19.46	20.00	0.826	.

* significant at the 5% level

**significant at the 1% level

Appendix F

Assessment of Confounding

Table F1. Examination of each Potential Confounder of the relationship between each Exposure and Outcome.

Exposure	Outcome		Externalizing Problems	Sleep Problems	Food Insecurity
Parental Depression	Total Internalizing Problems	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N
Parental Depression	Withdrawn	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N
Parental Depression	Somatic Complaints	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N
Physical or Verbal violence	Total Internalizing Problems	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N
Physical or verbal violence	Withdrawn	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N
Physical or verbal violence	Somatic Complaints	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N
Low Quality-Time	Total Internalizing Problems	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N
Low Quality-Time	Withdrawn	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N
Low Quality-Time	Somatic Complaints	With Exposure	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	Y	Y	N

Table F1. Examination each Potential Confounder of the relationship between each Exposure and Outcome (Continued)

Exposure	Outcome		Parental Social Support	Neighborhood disadvantage	Parental substance Use	Child's age
Parental Depression	Total Internalizing Problems	With Exposure	Y	Y	Y	N
		With Outcome in Unexposed	Y	Y	Y	N
		Change of 10% in Adjusted vs. Crude?	N	N	N	N
Parental Depression	Withdrawn	With Exposure	Y	Y	Y	N
		With Outcome in Unexposed	Y	Y	Y	N
		Change of 10% in Adjusted vs. Crude?	N	N	N	N
Parental Depression	Somatic Complaints	With Exposure	Y	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	N	N	N	N
Physical or Verbal violence	Total Internalizing Problems	With Exposure	Y	Y	Y	N
		With Outcome in Unexposed	Y	Y	Y	N
		Change of 10% in Adjusted vs. Crude?	N	N	N	N
Physical or verbal violence	Withdrawn	With Exposure	Y	Y	Y	N
		With Outcome in Unexposed	Y	Y	Y	N
		Change of 10% in Adjusted vs. Crude?	N	N	N	N
Physical or verbal violence	Somatic Complaints	With Exposure	Y	Y	Y	Y
		With Outcome in Unexposed	Y	Y	Y	Y
		Change of 10% in Adjusted vs. Crude?	N	N	N	N
Low Quality-Time	Total Internalizing Problems	With Exposure	Y	Y	Y	N
		With Outcome in Unexposed	Y	Y	Y	N
		Change of 10% in Adjusted vs. Crude?	N	N	N	N
Low Quality-Time	Withdrawn	With Exposure	Y	Y	Y	N
		With Outcome in Unexposed	Y	Y	Y	N
		Change of 10% in Adjusted vs. Crude?	N	N	N	N
Low Quality-Time	Somatic Complaints	With Exposure	Y	Y	Y	N
		With Outcome in Unexposed	Y	Y	Y	N
		Change of 10% in Adjusted vs. Crude?	N	N	N	N