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Patterns of change in implementation of state alcohol control policies in the United States, 1999–2011

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Abstract

Aims—To examine state alcohol control policy implementation by policy efficacy and intent.

Design—A descriptive longitudinal analysis of policy implementation.

Setting—The United States, 1999–2011.

Participants—Fifty states and the District of Columbia.

Measurements—Twenty-nine state-level policies were rated based on an implementation rating (IR; range = 0.0-1.0) gathered from the Alcohol Policy Information System, government and industry reports and other sources; and expert judgment about policy efficacy for addressing binge drinking and alcohol-impaired driving among the general population and youth, respectively.

Findings—On average, implementation of the most effective general population policies did not change [mean IR = 0.366 in 1999; 0.375 in 2011; slope for annual change = 0.001; 95% confidence interval (CI) for the slope -0.001, 0.002]. In contrast, implementation increased over time for less effective policies (mean IR = 0.287 in 1999; 0.427 in 2011; slope for annual change compared with most effective policies = 0.009; slope 95% CI = 0.002–0.007), for youth-oriented policies (mean IR = 0.424 in 1999; 0.511 in 2011; slope for annual change compared with most effective policies = 0.005–0.009), and for impaired driving policies (mean IR = 0.493 in 1999; 0.608 in 2011; slope for annual change compared with most effective policies = 0.007–0.014).

Conclusions—Implementation of politically palatable state alcohol policies, such as those targeting youth and alcohol-impaired driving, and less effective policies increased during 1999–2011 in the United States, while the most effective policies that may maximally protect public health remained underused.

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Alcohol; legislation; policy; public health

INTRODUCTION

Excessive alcohol use, including alcohol use disorders and binge drinking, causes both acute and chronic negative social and health consequences that are burdensome public health problems throughout the world [1–3]. The World Health Organization notes that alcohol '... is a major global contributing factor to death, disease and injury' and results in approximately 2.5 million deaths world-wide each year [4]. In the United States alone, alcohol contributes to an estimated 80 000 deaths and \$223 billion in social and economic costs annually, including costs resulting from lost productivity, health-care and criminal justice expenditures [5]. Nearly half of these costs are borne by government and public funds.

Control policies can reduce excessive alcohol consumption and the various social, health and economic harms that result [6,7]. The evidence supporting the effectiveness of policy strategies is well documented [6,8–15], but effective policies are often underutilized [16]. Alcohol researchers, most prominently Robin Room, have noted that effective strategies for reducing the public health burden of alcohol are generally unpopular with legislators and the public and therefore are less likely to be implemented, while politically popular strategies are generally not very effective [6,17–20]. Often the most effective strategies in public health are those that address the underlying social causes of health concerns [21] (e.g. the availability of alcohol) [20,22] in a broad population of people, rather than in specific groups [21]. However, the feasibility and acceptability to the public and to legislators of population strategies can be barriers to their implementation [21,23]. Popular support plays an important role in passing legislation related to alcohol [24–28]. Public opinion surveys generally show low levels of support for effective policies, such as raising prices for consumer goods (e.g. tax, price restrictions), unless the funds raised are directed towards a specific purpose (e.g. treatment for those who have problems with alcohol) [25,28]. Tradeoffs that substitute weaker for stronger policies are often made in the political process required to implement policies [7,17,23,25,29]. The public may be more supportive of policies they perceive will apply to someone else, such as drunk drivers or individuals under the legal drinking age [23,25].

The general contention that effective policies are unpopular and popular strategies are ineffective has some anecdotal support and is generally accepted by alcohol policy researchers [17,18,29]. However, it has not been examined empirically in the United States. In a series of studies on state alcohol control policies we created two measures that characterize implementation for 29 unique policies in the United States for 1999–2011 by their efficacy and targeted population. The first is a set of four ratings of the relative efficacy of individual policies for reducing binge drinking and alcohol-impaired driving among the general population (i.e. adults) and among youth [30], respectively. The second is a measure of the strength of implementation [31] that distinguishes between policies on a given topic

that have specific provisions that may make them more or less effective in practice. These measures allowed us to examine policy implementation in four groups of policies (effective for the general population, effective for youth, effective for impaired driving and comparatively less effective policies) and whether implementation differed between groups over time.

We hypothesized that for each of four efficacy domains, policies with higher efficacy ratings were less likely to be implemented than policies with lower efficacy ratings. We further hypothesized that alcohol-impaired driving policies and policies targeting youth would be more likely to be implemented than policies rated as effective for addressing binge drinking among the general population. Data on the implementation of alcohol control policies over time that account for their relative efficacy may heighten awareness about gaps in policy.

METHODS

We used publicly available data on policy implementation in 50 US states and the District of Columbia from 1999 to 2011, a period that maximized the amount of consistently collected data. The primary data source was the Alcohol Policy Information System (APIS) [32]. Other sources included reports by the National Highway Traffic Safety Administration, the Insurance Institute for Highway Safety, the National Alcohol Beverage Control Association and the alcohol industry [33–38] and original legal research on state statutory and case law to verify information from other sources and fill in gaps in the available data conducted by a trained research lawyer using the WestLaw Next® database.

We transformed data from legal code into numerical variables for quantitative analysis. We created two measures of policy implementation. The first measure indicated whether or not the state had a given policy (coded as 1/0). The second measure was an implementation rating (IR) based on provisions that were collected consistently and available in all states across the study period. The IR was developed in consultation with experts based on the policy's statutory design to emphasize specific provisions within each policy that made it broadly applicable, effective or enforceable. IR scores ranged from 0.0 (no policy) to 1.0 (full implementation). Higher scores reflect greater restriction on alcohol and were scaled to reflect the presumed strength and additive effects of the provisions. Additional details are available elsewhere [31]. The scoring criteria for each policy were uniform across all states and years, but the IR varied across states and years based on implementation in each state. Data were available on 29 state-level policies during our study period, resulting in 19 227 unique state–policy–years (51 states \times 29 policies \times 13 years). A composite measure using the IR was associated inversely with binge drinking prevalence among adults [31].

Ratings of policy efficacy

We used efficacy ratings (ER) to create four conceptually distinct policy groupings. ER were created using a modified Delphi panel of 10 alcohol policy experts [30,39]. At the outset of the study prior to collecting implementation data the panelists independently rated the efficacy of 47 policies for addressing binge drinking and alcohol-impaired driving among both the general population and among youth on a five-point Likert scale (1 = low efficacy, 5 = high efficacy). The present analysis includes 29 of 47 policies for which

consistently collected data were available throughout our study period. Ten policies did not exist in the United States or there was no variation between states, and eight policies had inadequate data across all states and over time. These 18 policies had lower average ER (2.4 for adult binge drinking; 2.3 for adult impaired driving; 2.3 for youth binge drinking; and 2.3 youth impaired driving) than the included policies (2.5 for adult binge drinking; 2.6 for adult impaired driving; 2.8 for youth binge drinking; and 3.0 youth impaired driving). Additional details about the policy rating process and panelists are available elsewhere [30,40]. Policies were grouped by ER across domains of binge drinking and impaired driving for both adults and youth.

A description for each of the 29 policies, its ER and corresponding IR is available in Supporting information, Appendix S1.

Analysis

We conducted descriptive and comparative analyses of the implementation data. First we examined the state-specific implementation of having any policy compared with no policy (yes/no) for each of the 29 policies. Secondly, we examined the mean IR for each individual policy across all states. Next we examined whether the trend of IR over time differed in each of four efficacy domains: efficacy for reducing (i) binge drinking in the general population; (ii) alcohol-impaired driving in the general population; (iii) binge drinking among youth; and (iv) alcohol-impaired driving among youth. Then we examined the mean IR for each of these outcomes across all 29 policies together, and within each of four policy groupings. Multivariable models were conducted using the generalized estimating equations (GEE). State was included in the model as a fixed effect and each of the 29 policies within each state (51 states \times 29 policies) was included individually as a repeated variable over time. This modeling specification accounted for state-level average implementation and the correlation of policy implementation within states over time. All statistical analysis was conducted with SAS statistical software and the GEE analysis was conducted using the Genmod procedure in SAS.

RESULTS

Individual policy implementation

The implementation of each of the 29 policies in 1999 and 2011 is shown in Table 1. Data are presented for each policy individually and overall for the number of states with a policy and the mean IR across all states.

An increase in implementation of alcohol control policies occurred during the study period. Across all 29 policies the average number of states (of 51) with any particular policy was 32.9 in 1999. By 2011 the average number of states with implemented policies was 37.0. Similarly, the average IR across all 29 policies increased from 0.38 in 1999 to 0.44 in 2011. The parallel change in these two measures suggests that the change in policy implementation was due to adoption of new policies, rather than strengthening the implementation of existing ones. We provide three examples to illustrate our findings for individual policies. The most commonly implemented policy in 1999 was a prohibition on furnishing alcohol to

minors. All 50 states plus the District of Columbia had some type of policy restricting furnishing to minors. There was no change in the number of states with a furnishing to minors policy by 2011. Similarly, the mean IR was 0.74 in 1999 and 0.73 by 2011. During the study period the policy that was most widely adopted was ignition interlocks for impaired driving offenders. In 1999 only four states had this policy, but by 2011 33 states did. Similarly, the mean IR for the ignition interlock policy rose from 0.04 in 1999 to 0.42 in 2011. In contrast, the implementation of restrictions on days of sale eroded substantially, with seven states rescinding policies restricting alcohol sales on Sunday during the study period. The mean IR for days of sale restrictions rose from 0.32 in 1999 to 0.19 in 2011.

Policy implementation by efficacy rating

We found statistically significant relationships between ER and policy implementation measured by IR over time (Table 2). Policies with high ER for addressing binge drinking in youth populations and alcohol-impaired driving in general and youth populations on average had greater implementation for our 29 policies during the period 1999–2011. However, effective policies targeting the general population were less likely to increase in implementation relative to less effective policies in addressing binge drinking in general and youth populations, and impaired driving in youth. For example, in a model examining the relationship between ER for reducing binge drinking in the youth population and IR for our 29 policies we observed a significant negative interaction between ER and IR over time [slope for annual change = -0.005; 95% confidence intervals (CI) for the slope = -0.006, -0.004; P < 0.001], indicating less implementation over time of efficacious policies compared with less efficacious policies. We observed similar findings for ER for reducing binge drinking and for alcohol-impaired driving among youth for these same 29 policies. We observed the same overall increase in IR among our 29 policies when using the ER for impaired driving in the general population.

Policy implementation by group over time

We created four groups of policies according to their ER across domains of binge drinking and impaired driving for both adults and youth, respectively (Table 3). These groupings and their corresponding mean ER are shown in Table 3. Policies that received high ER across all four domains were categorized as 'effective population' policies. Policies that received high ER for youth binge drinking and impaired driving, but comparatively low ER for adult binge drinking and impaired driving were 'effective youth' policies. Policies that were rated as high for addressing both youth and adult impaired driving, but received lower ER for youth and adult binge drinking, were 'effective impaired driving' policies. Policies that received low ER across all four domains were 'less effective' policies.

Some differences in implementation existed across the policy groupings (Table 3). The 'effective population' policies (13 policies) were implemented, on average, in 31.0 states in 1999 and in 31.9 states by 2011. In contrast, 'effective impaired driving' policies (three policies) were implemented on average in 45.7 states in 1999 and in 46.3 states by 2011. The seven 'effective youth' policies were also more commonly implemented, occurring in 39.3 states on average in 1999 and increasing to 43.4 by 2011. The six 'less effective' policies were the least commonly implemented in 1999, occurring in 22.7 states on average

in 1999. On average, implementation of these policies increased to 34.0 states by 2011, the largest increase in the four policy groupings. Similar findings were observed when examining the average IR.

Figure 1 shows the mean IR within each of four policy groupings across all years in our study period, and illustrates that while the average implementation score was essentially unchanged among 'effective population' policies, it increased for 'effective impaired driving' policies, 'effective youth' policies and 'less effective' policies.

In multivariable analyses to explore differences in implementation between policy groupings (Table 4), we found that 'effective population' policies did not change over the study period. This policy group served as the reference group for our analysis. In comparison, 'effective impaired driving' policies and 'effective youth' policies were more commonly implemented at the beginning of the study period (1999) and also increased significantly during the study period. 'Less effective' policies were less likely to be implemented at the beginning of the study period than 'effective population' policies. However, these policies were adopted in 11.3 additional states on average between 1999 and 2011. Findings were similar for analysis using the any policy measure and the average IR for those policy groups.

DISCUSSION

In the United States during the period from 1999 to 2011 we observed a small overall increase in the implementation of 29 state alcohol control policies. This increase occurred among specific types of policies and not among others. At the start of the study, policies targeting youth and alcohol-impaired driving were implemented at a high level and increased during the study period. Less effective policies had low levels of implementation in 1999, but increased significantly from 1999 to 2011. The most effective group of policies was underutilized in comparison to other policy groups we examined, and did not increase during the course of the study period.

This evidence provides empirical support for the observation by alcohol policy researchers that effective policies are relatively politically unpopular, and less effective policies are more politically popular. The common thread across these findings is that willingness exists among state legislatures in the United States to implement legislation to address problems associated with excessive alcohol use, specifically for underage drinking and alcohol-impaired driving. However, as evidenced by our findings, there is apparent reluctance to address those problems using policies that effectively restrict excessive drinking in the general population.

We used two different, but complementary, measures of policy implementation: whether or not a specific policy existed, and a rating of the strength of implementation of each policy according to various components that made it more restrictive, more enforceable or applied to more people or in more circumstances. Overall, our main findings were consistent across both these measures. There are some important advantages of employing both measures. The average implementation rating was able to detect areas where states worked to strengthen an existing policy over time. For example, nearly all states had a law making it

illegal *per se* to operate a motor vehicle with a blood alcohol concentration (BAC) at or above 0.08 in 1999. The change in a policy's average IR revealed shifts in the strength of implementation within those states over time. However, by using both measures we were able to document that most of the change that occurred in policies over time appears to have been driven by the adoption of new policies where no policy existed previously, rather than strengthening of existing policies.

The most effective policies are likely to reduce the problems associated with excessive drinking because they reduce drinking overall. Widespread implementation of effective policies may have a negative impact on future sales of alcohol products, and on this basis are likely to be opposed by alcohol-related industries. It is important to be aware of the tension between public health and economic interests when considering the adoption of alcohol control policies. Industry may try to influence both public opinion and views of legislators about the role of policy. The tension between public health goals and industrial economic interests has been described elsewhere [17,20,29], and probably plays a significant role in the lack of adoption of the most effective policies.

There are some important caveats and limitations of this analysis to acknowledge. Our ratings of efficacy were based on the opinion of a select group of alcohol policy experts. A different group may have reached a different consensus on the efficacy ratings of these policies. However, the policies that received high ER by experts in our review are also the policies with the strongest evidence of effectiveness for reducing excessive drinking among the general population. In a prior study we found a strong positive correlation between ER and ratings of the strength of evidence supporting those ratings [30]. The most highly rated policies in our review [30] (e.g. increased alcohol taxes) were those recognized in major reviews of scientific evidence as effective strategies to address problems resulting from excessive drinking [6,8,9]. We were limited to examining policies for which consistently collected data across all states during our study period were available. It is possible that the implementation of policies for which we did not have data were different than the policies where data were available. However, our policies covered most of the major state alcohol control policies in the United States, including those available in the APIS.

We did not assess any policies that promoted education about the risks of alcohol use. These policies were not nominated for consideration by our panel of experts because they were judged to be ineffective, and our study was restricted to policies believed by experts to be at least somewhat effective [30]. It is possible that an examination of all possible policies might have found even greater trends towards greater implementation of ineffective policies not included in the study. Alcohol use among college students in the United States is one area where this phenomenon can be observed. College students as a group tend to drink alcohol more heavily than most other segments of the population in the United States [1,41]. The National Institute on Alcohol Abuse and Alcoholism College Drinking Task Force concluded that educational efforts were ineffective for reducing drinking and related problems. However, nearly every college in a large national sample of schools used educational approaches to address student drinking [42]. In contrast, very few colleges in this same sample implemented, or were even working to implement, the most effective policies as identified by the College Drinking Task Force [42].

We found general support for our hypothesis. Policies that are effective for addressing drinking by youth and alcohol-impaired driving were more commonly implemented than policies restricting adult consumption. Secular shifts in the United States during our study period, including the rise of libertarian political thinking, the consolidation of the alcohol industry and changing campaign financing laws, may have influenced the implementation of alcohol control policies and account for our findings. State legislatures and prevention advocates should be aware of these findings and consider policy approaches that are underutilized but likely to be effective. A closer examination of the political conditions surrounding implementation of effective policies may be important to understand more clearly the role of public opinion on policy adoption, and the ways in which vested interests (e.g. alcohol-related industries) work to counteract the adoption and implementation of effective policies.

Declaration of interests

The authors have no conflicts to declare.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1

Efficacy ratings and implementation indices for 29 policies with policy scores.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Implementation of 29 state alcohol control policies in the United States, 1999-2011.

	1999		2011		<u>1999-2011</u>	
Policy	Number of states with a policy ^a	Mean policy implementation rating ^C	Number of states with a policy ^a	Mean policy implementation rating ^C	Change in number of states with a policy ^a	Change in mean implementation rating ^c
Mean across all policies	32.9	0.38	37.0	0.44	4.0	0.06
Tax ^b	NA	0.48	NA	0.49	NA	0.00
Outlet density ^b	NA	0.73	NA	0.73	NA	0.01
Furnishing to minors prohibited	51	0.74	51	0.73	0	-0.01
False ID prohibited	50	0.51	51	0.55	1	0.04
BAC 0.08 illegal per se	49	0.35	51	0.71	2	0.36
Administrative license revocation	49	0.42	49	0.40	0	-0.02
Alcohol beverage control agency	48	0.43	48	0.48	0	0.05
Direct shipment of alcohol prohibited	48	0.52	48	0.44	0	-0.08
Sales to intoxicated prohibited	47	0.45	48	0.46	1	0.01
Graduated driver's license	46	0.23	50	0.42	4	0.19
Minimum legal drinking age	44	0.50	47	0.57	3	0.07
Dram shop	43	0.51	45	0.52	2	0.01
Hours of sale restriction	43	0.53	44	0.53	1	0.00
Roadside sobriety checkpoints	39	0.71	39	0.71	0	0.00
Zero tolerance	36	0.36	37	0.39	1	0.02
Use lose	33	0.45	41	0.62	8	0.16
Wholesale price restriction	32	0.24	33	0.25	1	0.01
Retail price restriction	31	0.26	35	0.32	4	0.06
Open container prohibited in motor vehicle	26	0.46	44	0.84	18	0.38
Social host laws	26	0.29	31	0.33	5	0.04
Minimum age of server	26	0.25	26	0.26	0	0.01
Local option	20	0.08	19	0.06	-1	-0.02
Days of sale restriction	20	0.32	13	0.19	-7	-0.13
Fetal alcohol syndrome warning signs	19	0.36	24	0.43	5	0.07
State monopoly	18	0.23	18	0.23	0	0.00
House party laws	15	0.17	27	0.30	12	0.13
Keg registration	13	0.09	29	0.18	16	0.09
Responsible beverage service training	13	0.23	17	0.29	4	0.06
Ignition interlock laws	4	0.04	33	0.42	29	0.38

NA = not applicable; BAC = blood alcohol concentration.

 a Total number of states (plus the District of Columbia) is 51.

 b Taxes and outlet density are based on a continuous measure, pooled across all study years and ranked by decile.

 $^{\it C}$ Implementation score includes all 51 states, including states with no policy as 0.0.

Table 2

Interaction effects^a between policy domain efficacies and implementation trend, 1999-2011.

Models	Predictors	Beta (95% CIs)	P-value
Model I (efficacy on binge drinking in general population)	Efficacy on binge drinking in general population	0.012 (-0.003, 0.028)	0.110
	Implementation trend	0.013 (0.010, 0.015)	< 0.001
	Efficacy \times trend interaction	-0.003 (-0.004, -0.002)	< 0.001
Model II (efficacy on binge drinking in youth)	Efficacy on binge drinking in youth population	0.044 (0.019, 0.068)	0.001
	Implementation trend	0.019 (0.015, 0.023)	< 0.001
	Efficacy \times trend interaction	-0.005 (-0.006, -0.004)	< 0.001
Model III (efficacy on impaired driving in general population)	Efficacy on alcohol-impaired driving in general population	0.021 (0.007, 0.035)	0.003
	Implementation trend	0.006 (0.003, 0.009)	< 0.001
	Efficacy \times trend interaction	-0.001 (-0.001, 0.001)	0.781
Model IV (efficacy on impaired driving in youth)	Efficacy on alcohol-impaired driving in general population	0.063 (0.038, 0.088)	< 0.001
	Implementation trend	0.009 (0.005, 0.012)	< 0.001
	Efficacy \times trend interaction	-0.001 (-0.002, -0.001)	0.048

^{*a*}Regression models predicting the outcome of implementation ratings were based on individual state-policy-year observations (n = 51 states and DC × 29 policies × 13 years = 19 227). CI = confidence interval.

Table 3

Grouping of 29 state alcohol control policies by efficacy rating [1-4] and prevention target.

		Mean efficacy scores			
Policy grouping	Policies included	Adult binge drinking	Adult alcohol-impaired driving	Youth binge drinking	Youth alcohol-impaired driving
Effective general population policies (<i>n</i> = 13)	Alcohol excise taxes (state); state alcohol control systems (monopoly); outlet density restrictions; retail price restrictions; retail price restrictions; ABCs present, functional, adequately staffed; dram shop liability laws; hours of sale restrictions; sales/service to intoxicated patrons prohibited; local option permissible; social host laws (civil liability); days of sale restriction (Sunday sales); responsible beverage service training	3.4	3.3	3.2	3.1
Effective youth- oriented policies (<i>n</i> = 7)	Minimum legal drinking age laws (21 years); use alcohol/lose license; zero tolerance laws; furnishing alcohol to minors prohibited; graduated drivers license laws; false ID laws; House Party laws (social host, criminal liability)	1.5	1.5	3.3	3.6
Effective impaired driving polices (n=3)	BAC 0.08/per se laws; sobriety checkpoints; administrative license revocation	2.7	3.8	2.4	3.3
Less effective policies (<i>n</i> = 6)	Minimum age of server/seller; direct shipment/ home delivery of alcohol restricted; FAS warning signs; keg registration laws; ignition interlock laws for DUI offenders; open	1.8	2.1	2.1	2.2

		Mean efficacy scores			
Policy grouping	Policies included	Adult binge drinking	Adult alcohol-impaired driving	Youth binge drinking	Youth alcohol-impaired driving
	container laws, automobiles				

DUI = driving under the influence; FAS = fetal alcohol spectrum; BAC = blood alcohol concentration; ABCs = Alcohol Beverage Control agencies.

	<u>Number of states with a polic</u>	y ^a			Mean policy implementation	ı score ^a		
	666I	2011	Change 1999-2011	Change over time (mean 95% confidence intervals)	1999	2011	Change 1999-2011	Change over time (mean 95% confidence intervals)
Effective general population policies	31.0	31.9	0.9	$0.008^{\mathcal{C}} (-0.0004, 0.016)$	0.366	0.375	00.0	$0.001^{\mathcal{C}} (-0.001, 0.002)$
Difference from referent (mean, 95% confidence intervals)	$\operatorname{Referent}^{b}$				$\operatorname{Referent}^{b}$			
Effective youth-oriented policies	39.3	43.4	4.1	$0.042^{***}(0.023, 0.061)$	0.424	0.511	0.087	$0.007^{st}(0.005, 0.009)$
Difference from referent (mean, 95% confidence intervals)	$0.746^{***}(0.439, 1.054)$				$0.050^{*}(0.009,0.091)$			
Effective impaired driving polices	45.7	46.3	0.6	0.003 (-0.018, 0.023)	0.493	0.608	0.115	$0.0105^{***}(0.007, 0.014)$
Difference from referent (mean, 95% confidence intervals)	$1.808^{***}(1.236, 2.381)$				$0.136^{***}_{(0.078, 0.194)}$			
Less effective policies	22.7	34.0	11.3	$0.010^{***}(0.049, 0.087)$		0.427	0.140	$0.009^{***}(0.002, 0.007)$
Difference from referent	-0.584^{***} (-0.872 , -0.296)				-0.0588^{*} (-0.109 , -0.009)			
$n = 19\ 227$ state-policy-years. ** $P < 0.01$.								

 d Total number of states (plus the District of Columbia) is 51.

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b Referent is the policy implementation in the 'effective general population' policies in 1999, compared with each of three other groups in 1999.

^cReferent is the estimated slope of trends in policy implementation in the 'effective general population' policies during 1999-2011, compared to the estimated slope of the three other groups during 1999-2011.

 $^{*}_{P < 0.05.}$

*** P < 0.001.

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Table 4

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