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Dental Composite Restorations and Psychosocial Function in Children

WHAT'S KNOWN ON THIS SUBJECT: Dental composites composed of bisphenol A (BPA) derivatives are common alternatives to amalgam, but may release BPA. Gestational BPA exposure has been associated with poorer behavior in children. A safety trial of amalgam found worse psychosocial outcomes for children randomized to composites.

WHAT THIS STUDY ADDS: In the trial, greater exposure to bisphenol-A-glycidyl-methacrylate-based dental composite in children aged 6 to 10 years was associated with worse self-reported psychosocial functioning at 5-year follow-up. There were no such associations with exposure to dental amalgam or urethane-dimethacrylate-based polyacid-modified composite (compomer).

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KEY WORDS

composite dental resin, composite resins, bisphenol A-glycidyl methacrylate, compomers, child behavior, behavioral symptoms, affective symptoms

ABBREVIATIONS

BASC-SR—Behavior Assessment for Children–Self-Report
bisGMA—bisphenol A-glycidyl methacrylate
BPA—bisphenol A
CBCL—Child Behavior Checklist
NECAT—New England Children's Amalgam Trial
UDMA—urethane dimethacrylate

abstract

BACKGROUND AND OBJECTIVE: Resin-based dental materials may intraorally release their chemical components and bisphenol A. The New England Children's Amalgam Trial found that children randomized to amalgam had better psychosocial outcomes than those assigned to composites for posterior tooth restorations. The objective of this study was to examine whether greater exposure to dental composites is associated with psychosocial problems in children.

METHODS: Analysis of treatment-level data from the New England Children's Amalgam Trial, a 2-group randomized safety trial comparing amalgam with the treatment plan of bisphenol A-glycidyl methacrylate (bisGMA)-based composite and urethane dimethacrylate–based polyacid-modified composite (compomer), among 534 children aged 6 to 10 years at baseline. Psychosocial function at follow-up (n = 434) was measured by using the self-reported Behavior Assessment System for Children (BASC-SR) and parent-reported Child Behavior Checklist (CBCL).

RESULTS: Children with higher cumulative exposure to bisGMA-based composite had poorer follow-up scores on 3 of 4 BASC-SR global scales: Emotional Symptoms (β = 0.8, SE = 0.3, P = .003), Clinical Maladjustment (β = 0.7, SE = 0.3, P = .02), and Personal Adjustment (β = –0.8, SE = 0.2, P = .002). Associations were stronger with posterior-occlusal (chewing) surfaces, where degradation of composite was more likely. For CBCL change, associations were not statistically significant. At-risk or clinically significant scores were more common among children with greater exposure for CBCL Total Problem Behaviors (16.3% vs 11.2%, P-trend = .01) and numerous BASC-SR syndromes (eg, ≥13 vs 0 surface-years, Interpersonal Relations 13.7% vs 4.8%, P-trend = .01). No associations were found with compomer, nor with amalgam exposure levels among children randomized to amalgam.

CONCLUSIONS: Greater exposure to bisGMA-based dental composite restorations was associated with impaired psychosocial function in children, whereas no adverse psychosocial outcomes were observed with greater urethane dimethacrylate–based compomer or amalgam treatment levels. *Pediatrics* 2012;130:e328–e338

Each author has participated sufficiently in the work to take public responsibility for appropriate portions of the content. Drs Maserejian, Trachtenberg, McKinlay, and Bellinger contributed to conception and design; Drs McKinlay, Bellinger, and Tavares were responsible for acquisition of data; Drs Maserejian, Trachtenberg, Tavares, Hauser, and Bellinger and Mr Shrader were responsible for analysis and interpretation of data; Dr Maserejian and Mr Shrader were responsible for drafting of the manuscript; and Drs Maserejian, Hauser, Trachtenberg, McKinlay, Tavares, and Bellinger and Mr Shrader were responsible for critical revision of the manuscript for important intellectual content. Each author has given final approval to the submitted manuscript.

This trial has been registered at www.clinicaltrials.gov (identifier NCT00065988).

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(Continued on last page)

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Dental caries is the most common chronic disease in US children; more than half have caries by age 7 and 80% have decayed or filled teeth by adolescence.[1] Composite restorations are becoming the preferred treatment of dental caries, with more than 10 million placed yearly in US children alone.[2] As the popularity of dental amalgam decreases because of concerns with mercury and cosmetic preferences, composites have replaced an estimated 81% of these fillings, and their use escalates as debates over the regulation of amalgam continue.[2]

Components of dental composite materials, such as epoxy resins and acrylic monomers, may have adverse effects.[3] Recent attention has focused on bisphenol A (BPA) release from dental resins because of numerous experiments showing adverse effects of BPA.[4–6] In dentistry, BPA is used in the synthesis of monomers, such as bisphenol-A-diglycidyl-dimethacrylate (bisGMA), traditionally the main source monomer for composites. Elution of BPA may result from impurities left after resin synthesis or from resin degradation.[6] The monomer urethane dimethacrylate (UDMA) can be used in place of BPA-derived monomers and has greater thermal stability and mechanical strength.[7]

There are limited data on potential human health effects of BPA exposure,[8–10] but animal studies have shown that early life exposure is a sensitive window.[11] Regarding psychological outcomes, BPA exposure in rodent experiments resulted in increases in defensive aggression, activity and hyperactivity, impaired learning of avoidance tasks, and altered play.[11–13] Emerging studies in pediatric populations are supportive of laboratory findings. For example, a study of 249 mothers and their children suggested that prenatal BPA exposure was associated with anxiety, depression, and hyperactivity problems during early childhood, particularly among girls.[14,15]

The potential role of dental materials as sources of BPA exposure and related outcomes has been controversial. A prevailing assumption is that monomers released from dental composites would have no systemic health effects because exposure is acute, during dental treatment. Composite restorations degrade with time,[16,17] however, allowing continued, long-term release of their compounds into the oral environment. Furthermore, BPA effects are observed in experimental studies at chronic low doses,[9] similar to concentrations observed in saliva or urine after dental material placement.[5,6,18,19] Although dental amalgam has been scrutinized given its mercury content,[20–22] the safety of its most common alternatives, composites, remains an unresolved issue.

No studies have assessed the long-term human health effects of bisGMA-based dental materials. The New England Children's Amalgam Trial (NECAT) was a National Institutes of Health–funded randomized clinical trial of neuropsychological and renal effects of dental amalgam in children over 5 years of follow-up. Results showed no harmful effects of amalgam.[20] Contrary to the original hypothesis, NECAT found worse psychosocial outcomes for children who received the comparison treatment plan, resin-composites.[23] In particular, children assigned to composites had statistically significantly worse psychosocial function scores on Emotional Symptoms and Personal Maladjustment domains, and less favorable improvement in scores for Anxious/Depressed, Delinquent, and Total Problem Behaviors. A thorough investigation considering exposure levels is important to substantiate these findings.

Our objective was to test the hypothesis that greater exposure to dental composites is associated with greater impairments in psychosocial function among children. By using NECAT data, we examined 2 resin-based composite materials (UDMA-based compomer and bisGMA-based composite) and used the data on children randomized to amalgam to assess potential unmeasured confounding by severity of dental disease.

METHODS

Study Design and Participants

NECAT data were collected from 1997 to 2005 at 6 community dental clinics in Boston and Maine. A total of 5116 children were screened and 598 were eligible to participate in a 5-year safety trial of amalgam. Eligibility criteria were the following: aged 6 to 10 years; English fluency; no amalgam restorations; $\geq$2 posterior teeth with caries requiring restoration on occlusal surfaces; and, by parent-report, no physician-diagnosed psychological, behavioral, neurologic, immunosuppressive, or renal disease. Written parental consent and child assent were obtained for 534 children. The study was approved by the institutional review boards of participating sites. Details of the study design have been published.[20,23,24]

Randomization to treatment plan of amalgam versus composites for posterior restorations was used to ensure similarity in characteristics of children and no self-selection in treatment materials. Once randomized, exposure levels varied by individuals' treatment needs; thus, we applied methods typical for observational cohort studies for this analysis.

Dental Materials and Interventions

For children assigned to the resin-based composites treatment plan, compomer (Dyract AP, by Dentsply Caulk, Milford, DE) was used in primary teeth, and composite (Z100, by 3M ESPE, St Paul, MN) was used in permanent teeth. Z100 is a radiopaque dental composite, with zirconia/silica filler (85% by weight) with particle size range 3.5 to 0.01 μm. Its main source

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monomers (each 5% to 10% by weight) are bisGMA and triethylene-glycol dimethacrylate. Compomers are polyacid-modified composites that contain 72% (by weight) strontium-fluorosilicate-glass for fluoride release. The Dyract resin is composed of UDMA and carboxylic-acid-modified-dimethacrylate. For children assigned to amalgam, Dispersalloy (by Dentsply Caulk) was applied for posterior teeth; anterior teeth were treated with compomer/composite as in standard practice. Children had semiannual dental examinations and treatment visits as needed throughout the 5-year follow-up.

Urine/blood specimens collected and analyzed for mercury content were discarded, per protocol, upon NECAT's completion. Previous in vitro and in vivo studies have shown that Z100 composite released BPA, bisGMA, bisDMA, and BPA diglycidylether.[18,19,25–28] Dyract did not release detectable BPA or bisGMA in eluates from filled tooth samples.[29]

Psychosocial Assessment Measures

Psychosocial assessments were made by using 2 validated instruments at baseline and follow-up: (1) Child Behavior Checklist (CBCL) parent-report,[30] and (2) Behavior Assessment for Children Self-Report (BASC-SR).[31] Both are widely used in screening children and adolescents for psychosocial problems,[32] yielding global T-scores (mean 50, SD = 10) and core syndrome scores (see Table 3 footnotes). Examiners were trained and certified by 1 supervising psychologist (D.C.B.) and continuously monitored for quality control.

Statistical Analysis

The primary outcomes were (1) BASC-SR score at study completion, and (2) CBCL change score from baseline (before dental treatment) to study completion 5 years later. After excluding children missing outcome data, sample sizes for analyses were $n = 415$ for BASC-SR, and $n = 351$ for CBCL, providing 80% power to detect a correlation of 0.15 between exposure levels and psychosocial scores. Because BASC-SR was developed for children aged ≥8 years, change in BASC-SR was a secondary outcome explored among participants aged ≥8 years at baseline ($n = 197$).

To be consistent with the randomly assigned treatment plan, preliminary analyses examined total composites (compomer plus composite) in association with outcomes. Effect modification by material type was evaluated because of the biological plausibility that bisGMA-based and UDMA-based composites have distinct chemical properties and potential effects. For each material, cumulative exposure level was calculated by using surface-years (each treated surface weighted by number years present in the mouth). Given our previous finding that treatment on posterior-occlusal surfaces was most strongly associated with biomarkers of amalgam restorations,[22] presumably owing to chewing effects, we also evaluated posterior-occlusal surface-years.

Loess smoothing plots were used to assess the linearity of associations between exposure level and psychosocial function scores in preliminary analyses. Multivariable generalized linear regression models were used to obtain β estimates for continuous and categorical exposure measures. Exposure categories were none and, among the exposed, tertiles. In secondary analyses, the presence of scores in the clinical range were examined by using multivariable logistic regression. Multivariable models were determined by directed acyclic graphs,[33] which considered factors relevant in previous NECAT analyses and other studies of environmental toxicant-neurodevelopment associations[23]: age, gender, race/ethnicity, socioeconomic status, geographic site, primary caregiver's marital status, blood lead level, and any maternal self-reported exposure during pregnancy to alcohol or illicit substances. Effect modification by age and gender were investigated, but no interactions were found.

To evaluate the possibility of residual confounding, we replicated all analyses by using amalgam exposure levels separately in primary teeth and permanent teeth, and conducted all analyses again within assigned treatment arm. Results consistent between amalgam and composites would suggest that findings were a result of confounding by factors associated with severity of dental disease/treatment (ie, exposure level) on primary or permanent teeth, rather than dental material. Statistical analyses were conducted at significance level $\alpha = 0.05$ by using SAS version 9.2 (SAS Institute, Inc, Cary, NC).

RESULTS

Follow-up data for either the BASC-SR or CBCL were available for 434 children (81.3% of the total NECAT cohort). Children excluded owing to missing data were similar to children in the final analytic sample in age, caries, assigned treatment, and baseline CBCL Total Problem Behaviors score, although more likely to be nonwhite race (58.0% vs 34.3%). Children assigned to composites ($n = 217$) had a mean (SD) 38.1 (24.2) surface-years total composites exposure, and most received both compomer and composite given their mixed dentition at baseline (Table 1). Children assigned to amalgam ($n = 217$) were largely (59.4%) unexposed to composites; exposure resulted from composite use for anterior teeth. As treated, children with higher cumulative exposure to dental compomer/composite during the 5-year study were more likely to be girls and have greater treatment needs at baseline compared with children with lower exposure (Table 2).

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TABLE 1 Dental Materials Exposure During the 5-Year Trial Among Children in This Analysis

	Assigned Treatment[a]		Treatment(s) Received[b]		
	Composites n = 217	Amalgam n = 217	Compomer n = 241	Composite n = 220	Amalgam n = 216
Received both compomer and composite, n (%)	148 (68.2)	12 (5.5)	160 (66.4)	160 (72.7)	14 (6.5)
Exposure levels, mean (SD)					
Number of surfaces restored during the trial					
Total (compomer, composite, or amalgam)	12.9 (7.7)	12.7 (8.3)	14.4 (8.0)	15.5 (8.3)	13.0 (8.4)
Compomer	7.9 (5.9)	0.9 (2.6)	8.0 (5.5)	6.6 (6.3)	1.0 (2.8)
Composite	5.0 (5.8)	1.2 (3.1)	3.8 (4.9)	6.1 (5.6)	1.3 (3.2)
Amalgam	0.0 (0.6)	10.5 (6.2)	2.6 (5.8)	2.8 (6.0)	10.6 (6.1)
Surface-years					
Compomer, primary teeth	21.3 (20.3)	2.2 (6.1)	21.1 (19.2)	17.0 (20.3)	2.5 (7.0)
Composite, permanent teeth	16.9 (19.5)	3.8 (10.9)	13.1 (16.7)	20.4 (19.2)	4.1 (11.6)
Amalgam, primary teeth	0	20.7 (19.4)	6.1 (16.1)	4.7 (12.3)	20.8 (19.4)
Amalgam, permanent teeth	0.1 (1.9)	10.8 (12.3)	2.1 (6.9)	3.1 (8.7)	11.0 (12.3)

[a] Randomization to a treatment plan for posterior teeth caries of compomer/composite versus amalgam was stratified by geographic location and number of teeth with caries at baseline (2–4 vs ≥5). The CONSORT flow diagram showing the progress of all randomized patients throughout the trial, including recruitment, randomization, and follow-up, was previously published.[20]
[b] Columns present data for children who received any restoration treatment on posterior or anterior teeth with each specific material, and are not mutually exclusive. Among children randomized to the composites treatment plan, compomer was used for primary dentition and composite for permanent dentition. Among children randomized to amalgam treatment, compomer or composite was used for anterior tooth surfaces per NECAT protocol and standard clinical practice. One participant in the amalgam group refused amalgam restorations and received compomer only. Two participants in the composites group received amalgam from out-of-study dentists. Materials applied were Dyract compomer (UDMA-based resin), Z100 composite (bisGMA-based resin), and Dispersalloy amalgam.

In preliminary analyses, effect modification of composites by materials placed on primary (UDMA-based compomer) versus permanent (bisGMA-based composite) teeth was apparent. In contrast, amalgam associations were similar for primary and permanent teeth. All subsequent analyses were conducted separately for compomer and composite, and for parallel comparison, separated by primary/permanent teeth for amalgam.

UDMA-based compomer had no statistically significant or consistent associations with BASC-SR scores or CBCL change scores (Table 3). In contrast, greater bisGMA-based composite exposure was consistently associated with higher BASC-SR scores on Emotional Symptoms and Clinical Maladjustment, and lower scores on Personal Adjustment, all indicating worse psychosocial functioning at the end of follow-up. Linear trends were also significant for 3 core syndromes of interest, Depression, Attitude to School, and Interpersonal Relations, as well as most other individual syndromes (Supplemental Table 4). Findings for BASC-SR change scores were similar. For CBCL change scores, results generally indicated less improvement with greater composites exposure, but were statistically significant only for Activities Competence (2.6-point difference between highest tertile and unexposed, P trend = .03).

The magnitudes of associations between composite and BASC-SR psychosocial scores were stronger for posterior-occlusal surface exposure. For example, each additional 10 posterior-occlusal surface-years (eg, from 2 surfaces each present in the mouth 5 years) was associated with a reduction in BASC-SR Personal Adjustment score of 2.2 points ($P < .0001$), compared with 0.8 points ($P = .002$) using total surface-years (Table 3). Trends toward less favorable scores with increasing dose are illustrated in Fig 1. For BASC-SR, differences ranging from 2 to 6 points between higher and lower exposure groups were found for all core syndromes contributing to Emotional Symptoms Index ($P = .002$), Personal Adjustment ($P < .0001$), and Clinical Maladjustment ($P = .02$), except Atypicality ($P = .18$). CBCL differences were not statistically significant. The CBCL Anxious/Depressed ($P = .07$) or Delinquent ($P = .16$) change scores among children with >15 posterior-occlusal surface-years shifted downward (by 3 to 4 points), whereas the scores of children with lower exposures improved slightly.

Overall, fewer than 10% of children had follow-up psychosocial scores in at-risk or clinically significant ranges. Clinically concerning scores on many BASC-SR core syndromes, as well as CBCL Total Problem Behaviors, were more common among children who had greater composite exposure (Fig 2). For example, Total Problem Behavior scores of concern were present in 16.3% of children in the highest (≥13 surface-years) versus 6.3% in the lowest exposed tertile (0.1–5.0 surface-years, P trend = .01). In addition to BASC-SR Anxiety, Depression, and Interpersonal Relations, similar trends were statistically significant for Social Stress, Sense of Inadequacy, Locus of Control, Sensation Seeking, Relations with Parents, Self-Esteem, Self-Reliance, and the overall Emotional Symptoms Index ($P = .006$).

There were no consistent associations between amalgam exposure levels on permanent teeth (Table 3, Supplemental Table 4) or primary teeth (data not

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TABLE 2 Baseline Characteristics of Participants, Overall and by Total Composites (Compomer or Composite) Surface-Years Exposure Level

	Total Analytic Sample	Exposure Level (Surface-Years Category) (Tertile among Exposed)			
		0	0.1–16	16.1–39.9	≥40
n	434	133	101	100	100
Age, mean (SD)	8.1 (1.4)	8.2 (1.3)	7.9 (1.4)	8.1 (1.2)	8.0 (1.5)
Gender, *n* (%)					
Female	227 (52.3)	70 (52.6)	52 (51.5)	46 (46.0)	59 (59.0)
Male	207 (47.7)	63 (47.4)	49 (48.5)	54 (54.0)	41 (41.0)
No. of carious teeth, mean (SD)	5.2 (2.9)	4.7 (2.7)	4.5 (2.7)	5.0 (2.8)	6.8 (2.7)
No. of carious surfaces, mean (SD)	9.3 (6.6)	8.5 (6.4)	7.7 (5.5)	8.6 (6.3)	12.7 (7.3)
Race/ethnicity, *n* (%)[a]					
Non-Hispanic white	285 (65.7)	82 (61.7)	74 (73.3)	62 (62.0)	67 (67.0)
Non-Hispanic black	83 (19.1)	34 (25.6)	14 (13.9)	18 (18.0)	17 (17.0)
Hispanic (nonmixed)	28 (6.5)	7 (5.3)	4 (4.0)	12 (12.0)	5 (5.0)
Other	38 (8.8)	10 (7.5)	9 (8.9)	8 (8.0)	11 (11.0)
Socioeconomic status, *n* (%)[b]					
Low	117 (27.0)	41 (30.8)	24 (23.8)	37 (37.0)	15 (15.0)
Medium	211 (48.6)	69 (51.9)	51 (50.5)	38 (38.0)	53 (53.0)
High	106 (24.4)	23 (17.3)	26 (25.7)	25 (25.0)	32 (32.0)
Marital status of primary caregiver, *n* (%)[c]					
Single, never married	78 (18.1)	24 (18.3)	18 (18.0)	21 (21.0)	15 (15.0)
Married	281 (65.2)	85 (64.9)	67 (67.0)	64 (64.0)	65 (65.0)
Separated/divorced/widowed	72 (16.6)	22 (16.8)	15 (15.0)	15 (15.0)	20 (20.0)
Geographic Location, *n* (%)					
Urban (Boston, MA)	220 (50.7)	78 (58.7)	38 (37.6)	53 (53.0)	51 (51.0)
Rural (Farmington, ME)	214 (49.3)	55 (41.4)	63 (62.4)	47 (47.0)	49 (49.0)
Drinking water source, *n* (%)					
Bottled	122 (28.1)	38 (28.6)	28 (27.7)	27 (27.0)	29 (29.0)
Tap	157 (36.2)	46 (34.6)	40 (39.6)	37 (37.0)	34 (34.0)
Mixed	115 (26.5)	35 (26.3)	24 (23.8)	28 (28.0)	28 (28.0)
Don't know	40 (9.2)	14 (10.5)	9 (8.9)	8 (8.0)	9 (9.0)
Fruits and vegetables servings/day, mean (SD)[c]	1.3 (0.6)	1.4 (0.7)	1.3 (0.6)	1.3 (0.6)	1.2 (0.5)
Gum-chewing frequency, *n* (%)[c]					
Not at all	30 (7.0)	10 (7.6)	7 (7.0)	9 (9.0)	4 (4.0)
Occasionally	360 (83.5)	108 (82.4)	79 (79.0)	82 (82.0)	91 (91.0)
Daily	41 (9.5)	13 (9.9)	14 (14.0)	9 (9.0)	5 (5.0)
Blood lead level, mean (SD) mg/dL[c]	2.3 (1.8)	2.6 (1.9)	2.3 (1.9)	1.9 (1.2)	2.5 (1.7)
Premature birth, *n* (%)					
Yes	51 (11.8)	14 (10.5)	12 (11.9)	12 (12.0)	13 (13.0)
No	345 (79.5)	105 (79.0)	81 (80.2)	79 (79.0)	80 (80.0)
Missing	38 (8.8)	14 (10.5)	8 (7.9)	9 (9.0)	7 (7.0)
Birth weight, g, mean (SD)[c]	3361 (545)	3325 (514)	3351 (558)	3377 (599)	3402 (523)
Maternal alcohol or illicit drug exposure during pregnancy, *n* (%)[d]					
Yes	142 (32.7)	49 (36.8)	31 (30.7)	31 (31.0)	31 (31.0)
No	254 (58.5)	70 (52.6)	62 (61.4)	60 (60.0)	62 (62.0)
Missing	38 (8.8)	14 (10.5)	8 (7.9)	9 (9.0)	7 (7.0)

[a] Race/ethnicity was self-reported by the parent of the child. The "other" category included individuals who identified themselves as Asian, Native American, multiracial (specified), or other (specified).

[b] Socioeconomic status index was calculated by using household income and education level of the primary caregiver and standardized to the US population.

[c] Three children were missing baseline data on marital status of primary caregiver, fruit/vegetable intake, and gum-chewing frequency. Seven children were missing data on baseline blood lead level. Forty-one children were missing data on birth weight, which was self-reported by the parent.

[d] Self-reported by mother of the child. Illicit drugs included marijuana, crack cocaine, heroin, methadone, hallucinogens, and amphetamines.

shown) and psychosocial function. Four statistically significant findings for Interpersonal Relations, Self-Reliance, Anxious/Depressed, and Delinquent Behaviors were in the direction of greater improvement with increasing amalgam exposure.

Additional analyses conducted within randomized treatment arms confirmed findings, with notably larger associations for BASC-SR Anxiety change score for bisGMA-based composite (10 posterior-occlusal surface-years, mean 3.9, SE = 1.2, P = .004; permanent-tooth amalgam mean –0.2, SE = 1.5, P = .91) and Depression (mean 2.8, SE=1.2, P = .02; permanent-tooth amalgam mean 1.2, SE = 1.5, P = .43).

DISCUSSION

These findings indicate that exposure to bisGMA-based dental composite resins may impair psychosocial health in children. With increasing level and duration of exposure to bisGMA-based composite over 5 years of follow-up, children reported more anxiety, depression, social stress, and interpersonal-relation problems, and were more likely to have clinical-range scores for parent-reported total problem behaviors. No similar associations were found for amalgam permanent tooth exposure levels or in the previously reported[23] intent-to-treat randomized group analysis; thus, unmeasured/unknown confounding by factors associated with severity of dental disease on permanent teeth is unlikely to explain our findings for bisGMA-based composite. UDMA-based polyacid-modified composite (compomer) had no associations with psychosocial function scores.

Owing to the lack of relevant biomarker data in NECAT, we were unable to examine whether children with greater composite exposure had increased concentrations of potentially leached monomers, such as bisGMA, or BPA, which may plausibly cause the observed

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TABLE 3 Psychosocial Function Scores, by Cumulative Exposure (Surface-Years [SY]) to UDMA-based Compomer, BisGMA-based Composite, and Amalgam Dental Restorations

	Compomer (Primary Teeth)[a]								Composite (Permanent Teeth)[a]								Amalgam (Permanent Teeth)[a]							
	Total SY						Posterior-Occlusal SY		Total SY						Posterior-Occlusal SY		Total SY						Posterior-Occlusal SY	
	0	0.1–10.0	10.1–22.9	≥23.0	10-SY β (SE)	P	10-SY β (SE)	P	0	0.1–9.0	9.1–22.9	≥23.0	10-SY β (SE)	P	10-SY β (SE)	P	0	0.1–9.0	9.1–22.9	≥23.0	10-SY β (SE)	P	10-SY β (SE)	P
BASC-SR Year 5 T-Score, adjusted mean (SE)																								
No. participants	182	83	72	78					204	73	67	71					264	59	56	36				
Median SY	0	4.9	15.8	38.0					0	3.8	14.0	36.6					0	4.3	14.5	30.0				
Emotional symptoms index[b]	46.9	47.9	47.8	47.8	−0.003	.99	0.3	.60	46.6	47.6	48.4	49.4	0.8	.003[h]	1.7	.002[h]	47.8	46.6	46.7	47.3	−0.1	.72	−0.5	.49
	(1.5)	(1.6)	(1.6)	(1.7)	(0.2)		(0.5)		(1.5)	(1.6)	(1.7)	(1.7)	(0.3)[h]		(0.5)[h]		(1.4)	(1.8)	(1.8)	(2.0)	(0.4)		(0.7)	
Clinical maladjustment[c]	46.4	47.4	47.9	47.1	−0.1	.74	0.1	.84	46.6	46.6	47.8	49.1	0.7	.02[h]	1.4	.02[h]	47.5	46.0	45.8	47.6	−0.1	.87	−0.4	.58
	(1.6)	(1.7)	(1.7)	(1.8)	(0.3)		(0.6)		(1.6)	(1.7)	(1.8)	(1.8)	(0.3)[h]		(0.6)[h]		(1.5)	(1.9)	(1.9)	(2.1)	(0.4)		(0.8)	
School maladjustment[d]	52.4	52.1	54.0	51.7	−0.3	.37	−0.4	.58	52.5	52.2	52.8	54.2	0.5	.07	0.5	.42	52.3	51.8	54.5	53.5	0.5	.34	0.5	.56
	(1.8)	(1.9)	(1.9)	(2.0)	(0.3)		(0.6)		(1.7)	(1.9)	(2.0)	(2.0)	(0.3)		(0.7)		(1.7)	(2.1)	(2.1)	(2.3)	(0.5)		(0.8)	
Personal adjustment[e]	50.3	49.9	48.8	48.5	−0.2	.35	−0.8	.14	50.5	49.8	47.7	47.7	−0.8	.002[h]	−2.2	<.0001[h]	49.2	50.4	50.3	50.1	0.4	.31	0.7	.35
	(1.5)	(1.6)	(1.6)	(1.7)	(0.2)		(0.5)		(1.4)	(1.6)	(1.7)	(1.7)	(0.2)[h]		(0.5)[h]		(1.4)	(1.7)	(1.7)	(1.9)	(0.4)		(0.7)	
Core syndromes																								
Anxiety	44.7	46.2	45.2	45.4	−2.0	.54	0.1	.84	44.3	45.7	46.7	46.2	0.4	.14	1.3	.03[h]	45.8	44.5	44.3	43.6	−0.6	.16	−1.2	.13
	(1.6)	(1.8)	(1.8)	(1.9)	(0.3)		(0.6)		(1.6)	(1.8)	(1.9)	(1.9)	(0.3)		(0.6)[h]		(1.6)	(1.9)	(1.9)	(2.1)	(0.4)		(0.8)	
Depression	50.6	50.0	51.7	50.1	−0.1	.62	−0.05	.92	50.5	50.5	50.8	52.0	0.5	.04[h]	1.0	.05[h]	50.8	50.1	50.3	52.1	0.4	.34	0.5	.49
	(1.4)	(1.5)	(1.5)	(1.6)	(0.2)		(0.5)		(1.4)	(1.5)	(1.6)	(1.6)	(0.2)[h]		(0.5)[h]		(1.4)	(1.7)	(1.7)	(1.9)	(0.4)		(0.7)	
Attitude to school	51.7	51.1	53.5	50.0	−0.4	.18	−0.4	.50	51.5	51.7	50.9	54.4	0.8	.02[h]	0.8	.24	51.6	52.0	52.0	53.8	0.4	.40	0.4	.67
	(1.8)	(2.0)	(2.0)	(2.1)	(0.3)		(0.7)		(1.8)	(2.0)	(2.1)	(2.1)	(0.3)[h]		(0.7)		(1.8)	(2.2)	(2.2)	(2.4)	(0.5)		(0.9)	
Interpersonal relations	52.5	52.5	52.4	51.7	−0.2	.44	−0.5	.26	52.8	53.3	50.3	51.4	−0.6	.005[h]	−1.5	.001[h]	52.1	52.5	53.3	52.9	0.4	.27	0.7	.25
	(1.3)	(1.4)	(1.4)	(1.4)	(0.2)		(0.4)		(1.2)	(1.4)	(1.4)	(1.4)	(0.2)[h]		(0.5)[h]		(1.2)	(1.5)	(1.5)	(1.7)	(0.3)		(0.6)	
BASC-SR Change Score (among children age ≥8 y at baseline), adjusted mean (SE)																								
No. participants	97	49	33	18					85	29	35	48					119	28	29	21				
Median SY	0	4.0	15.8	30.0					0.0	4.6	13.3	38.9					0.0	4.5	17.5	30.5				
Emotional symptoms index[b]	−5.4	−4.2	−6.3	−8.7	−0.7	.32	−0.4	.75	−5.9	−6.0	−7.8	−2.6	0.8	.02[h]	1.8	.01[h]	−5.1	−7.0	−5.9	−5.1	0.1	.90	−0.2	.85
	(2.6)	(2.6)	(2.7)	(3.4)	(0.7)		(1.4)		(2.4)	(2.9)	(2.9)	(2.7)	(0.4)[h]		(0.7)[h]		(2.4)	(2.9)	(2.9)	(3.2)	(0.6)		(1.0)	
Clinical maladjustment[c]	−3.8	−4.7	−4.1	−8.0	−0.6	.45	−0.1	.96	−4.5	−5.0	−7.3	−1.5	0.7	.06	1.6	.04[h]	−4.1	−5.8	−4.7	−2.7	0.3	.63	0.6	.61
	(2.7)	(2.8)	(2.8)	(3.6)	(0.8)		(1.5)		(2.5)	(3.0)	(3.0)	(2.8)	(0.4)		(0.8)[h]		(2.6)	(3.1)	(3.0)	(3.4)	(0.7)		(1.1)	
School maladjustment[d]	0.03	1.4	2.9	6.1	1.7	.04[h]	3.5	.03[h]	0.9	2.6	2.3	3.4	0.4	.36	1.1	.22	1.8	−0.4	3.7	−0.6	−0.1	.93	−0.4	.73
	(3.0)	(3.1)	(3.1)	(4.0)	(0.8)[h]		(1.6)[h]		(2.9)	(3.4)	(3.4)	(3.2)	(0.4)		(0.9)		(2.9)	(3.5)	(3.4)	(3.8)	(0.8)		(1.2)	
Personal adjustment[e]	0.6	−2.2	0.4	−2.2	−0.8	.29	−1.4	.34	0.3	0.6	−0.5	−3.6	−1.0	.02[h]	−2.3	.004[h]	−1.6	−0.1	2.2	2.7	1.2	.09	2.1	.07
	(2.8)	(2.9)	(2.9)	(3.6)	(0.8)		(1.5)		(2.6)	(3.1)	(3.1)	(2.9)	(0.4)[h]		(0.8)[h]		(2.6)	(3.2)	(3.1)	(3.4)	(0.7)		(1.1)	
Core syndromes																								
Anxiety	−6.2	−5.8	−5.6	−8.4	−0.1	.91	0.6	.68	−6.4	−6.5	−7.7	−3.1	0.7	.10	1.6	.04[h]	−5.4	−6.9	−6.8	−6.3	−0.3	.64	−0.4	.70
	(2.8)	(2.9)	(2.9)	(3.7)	(0.8)		(1.5)		(2.6)	(3.1)	(3.1)	(2.9)	(0.4)		(0.8)[h]		(2.6)	(3.2)	(3.1)	(3.5)	(0.7)		(1.1)	
Depression	−1.4	−2.1	−3.3	−6.3	−1.3	.09	−1.5	.29	−2.4	−2.4	−6.2	−1.2	0.6	.12	0.9	.26	−2.9	−3.5	−2.1	0.6	0.9	.18	1.1	.33
	(2.7)	(2.8)	(2.8)	(3.6)	(0.8)		(1.5)		(2.6)	(3.0)	(3.1)	(2.9)	(0.4)		(0.8)		(2.6)	(3.1)	(3.1)	(3.4)	(0.7)		(1.1)	
Attitude to school	−0.7	−0.01	2.2	3.9	1.5	.10	4.0	.03[h]	−0.4	1.4	0.9	4.1	0.8	.08	1.4	.16	1.1	0.3	−0.4	1.6	−0.04	.97	−0.5	.74
	(3.4)	(3.5)	(3.5)	(4.4)	(0.9)		(1.8)[h]		(3.2)	(3.8)	(3.8)	(3.6)	(0.5)		(1.0)		(3.2)	(3.9)	(3.8)	(4.2)	(0.8)		(1.4)	

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TABLE 3 Continued

	Compomer (Primary Teeth)[a]								Composite (Permanent Teeth)[a]								Amalgam (Permanent Teeth)[a]							
	Total SY						Posterior-Occlusal SY		Total SY						Posterior-Occlusal SY		Total SY						Posterior-Occlusal SY	
	0	0.1–10.0	10.1–22.9	≥23.0	10-SY β (SE)	P	10-SY β (SE)	P	0	0.1–9.0	9.1–22.9	≥23.0	10-SY β (SE)	P	10-SY β (SE)	P	0	0.1–9.0	9.1–22.9	≥23.0	10-SY β (SE)	P	10-SY β (SE)	P
Interpersonal relations	3.5 (2.6)	2.1 (2.7)	2.9 (2.7)	7.1 (3.4)	0.4 (0.7)	.57	0.05 (1.4)	.97	3.0 (2.5)	5.0 (3.0)	3.6 (3.0)	1.4 (2.8)	−0.7 (0.4)	.05	−1.7 (0.7)	.03	2.6 (2.5)	2.4 (3.0)	3.7 (2.9)	7.4 (3.3)	1.3 (0.7)	.06	2.3 (1.1)	.03
CBCL Change Score, adjusted mean (SE)																								
No. participants	155	65	62	69					178	64	55	54					225	50	44	32				
Median SY	0	5.0	16.1	40.3					0	3.8	13.3	36.6					0	4.3	14.1	30.0				
Competence[f]	−0.4 (2.3)	−1.0 (2.5)	−0.1 (2.4)	0.1 (2.5)	0.4 (0.3)	.20	0.4 (0.6)	.55	0.3 (2.3)	−0.5 (2.4)	−0.3 (2.5)	−1.2 (2.5)	−0.5 (0.3)	.10	−0.5 (0.7)	.47	−0.4 (2.2)	1.4 (2.6)	−0.5 (2.6)	−0.7 (2.8)	−0.4 (0.5)	.40	−0.3 (0.9)	.74
Total problem behaviors[g]	−1.7 (2.1)	−1.8 (2.4)	1.7 (2.4)	−1.5 (2.4)	−0.1 (0.3)	.83	0.5 (0.7)	.44	−0.8 (2.2)	−1.2 (2.3)	−0.3 (2.4)	−1.5 (2.4)	0.1 (0.3)	.87	0.1 (0.7)	.93	−0.3 (2.1)	−1.8 (2.5)	0.5 (2.6)	−3.6 (2.6)	−0.7 (0.6)	.20	−1.4 (1.0)	.15
Internalizing problems	−1.5 (2.2)	−0.4 (2.4)	1.8 (2.4)	−1.1 (2.5)	−0.1 (0.3)	.87	0.3 (0.7)	.68	−0.9 (2.2)	−0.8 (2.4)	0.7 (2.5)	−0.7 (2.5)	0.1 (0.3)	.72	0.7 (0.8)	.37	0.2 (2.2)	−2.1 (2.6)	−0.6 (2.6)	−2.5 (2.7)	−0.8 (0.6)	.16	−1.6 (1.0)	.11
Externalizing problems	1.0 (2.0)	0.7 (2.2)	2.6 (2.2)	1.1 (2.2)	−0.2 (0.3)	.57	0.4 (0.6)	.56	1.6 (2.0)	1.3 (2.2)	0.6 (2.3)	1.2 (2.3)	0.03 (0.3)	.92	−0.4 (0.7)	.53	1.7 (2.0)	0.9 (2.3)	3.3 (2.4)	−0.9 (2.4)	−0.3 (0.5)	.52	−0.9 (0.9)	.34
Core syndromes																								
Attention problems	−2.2 (1.2)	−2.0 (1.3)	−0.3 (1.3)	−2.2 (1.3)	−0.03 (0.2)	.88	0.03 (0.4)	.94	−1.7 (1.2)	−1.9 (1.3)	−1.8 (1.3)	−1.6 (1.3)	0.02 (0.2)	.90	−0.1 (0.4)	.75	−1.7 (1.2)	−1.4 (1.4)	−2.5 (1.4)	−1.8 (1.4)	−0.3 (0.3)	.29	−0.6 (0.5)	.27
Withdrawn	−1.7 (1.2)	−1.9 (1.3)	−1.2 (1.3)	−1.5 (1.3)	0.003 (0.2)	.99	0.1 (0.4)	.77	−1.8 (1.2)	−1.8 (1.3)	−1.8 (1.4)	−0.5 (1.4)	0.4 (0.2)	.06	0.6 (0.4)	.15	−1.4 (1.2)	−1.7 (1.4)	−1.2 (1.4)	−2.3 (1.5)	−0.3 (0.3)	.34	−0.5 (0.5)	.33
Anxious/depressed	−1.5 (1.2)	−1.1 (1.3)	0.2 (1.3)	−1.4 (1.3)	−0.002 (0.2)	.99	0.1 (0.4)	.71	−1.1 (1.2)	−1.8 (1.3)	−0.6 (1.4)	−0.4 (1.4)	0.2 (0.2)	.23	0.8 (0.4)	.07	−0.6 (1.2)	−1.4 (1.4)	−0.6 (1.4)	−2.7 (1.5)	−0.5 (0.3)	.08	−1.1 (0.5)	.03
Delinquent behaviors	−2.1 (1.3)	−1.6 (1.5)	0.2 (1.5)	−0.8 (1.5)	0.2 (0.2)	.30	0.9 (0.4)	.05	−1.6 (1.4)	−1.5 (1.5)	−0.4 (1.5)	−1.3 (1.5)	0.2 (0.2)	.32	0.7 (0.5)	.16	−0.7 (1.3)	−1.5 (1.6)	−1.5 (1.6)	−3.5 (1.6)	−0.7 (0.3)	.06	−1.4 (0.6)	.02
Aggression	−1.2 (1.1)	−1.2 (1.2)	0.1 (1.2)	−0.7 (1.2)	−0.1 (0.2)	.66	0.1 (0.4)	.82	−0.8 (1.1)	−1.2 (1.2)	−1.0 (1.3)	−0.4 (1.3)	0.1 (0.2)	.60	0.02 (0.4)	.95	−0.7 (1.1)	−0.5 (1.3)	−1.1 (1.3)	−1.5 (1.4)	−0.3 (0.3)	.38	−0.5 (0.5)	.30

[a] Exposure levels indicate the cumulative exposure received during the trial (as treated, regardless of randomized treatment assignment). The amalgam exposure metric is restricted to amalgam in permanent tooth surfaces to allow a parallel comparison with the composite exposure metric. Multivariable models adjusted for age, gender, race/ethnicity (white, black, Hispanic, or other), socioeconomic status, geographic study region (rural or urban), blood lead level, primary caregiver's marital status, and maternal alcohol/tobacco/drug exposure during pregnancy.

[b] Emotional symptoms index is a global indicator composed of 2 scales from Clinical Maladjustment (Anxiety and Social Stress), 2 from Personal Maladjustment (Interpersonal Relations and Self-Esteem), and 2 from no other domain (Depression and Sense of Inadequacy). Higher scores indicate more problems.

[c] Clinical Maladjustment summary score is composed of Anxiety, Social Stress, Atypicality, Locus of Control, and for ages ≥12 y, Somatization. Higher scores indicate more problems.

[d] School Maladjustment summary score is composed of Attitude to School, Attitude to Teachers, and for ages ≥12 y, Sensation Seeking. Higher scores indicate more problems.

[e] Personal Adjustment summary score is composed of Interpersonal Relations, Relations with Parents, Self-esteem, and Self-reliance. Lower scores indicate more problems.

[f] Competence summary score is composed of Activities, Social Adaptation, and School competence subscales. Lower scores indicate more problems (ie, decreased competence). These scores do not contribute to the Total Problem Behaviors score from the CBCL.

[g] Total Problem Behaviors score is composed of Internalizing and Externalizing Problems scales, as well as 4 core syndromes: Social Problems, Thought Problems, Attention Problems, and Sex Problems. Higher scores indicate more problems on these global and core syndrome scores.

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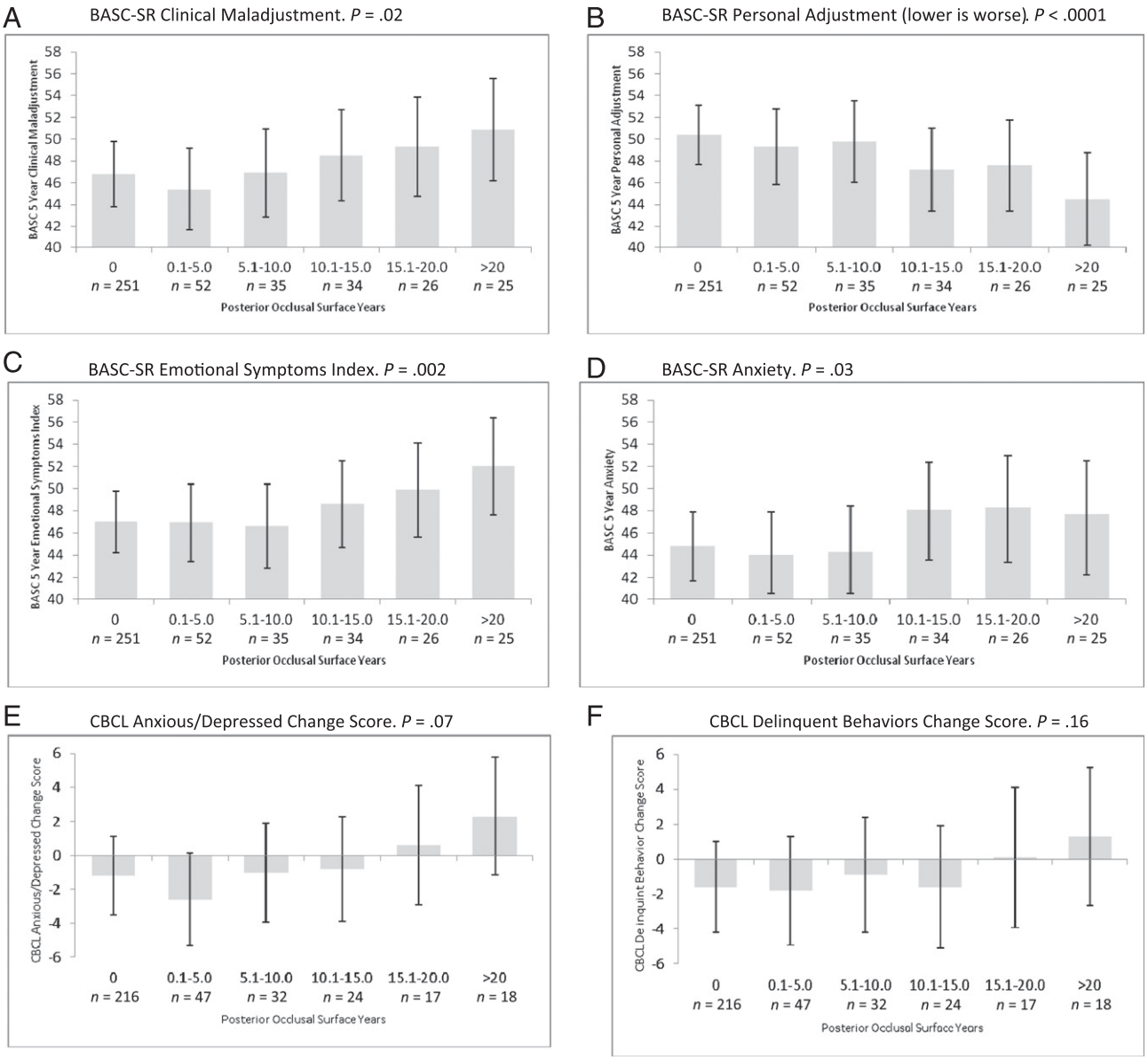

FIGURE 1
Multivariable-adjusted 5-year select psychosocial function scores and change scores, by cumulative exposure (surface-years) to BisGMA-based dental composite in posterior occlusal surfaces. Higher scores indicate poorer function for all domains except for the BASC-SR Personal Adjustment.

associations. Thus, it remains unclear whether our observed associations are attributable to BPA or to some other chemical component of the composite intervention. Numerous studies of the applied composite (Z100) have shown that it released BPA, bisGMA, bisDMA, and/or BPA diglycidylether,[18,19,25–27] including 1 study of 19 children showing that urinary BPA levels remained elevated 14 days after treatment.[28] Other bisGMA-based resins may have similar properties. In a cross-sectional study, Korean children with >10 resin-composites (unspecified manufacturers) had urinary BPA levels on average 2.7 μg/g creatinine higher than those with no fillings.[34] A recent meta-analysis concluded that, in the worst-case scenario, a full-crown posterior bisGMA-composite restoration might release 132.36 μmol after 24 hours, or on average 57.38 nmol, and that resin-based dental materials may contribute substantially to BPA exposure.[6] Compared with bisGMA-based resins, UDMA-resins have little or no effect on BPA exposure.[27,29,35] As new materials (eg, ormocer-based, silorane-based) are developed, thorough toxicological testing, including data on the long-term release of components, should be a requisite.

NECAT did not collect data on other common BPA exposure sources, such as consumption of canned foods/beverages,

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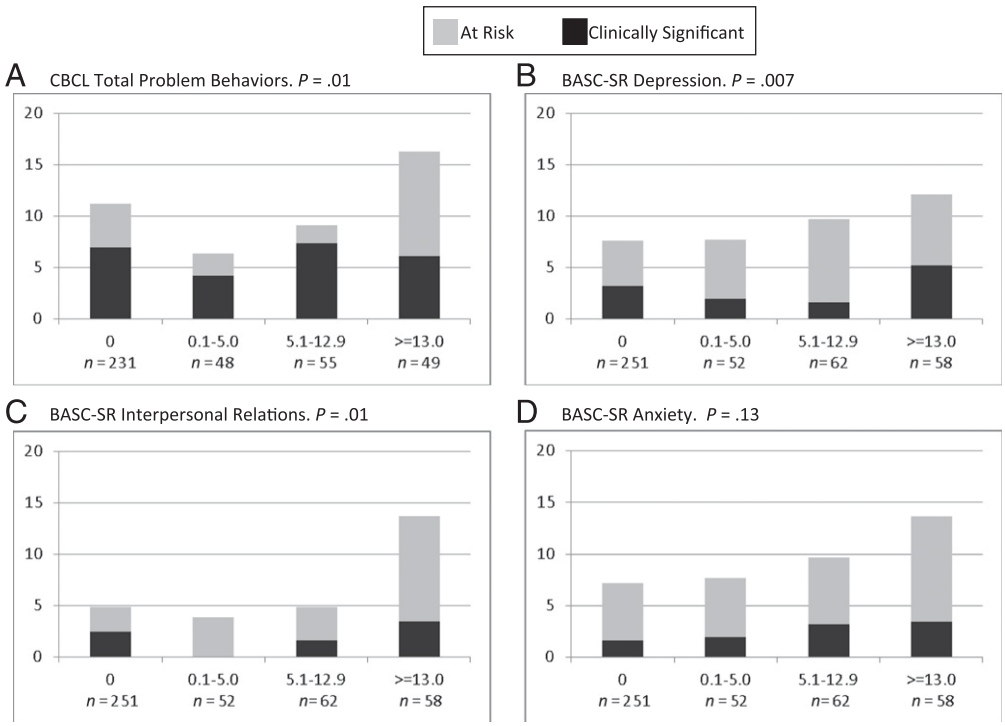

FIGURE 2

Percentage of children with at-risk or clinically significant select psychosocial function scores at end of 5-year follow-up, by cumulative exposure (surface-years) to BisGMA-based dental composite in posterior occlusal surfaces. *P* values are from multivariate logistic regression models adjusted for the factors listed in Table 3 footnotes. For CBCL, at-risk T-scores: 60–63, clinically significant ≥64. For BASC-SR Depression and Interpersonal Relations, at-risk: 60–69, clinically significant ≥70. BASC Anxiety at-risk: 60–64, clinically significant ≥65.

polycarbonate plastic container use, and thermal-receipts handling; however, the previously reported intent-to-treat findings were based on randomized treatment plan,[23] and randomization led to balance in most characteristics, including bottled versus tap water use and socioeconomic status, which may indicate BPA exposure. Randomization should also have accounted for methacrylate exposure from sealants, which were offered to all NECAT participants for caries prevention. In the current nonrandomized exposure analysis, the findings for bisGMA-based composite remained robust in multivariable models.

Our finding that cumulative exposure to composite on posterior-occlusal (chewing) surfaces was most strongly associated with poorer psychosocial outcomes supports the hypothesis that long-term release of resin components caused these associations. In NECAT, cumulative exposure to amalgam restorations on posterior-occlusal surfaces (versus all surfaces) was more strongly correlated with urinary mercury concentrations, well after the initial placement of amalgam.[22] Studies have shown that chewing increases the release of mercury from dental amalgam.[36,37] Composite restorations have decreased longevity compared with amalgam, and, as shown in previous analyses of NECAT, posterior composites underwent more repairs or replacements.[17] Thus, it is plausible that the combination of mechanical and chemical/enzymatic degradation, exacerbated by chewing on posterior-occlusal surfaces, promotes the release of chemicals from composites throughout the life of the restoration.

Although both the BASC-SR and CBCL are validated and widely used in clinical and research settings, we found fewer significant associations by using the CBCL than using the BASC-SR. These differences may be because of distinctions in the scales or their administration. The BASC was derived conceptually, considering clinically relevant material, rather than the more empirically derived CBCL. BASC anxiety and depression scores have been associated with greater gestational BPA exposure among girls in early childhood.[15] In NECAT, the BASC was self-reported, whereas the CBCL was parent reported. A longitudinal study spanning 24 years showed that when there are multiple informants for psychosocial assessment, informant-differences in rating internalizing problems become greater as children get older, and overall, children/adolescents typically self-report more internalizing and externalizing problems than obtained by parent/teacher report.[38] Thus, it is possible that that self-report by NECAT participants (aged 11–16 years at

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follow-up) more accurately reflected their psychosocial problems; however, the discrepancy between the BASC-SR and CBCL necessitate additional studies to confirm our results.

Our observed effect sizes, within the SD of both psychosocial instruments, nevertheless may indicate clinically meaningful consequences at both the individual and population levels. Shifting the mean value of psychosocial function scores in a population, even by a modest amount, will predictably produce a large change in the prevalence of clinical cases.[39,40] This analysis found clinically significant scores were 2 to 4 times more common among children with higher composite exposure. Generally, unexposed children tended to be similar to those with low-moderate exposure, which is expected because randomization presumably balanced genetic and other primary contributors of psychosocial functioning.

In conclusion, greater exposure to bisGMA-based dental composite, but not UDMA-based polyacid-modified compomer, was associated with impaired self-reported psychosocial function in children. Given that most children received both compomer and composite, additional studies that randomize participants to only 1 type of material are warranted. Nevertheless, the current findings were strong in magnitude, highly statistically significant, and robust in sensitivity analyses. A causal association between bisGMA-based composite and psychosocial health is supported by (1) the previously reported randomized "intent-to-treat" results,[23] (2) lack of associations with amalgam permanent tooth exposure levels, and (3) lack of self-selection to restorative material. Together with a separate National Institutes of Health–funded randomized trial among Portuguese children,[21] these trials definitively showed that among children aged ≥6 years, through 5 to 7 years of follow-up, amalgam did not adversely affect neuropsychological measures, whereas bisGMA-based composite was associated with poorer psychosocial outcomes and required more replacement and repair. Thus, there is no evidence to support that clinicians should systematically remove amalgam in posterior teeth to replace with bisGMA-based composite. Given the potential risks and decreased durability of composite, combined with transient increases in plasma mercury concentrations resulting from amalgam removal,[41,42] such procedures might carry more risk than benefit. Longitudinal trials are needed to examine modern-day resin-based dental materials for the long-term release of their components and health effects.

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