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Prevalence of endocrine disorders among children exposed to Lavender Essential Oil and Tea Tree Essential Oils

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ABSTRACT

Background: Lavender essential oil and tea tree essential oil have become popular ingredients in personal care and household products in recent decades. Questions regarding the safety of these oils in pediatric populations have been raised, proposing a link between these essential oils and endocrine disruption in children, specifically prepubertal gynecomastia. To date, no epidemiological studies have been conducted to evaluate this proposed link.

Methods: This is a cross sectional study conducted among parents of children in the United States to identify the prevalence of endocrine disruption in children aged 2–15 years old. This study also evaluates the potential for a relationship between the exposure of lavender essential oil and tea tree essential oil products and endocrine disrupting outcomes.

Results: In 556 children with a mean age of 6.33 (SD = 3.92), prevalence of endocrine disruption was .016 (SD = 0.13). No cases of prepubertal gynecomastia were identified in either group, and prevalence of precocious puberty, delayed puberty, growth hormone deficiency, and hypothyroidism were all consistent with population norms. Total risk of endocrine disorders among those exposed (0.0194) did not differ from the risk of those unexposed (0.0069). The risk ratio was 2.796 (95% CI: 0.352, 22.163, $P = .458$).

Conclusion: Children who were regularly exposed to lavender or tea tree essential oils experienced the same risk of endocrine disorders as those who were not exposed.

1. Introduction

1.1. Background

Lavender essential oil and tea tree essential oil have become popular ingredients in personal care and household products in recent decades [1,2]. A major reason for the increase in their popularity is the concern regarding the potential risks associated with synthetic ingredients used in most products [3]. These two plant ingredients have been used in personal care for millennia and have been considered safe for all ages [4,5].

Questions regarding the safety of these oils in pediatric populations were posed in a 2007 manuscript discussing three pediatric case studies and a laboratory study [6]. These authors proposed a potential causal link between these ingredients and prepubertal gynecomastia, a rare endocrine-related disorder in young boys, and issued a call to action for epidemiological research to evaluate the potential for a relationship. Prepubertal gynecomastia refers to the growth of breast tissue in boys who have not yet reached the age of puberty and is typically idiopathic [7–9].

Subsequent case studies and laboratory studies have been published, with conflicting findings, but no clinical or epidemiological studies have been conducted to evaluate these claims [10–12]. In a recent publication, the proposed outcome was extended beyond prepubertal gynecomastia to apply to endocrine disorders of all types [11]. Endocrine disruptors are chemicals that mimic or interfere with hormones within the body. These chemicals are ubiquitous in the modern environment and can be found in household products and personal care products and pose a

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public health threat as they can adversely affect fertility, immune health, and even pediatric neurodevelopment [13,14]. Identification and avoidance of endocrine-disrupting chemicals in the environment is a public health priority [15].

As a result, cautions have been issued to the public, warning that exposure to these ingredients may cause endocrine disruption in children [16]. These cautions, however, are based on a small number of case reports and have not been examined in epidemiological studies. Case reports document novel situations, producing hypotheses for epidemiological research; alone, they are insufficient to provide conclusive evidence of benefit or harm because they are unable to meet the criteria for establishing causation [17].

In addition, the case reports upon which these claims are based contain multiple epidemiological and methodological errors, including misclassification of exposure status and failure to evaluate other known causal factors, such as dietary exposures, known endocrine disruptors, or obesity [11]. Exposure status was determined by asking the parents whether they had used products containing either essential oil. More than one of the cases of prepubertal gynecomastia attributed to lavender or tea tree essential oil in these reports was found, upon subsequent investigation, to be misclassification [18]. This is consistent with research on the sensitivity and specificity of this approach, which identifies a high false-positive and false-negative rate [10].

In vitro and in vivo studies evaluating the potential for endocrine disruption caused by these ingredients have also produced conflicting results. While the laboratory studies accompanying case reports have identified endocrine disrupting potential in these essential oils, numerous researchers in multiple continents have found no endocrine-disrupting potential in either oil [19–22]. Some methodological concerns have been raised regarding the way in which these laboratory studies were conducted, which may explain these inconsistencies in the published findings [23].

Evaluation of this proposed relationship through other scientific approaches also produces conflicting information. Ecological evidence does not support the causal claim, as the prevalence of prepubertal gynecomastia remains stable, after adjusting for other factors, despite tea tree and lavender sales price increasing during the same time period [24,25]. Tea tree essential oil sales have been projected to increase from $38.8 million in 2017 to $59.6 million by 2025 and the lavender oil market has been projected to reach $124.2 million by 2024 [26,27].

Furthermore, human studies evaluating the effects of these oils have not identified endocrine-disrupting potential, and clinical trials monitoring the adverse effects of these oils have not observed endocrine disruption in participants [28–37]. Finally, a study evaluating the potential for long-term high-dose lavender oil to interact with hormonal birth control taken by young women found that there was no interaction between the two [38].

This raises the question of whether those warnings were issued prematurely as there is no current epidemiological or clinical evidence of a causal relationship between prepubertal gynecomastia or any other form of endocrine disruption and the use of essential oil-based personal care products.

The criteria for establishing a causal relationship (covariation, temporal precedence, and nonspuriousness) have not yet been evaluated through clinical studies, despite the call for epidemiological studies and publication of additional conflicting findings in laboratory studies and case reports. Establishing a causal relationship requires the confirmation of the presence of a correlation and the evaluation of the correlation for temporal precedence to confirm that exposure precedes the outcome. Finally, the potential for a spurious relationship must be ruled out. This cross-sectional study addresses this gap in the literature by identifying whether a correlation exists between exposure to these ingredients and endocrine disorders. If a relationship is identified, future epidemiological research should evaluate temporality to determine whether the exposure precedes the outcome, and then additional studies should be conducted to determine whether the relationship is spurious or should be considered causal. This study is reported using the STROBE checklist for cross-sectional studies.

1.2. Objectives

The purpose of this cross-sectional study is to identify the lifetime prevalence of endocrine disruption, specifically prepubertal gynecomastia and precocious puberty, among children who are exposed to lavender and tea tree essential oils and to compare this prevalence with that observed in the general population. The secondary objective of this study is to compare the lifetime prevalence among exposed children with that observed in unexposed children to determine whether exposed children are more likely to develop prepubertal gynecomastia or to experience any form of endocrine disruption. This study utilizes established epidemiological research methods with a clinically validated instrument. If an association is discovered, further research is required to identify the source and direction of this relationship and to determine whether it is causal.

2. Methods

2.1. Study design

This is a cross-sectional study, conducted among parents of children in the United States, to identify the prevalence of endocrine disruption in children aged 2–15 years old exposed to products containing lavender and tea tree essential oils. This is the age group at risk of developing prepubertal gynecomastia or precocious puberty due to endocrine disruptors [39–41]. This study also evaluates the potential for a relationship between the exposure to lavender essential oil and tea tree essential oil products and endocrine-disrupting outcomes.

2.2. Setting

Participants were recruited from email databases of the research foundation, social media, and from pediatrician and clinician offices around the country. Data collection began on February 14, 2019, and is ongoing. This study evaluates the first year of data collected.

2.3. Participants

Participants qualified for inclusion in this study are those who live in the United States and had children who were between the ages of 2 years and 15 years old. This age range was selected because it allows sufficient time for the child to be exposed to one of the exposures of interest for a duration sufficient to contribute to the outcome, if such a relationship exists, and it continues through the age of puberty.

2.4. Ethical approval

The protocol for this study was approved by a central IRB and was carried out in compliance with the Helsinki declaration of 1964. This study was registered at Clinical Trials dot gov, #NCT04836364. Participants were informed about the risks and benefits of the study as well as confidentiality. All participants provided informed consent prior to data collection.

2.5. Variables

Data were obtained using the Aromatic Plant Ingredients and Child Health Survey (APICHS), a validated measurement instrument developed for this population [10]. This instrument provides accurate classification of the exposure status, far exceeding the typical approach of exposure classification of asking parents during a clinician visit whether their children use products containing these ingredients. The single question approach is prone to multiple forms of bias, ultimately resulting in misclassification. The APICHS has been found to have a positive predictive value of 97.22% with extremely low false-negative and false-positive rates. To further reduce misclassification, data collection occurred online, allowing the participants sufficient time to consider each potential exposure method and provide accurate information. This data collection format also eliminated the potential for interviewer bias.

Exposure was operationalized as weekly or more frequent contact with a lavender or tea tree essential oil-containing product for a period of four or more months. This is a more precise definition of exposure than what has been used in case reports on this topic, which either did not specify the duration of the exposure or referenced vague exposure durations.

The primary outcomes of prepubertal gynecomastia and precocious puberty were defined as having ever received a diagnosis of either condition. Endocrine disruption was defined as having ever received a diagnosis of prepubertal gynecomastia, precocious puberty, delayed puberty, diabetes (type 1 or 2), thyroid conditions (including hypo- and hyperthyroidism), Cushing's syndrome, hypopituitarism, or growth hormone deficiency.

Secondary outcomes include endocrine-related symptoms, which was defined as having experienced obesity, short stature, or failure to meet growth milestones. These symptoms are associated with endocrine disruption but are not known to be caused by endocrine disruptors. To ensure comprehensive evaluation of the potential for endocrine disruption, endocrine disorders and symptoms of endocrine disruption were evaluated separately.

2.6. Bias

Recall bias is one of the greatest threats to retrospective and cross sectional studies. To reduce the risk of recall bias, the APICHS measurement tool was used, which has a sensitivity and specificity of 100% and 92.86%, respectively [10].

Selection bias is also a concern with cross-sectional studies. This concern was addressed by targeting participants who self-identify as users of natural personal care products in the inclusion criteria. These individuals differ from the general population with regard to the exposure of interest as they are more likely to have used products with essential oils as active ingredients or fragrances. This reduces the selection bias as the findings should be generalized specifically to this population. Reduction of selection bias was further addressed through the wording in recruitment materials and data collection materials, which emphasized the inclusion criteria rather than either the exposure or the outcome of interest. This prevented participants from self-selecting due to either exposure or outcome status.

2.7. Sample size and power

A power analysis was conducted to determine the required sample size to detect the prevalence of prepubertal gynecomastia within a population of users of lavender essential oil. With a hypothesized frequency of 2.5% and a 95% confidence interval of 2%, a total of 235 patients are required.

The frequency for sample size estimation is based on findings from Johnson and Einav-Bachar, which indicate that gynecomastia affects approximately 50–60% of the male pubertal population, and that prepubertal gynecomastia accounts for approximately 5% of gynecomastia referrals among this population, producing a 2.5% incidence rate [42–45]. To accommodate the inclusion of both sexes and adjust for the fact that not all participants will be exposed to these ingredients, the sample size was doubled. To further account for potential lack of completion of the survey, missing data, or other irregularities, an additional 5% increase to sample size was included. This produced a total sample of 505 to meet the research objective of identifying the prevalence of prepubertal gynecomastia among pediatric patients who are regularly exposed to lavender and/or tea tree essential oils.

2.8. Quantitative variables

Demographic variables include age, sex, race, region, household income, maternal educational attainment, and paternal educational attainment. These were used as control variables in the analysis. In addition, a sex-specific analysis was conducted to evaluate the potential relationship between exposure and outcomes within each sex.

2.9. Statistical methods

2.9.1. Descriptives

The prevalence of endocrine disruptive disorders was calculated as the percentage of patients experiencing any of the following disorders: prepubertal gynecomastia, precocious puberty, delayed puberty, diabetes (type 1 or 2), thyroid conditions (including hypo- and hyperthyroidism), Cushing's syndrome, hypopituitarism, or growth hormone deficiency. In addition, the prevalence by age group and sex was established. Means, standard deviations, and ranges are provided for continuous exposure and outcome variables, and frequencies are provided for categorical exposure and outcome variables.

The exposure variable was created as both a dichotomous exposure variable and a continuous quantitative variable accounting for the number of exposures a child experienced. This allowed multiple forms of comparisons, including both establishment of any relationship that may exist and assessment for a dose-dependent relationship.

2.9.2. Comparison of lifetime prevalence with population norm

To compare prevalence rates of prepubertal gynecomastia among those with documented lavender or tea tree essential oil exposure to the population norm of 2.5%, a one-sample *t*-test was conducted. This test was also conducted to compare the rates of endocrine disruption collectively to population norms. Assumptions of independence and normality were evaluated. Both the Kolmogorov-Smirnov test and Shapiro-Wilk test were used to evaluate normality, and boxplots were used to examine data for outliers.

2.9.3. Risk ratio and dose response

To compare the risk of endocrine disruption outcomes, among those who were exposed to these essential oils and those who were not, the Fisher's exact test was used and an attributable fraction was identified. For these tests, exposure was classified as having one or more regular exposures to products containing lavender or tea tree oils, and those who were not exposed to any products were classified as unexposed.

To evaluate a potential dose–response relationship based on the extent of the exposure to these ingredients, binary logistic

regression was conducted. Assumptions of independence, lack of multicollinearity, and linearity of log odds were evaluated through a correlation matrix and Box Tidwell test. Goodness of fit for the model was evaluated using the Hosmer-Lemeshow goodness of fit test. Sensitivity analysis was conducted by removing each contributing variable to identify how it affected the overall model. Control variables that did not contribute significantly to the model for logistic regression were removed to improve the model. All data were analyzed using Stata v16.1 with a P value of .05 indicating significance.

3. Results

3.1. Descriptives

A total of 710 individuals viewed the study information and provided informed consent. After the evaluation of data including removal for non-completers and duplicate entries, a total of 556 children ($n = 556$) were represented in the final data analysis.

The mean age of the children in this sample was 6.33 (SD = 3.92). The sample was 85.79% white ($n = 477$) and 54.8% male ($n = 302$). Household income was approximately normally distributed and was above average, with 83.09% of the sample's household income above $50,000 annually. The most common household income range in the sample was $100,000 to $150,000, representing 149 children or 26.8% of the sample (Table 1). These demographics are consistent with other studies identifying those most likely to use natural products [46].

3.2. Prevalence and population norms

Exposure to lavender and tea tree essential oils was common, with 412 (74.10%) of the participants reporting exposure to at least one product containing one or both of these ingredients. Among children who were exposed to these ingredients ($n = 412$), the average child was exposed to 4.69 (SD = 5.05) products, with a range of 1–39 products.

Of the 556 children in this sample, nine children experienced an endocrine disruption-related disorder. This included two cases of precocious puberty, one case of delayed puberty, four cases of hypothyroidism, and one case of growth hormone deficiency. There were no cases of prepubertal gynecomastia, diabetes (type 1 or 2), hyperthyroidism, Cushing's syndrome, or hypopituitarism in this sample.

For each disorder identified, a one-sample t-test was conducted to evaluate whether the endocrine disorder was more prevalent among children with routine exposures to essential oil ingredients than population norms sourced from epidemiological studies in the literature. One goal of this study was to compare the lifetime prevalence of prepubertal gynecomastia in children exposed to lavender or tea tree essential oils with the population norm of 2.5%, but no cases of prepubertal gynecomastia were present in the sample, producing a prevalence of 0%.

For the outcome of precocious puberty, the prevalence was 0.49% (95% CI: 0.00%, 2.00%) among children exposed to these ingredients. This is consistent with the population norm of 0.02%, identified by Cesario [47], Kletter [48], and Kota [49]. This study found no difference in prevalence among children who are regularly exposed to lavender or tea tree essential oils and those who are not ($t(411) = 1.36$, $P = 0.176$).

To identify the prevalence of delayed puberty among children exposed to lavender essential oil or tea tree essential oil, prepubertal children were excluded. The prevalence of delayed puberty among pubertal children exposed to lavender or tea tree essential oils was found to be 1.39% (95% CI: 0.00%, 8.18%). This is consistent with the population norm of 2.5% [50,51]. There is no difference in the prevalence of delayed puberty between children regularly exposed to lavender and tea tree essential oils and those who are not ($t(411) = -0.80$, $P = .426$).

The prevalence of growth hormone deficiency among children exposed to lavender and tea tree essential oils was 0.49% (95% CI: 0.00%, 2.00%). The population prevalence is estimated to be between 0.025% and 0.01% [52]. A one-sample t-test was conducted to compare the prevalence identified in this study with the mean of the population norm, and no statistically significant difference was identified ($t(411) = 1.35$, $P = .178$). Children who are regularly exposed to lavender and tea tree essential oils experience the same prevalence of growth hormone deficiency as the general population.

The prevalence of hypothyroidism among children exposed to lavender and tea tree essential oils was found to be 0.73% (95% CI: -0.00%, 2.00%). This is consistent with the population norm of 0.135% [53]. This study found no difference in the prevalence of hypothyroidism among children who are regularly exposed to lavender or tea tree essential oils and those who are not ($t(411) = 1.41$, $P = .158$) (Table 2).

3.3. Exposed compared with unexposed

A two-sided Fisher's exact test was performed to identify the odds of endocrine disorders among those exposed compared with those unexposed. Risk among those exposed (0.0194) did not differ from the risk among those unexposed (0.0069), with a risk difference of 0.0125. The risk ratio was 2.796 (95% CI: 0.352, 22.163, $P = .458$). Children who were regularly exposed to lavender or tea tree essential oils experienced the same risk of endocrine disorders as those who were not exposed.

Table 1
Demographics and characteristics of the study population.

Variable	
Age, years, mean ± SD (range)	6.33 (3.92) (2–15)
Sex, n (%) (male)	302 (54.8)
Race, n (%)	
White	477 (85.79)
Black	5 (0.9)
Hispanic	13 (2.34)
Multiple ethnicity/other	61 (10.97)
Household income, n (%)	
< $50,000	94 (16.91)
$50,000 - $74,999	112 (20.14)
$75,000 - $99,999	113 (20.32)
$100,000 - $149,999	149 (26.80)
$150,000 +	88 (15.83)
Education, n (%) maternal/paternal)	
Highschool	41 (7.37)/80 (14.39)
Some college	151 (27.15)/133 (23.93)
Bachelor's degree	203 (36.51)/195 (35.07)
Master's degree	84 (15.11)/103 (18.53)
Doctoral degree	77 (13.85)/42 (7.55)
Unknown	0 (0)/3 (0.54)

Table 2
Prevalence of Endocrine Disruption Among Children Exposed to Essential Oils and t-tests comparing to population norms.

Endocrine disorder	Frequency	Percent (%)	t
Prepubertal gynecomastia	0	0	–
Precocious puberty	2	0.49	1.36
Delayed puberty	1	1.39	−0.80
Growth hormone deficiency	1	0.49	1.35
Hypothyroidism	4	0.73	1.41

3.4. Dose–response relationship

Binary logistic regression was performed to evaluate the impact of exposure to lavender and tea tree essential oils on the likelihood that children would develop endocrine system disorders as compared with those who were not exposed. The model contained 6 demographic control variables and the exposure variable of quantity of lavender/tea tree exposures. The full model containing all predictors was not statistically significant: χ [2] (18, $N = 552$) = 15.25, $P = .645$. The odds ratio for pediatric endocrine disorders for children exposed to lavender and tea tree essential oils versus those who were unexposed was 1.001 (95% CI: 0.853, 1.175, $P = .989$). There was no difference in endocrine-related outcomes among children who use lavender or tea tree essential oil-containing products and children who do not.

As shown in Table 3, none of the predictor variables in the model were significant at the $P = 0.05$ level, with the exception of race (Black). The odds ratio for Black children was 26.51 (95% CI: 1.264, 556.459). However, this sample only included 5 Black children and the confidence interval is extremely large, so the results should be interpreted with caution. A sensitivity analysis was conducted by removing each variable, one at a time, and re-running the analysis. The predictors remained insignificant in each additional analysis. The model as a whole explained between 2.7% (Cox and Snell R square) and 17.8% (Nagelkerke R squared) of the variance in endocrine disorders. This indicates that some other factor is responsible for endocrine disorders among these children.

3.5. Additional analyses

To comprehensively evaluate the potential for a relationship between these essential oils and endocrine-related disorders in children, an additional analysis on the symptoms of endocrine disruption was conducted. This included obesity, short stature, and failure to meet growth milestones.

In this sample, 8 children were diagnosed with obesity, 28 children were diagnosed with short stature, and 59 children were diagnosed with failure to meet growth milestones. The risk ratios of experiencing these symptoms were 0.121 among children exposed to lavender and tea tree essential oils and 0.160 among children who were not exposed. A Fisher's exact test was conducted to determine the risk ratio of 0.60 (95% CI: 0.482, 1.199, $P = .252$). There was no difference in the symptoms of endocrine disruption among children regularly exposed to lavender and tea tree essential oils and children who were not exposed.

To identify a potential dose-dependent relationship, logistic regression was performed. Control variables included sex, race, paternal educational attainment, maternal educational attainment, income, and age. The full model was statistically significant (χ [2] (17, $N = 547$) = 34.65, $P = .007$). The model explained between 11.3% (Cox and Snell R square) and 8.1% (Nagelkerke R square) of the variance in symptoms.

Of these variables, only paternal educational attainment was significant, with lower levels of education correlating with higher levels of obesity, short stature, or failure to meet growth milestones. This is consistent with the overall scientific literature. The odds ratio for symptoms of endocrine disruption in children exposed to lavender and tea tree essential oils versus those who were unexposed is 0.977 (95% CI: 0.918, 1.040, $P = .460$). There was no difference in the symptoms of endocrine disruption between children exposed to lavender and tea tree essential oils compared with those who were not exposed.

4. Discussion

4.1. Key results

The purpose of this study was to identify the prevalence of endocrine disorders in children who are regularly exposed to lavender and tea tree essential oils. A secondary objective was to identify the odds ratio of endocrine disorders in exposed children versus unexposed children.

This study comprehensively evaluated the potential for a relationship between the use of lavender and tea tree essential oils and endocrine disruption using multiple statistical models. Numerous methods were used for evaluating the sample in this study, and all found that there is no difference in the prevalence of endocrine disorders among children exposed to lavender or tea tree essential oil, compared with children who were not exposed.

4.2. Limitations

This is, to the best of our knowledge, the first and only epidemiological study to evaluate the proposed relationship between

Table 3
Logistic regression on endocrine disruption.

Predictor	Predictor	B	SE	OR	95% CI	*P* value
Exposure		0.001	0.082	1.001	0.8527, 1.1753	.989
Sex (female)		0.778	0.761	2.176	0.4901, 9.6637	.307
Race	**Black**	**3.278**[a]	**1.553**[a]	**26.5170**[a]	**1.2636, 556.4598**[a]	**.035**[a]
	Hispanic	2.112	1.332	9.1270	0.6702, 124.2978	.097
	Other	−0.089	1.140	1.0934	0.1170, 10.2188	.938
Paternal education	Some college	0.785	1.452	2.1933	0.1274, 37.7613	.589
	Collegedegree	0.834	1.455	2.3029	0.1330, 39.8615	.566
	Graduate degree	1.801	1.505	6.0813	0.3812, 116.2211	.230
	Doctoral degree	1.512	1.824	4.5352	0.1270, 162.0109	.407
Maternal education	Some college	−1.281	1.344	0.2778	0.0199, 3.8735	.341
	College degree	−1.781	1.404	0.1684	0.0108, 2.6389	.205
	Graduate degree	−1.238	1.493	0.2899	0.1550, 5.4231	.407
	Doctoral degree	−2.142	1.820	0.1174	0.0033, 4.1596	.239
Income	$50,000-$74,999	−1.257	1.326	0.2844	0.0212, 3.8225	.343
	$75,000-$99,999	-.0948	1.314	0.3874	0.0295, 5.0892	.471
	$100,000-$149,999	−0.950	1.169	0.3866	0.0390, 3.8287	.417
	$150,000 +	−0.570	1.164	1.7691	0.0181, 17.3350	.624
Age		0.138	0.096	1.1477	0.9501, 1.3865	.153

[a]Bold = significant at the $P < 0.05$ level.
[b]B = coefficient; SE = standard error; OR = odds ratio; CI = confidence interval.

essential oil use and endocrine disruption among children. The study was sufficiently powered to respond to the call to action issued in the 2007 manuscript and utilizes a measurement tool specifically developed and validated for this population. However, it should be interpreted within the context of its methodology and associated limitations.

In this study, no cases of prepubertal gynecomastia were identified, prohibiting a comparison between prevalence rates between groups. This is consistent with other reports, indicating that prepubertal gynecomastia is extremely rare. However, given the absence of identified cases of prepubertal gynecomastia, a comparison of prevalence between groups was not possible. This study was powered to identify a 2-fold increase in the prevalence of prepubertal gynecomastia, which is a much smaller increase than has been suggested. The study was powered to identify such a small increase for ensuring that any additional risk was identified. Therefore, if an increased risk of endocrine disruption does exist, it is too small to be identified in this sample and may therefore be of questionable clinical significance. This cross-sectional study confirms that prepubertal gynecomastia is extremely rare among children who are routinely exposed to lavender and tea tree essential oils. There is no evidence of any association between these two ingredients and endocrine disruption of any type, including prepubertal gynecomastia.

Moreover, this study was conducted primarily on white children. Future research should include children of color to confirm generalizability.

4.3. Interpretation

This study finds no evidence of a relationship between the use of lavender or tea tree essential oils and endocrine disruption in children. This is consistent with other human research in the literature. More research needs to be conducted to confirm these findings, specifically through larger cross-sectional studies and on larger subsets of children of color. Exposure to lavender and tea tree essential oil has become widespread, yet a subsequent increase in endocrine disruption prevalence has not been observed. Usage of products containing lavender essential oil and/or tea tree essential oil is not associated with increase in endocrine disruption among children. The claim that lavender and tea tree essential oils cause endocrine disruption in children cannot be substantiated through epidemiological studies.

Endocrine disruption in children remains a public health concern. Additional epidemiological studies should be conducted to identify the cause(s) of these disorders. Future research should focus on the identification of exposures with statistically and clinically significant relationships, using established criteria for the assignment of causation rather than case reports or speculation.

4.4. Generalizability

This study was conducted primarily on white children in the United States. It has been suggested that these ingredients only affect children of Hispanic descent. These findings should not be generalized to populations not sufficiently represented in the sample, including Black children and children of Hispanic descent. More research should be conducted on these populations to confirm that no relationship exists between exposure and endocrine disruption activity.

This study was also conducted on American children using products available in American markets. It is possible that synergistic activity may be present in formulations available in other countries. However, the claims of an association between these ingredients and endocrine disruption outcomes originated in the United States and primarily involve products marketed in the US; therefore, the lack of an epidemiological relationship between the two is generalizable beyond the North American continent. Furthermore, should a synergistic relationship exist, it would be attributable to the specific combination of ingredients that produces this effect and not individual ingredients.

5. Conclusion

This study provides evidence that lavender essential oil and tea tree essential oil are safe ingredients in formulations for personal care products for use in children. The prevalence of endocrine disorders among children exposed to these ingredients is consistent with the general population and the proposed links between these ingredients and endocrine disruption cannot be substantiated in epidemiological studies. Investigation on endocrine disruption, including prepubertal gynecomastia, in children should be continued, with prioritization of identification of potential causal agents.

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Author declaration

We the undersigned declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere.

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). She is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author and which has been configured to accept email from c.hires@franklinhealth.org.

Ethical statement for Franklin Health Research Center

Hereby, I, Christy Hires, MPH, CHES, consciously assure that for the manuscript "Prevalence of Endocrine Disorders Among Children Exposed to Lavender Essential Oil and Tea Tree Essential Oils" the following is fulfilled:

1) This material is the authors' own original work, which has not been previously published elsewhere.

2) The paper is not currently being considered for publication elsewhere.

3) The paper reflects the authors' own research and analysis in a truthful and complete manner.

4) The paper properly credits the meaningful contributions of co-authors and co-researchers.

5) The results are appropriately placed in the context of prior and existing research.

6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.

7) All authors have been personally and actively involved in substantial work leading to the paper and will take public responsibility for its content.

8) The protocol for this study was approved by a central IRB and was carried out in compliance with the Helsinki declaration of 1964. This study was registered at Clinical Trials dot gov, #NCT04836364.

9) All participants were informed about the risks and benefits of the study as well as confidentiality. All participants provided informed consent prior to data collection.

I agree with the above statements and declare that this submission follows the policies of Franklin Health Research Center as outlined in the Guide for Authors and in the Ethical Statement.

CRediT authorship contribution statement

Jessie Hawkins: Conceptualization, Methodology, Formal analysis, Writing – original draft, Supervision, Project administration. **Christy Hires:** Methodology, Investigation, Writing – original draft, Visualization. **Elizabeth Dunne:** Methodology, Investigation, Writing – review & editing. **Lindsey Keenan:** Methodology, Writing – review & editing.

Declaration of competing interest

The authors declare no conflicts of interest associated with this publication, and there has been no significant financial support for this work that could have influenced its outcome.

Visual abstract

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