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The impact of asthma medication guidelines on asthma controller use and on asthma exacerbation rates comparing 1997–1998 and 2004–2005

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ABSTRACT

Background: The relationship between asthma controller medication use and exacerbation rates over time is unclear at the population level.

Objective: To estimate the change in asthma controller medication use between 2 time periods as measured by the controller-to-total asthma medication ratio and its association with changes in asthma exacerbation rates between 1997–1998 and 2004–2005.

Methods: The study design was a cross-sectional population-level comparison between individuals from 1997–1998 and 2004–2005. Study participants were individuals aged 5 to 56 years identified as having asthma in the Medical Expenditure Panel Survey (MEPS). The main outcome measures were a controller-to-total asthma medication ratio greater than 0.5 and asthma exacerbation rates (dispensing of systemic corticosteroid or emergency department visit/hospitalization for asthma) in 1997–1998 compared with 2004–2005.

Results: The proportion of individuals with a controller-to-total asthma medication ratio greater than 0.5, when adjusted for other demographic factors, has improved by 16.1% (95% CI: 10.8%, 21.3%) for all individuals from 1997–1998 to 2004–2005. Annual asthma exacerbation rates did not change significantly in any group from 1997–1998 to 2004–2005 (0.27/year to 0.23/year). African American and Hispanic individuals with asthma had higher asthma exacerbation rates and a lower proportion with a controller-to-total asthma medication ratio greater than 0.5 than whites in both 1997–1998 and 2004–2005; however, these differences were not statistically significant.

Conclusions: An increase in asthma controller-to-total medication ratio in a sample reflective of the US population was not associated with a decreased asthma exacerbation rate comparing 1997–1998 and 2004–2005.

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Introduction

The first national asthma guideline was released by the National Asthma Education and Prevention Program in 1991, with updates in 1997, 2002, and 2007.¹ The guideline updates in 1997 and 2002 emphasize the appropriate use of asthma controller medications (see Fig 1 for a summary of key update recommendations). A previous study using the National Health Interview Survey examining trends from 1997–2004 suggests that asthma exacerbation rates have not improved over this time.² Another study suggests that asthma exacerbation rates are higher for African-American and Hispanic individuals

than white individuals in the United States³ and that specific racial and ethnic groups are not receiving guideline-concordant care.^{4–6}

Several studies suggest that an improvement in guideline implementation leads to improved asthma outcomes.^{7–9} Whether improved adherence to guidelines impacts asthma exacerbation rates at a population level and more specifically impact rates for African-American or Hispanic individuals is unknown. One of the leading explanations for why asthma exacerbations have not decreased is the continued underuse of asthma controller medications,^{3,10} an explanation that is not well supported by data that suggest a rapid expansion of asthma medication prescription expenditures across this same period.¹¹ In this study, we examine the impact of asthma medication guidelines on asthma controller use and on asthma exacerbation rates between 1997–1998 and 2004–2005 and the differential impact among white, African-American, and Hispanic individuals.

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1997 NAEPP Update

- (1) Separation of mild asthma into mild intermittent and mild persistent which included a definition of persistent as >2 days/weeks or >2 nights/month of asthma symptoms
- (2) Division of asthma medications into 2 general classes of quick relief and long-term-control medications
- (3) Stepwise treatment that suggested initiating treatment at a higher level to establish prompt control and then later pursue stepdown therapy

2002 NAEPP Update

- (1) Reaffirmed that inhaled corticosteroids (ICS) are effective controller medications
- (2) Chronic use of ICS is unlikely to cause significant adverse effects
- (3) Adding long-acting β -agonist (LABA) to ICS improves asthma outcomes

Fig. 1. Key changes in 1997 and 2002 National Asthma Education and Prevention Program updates.

Methods

Study sample

This was a cross-sectional study using the Medical Expenditure Panel Survey (MEPS) data from 1997–1998 and 2004–2005 as collected by the Agency for Healthcare Research and Quality. The MEPS, a large-scale collection of surveys, is organized into 2 parts: the Household Component and the Insurance Component. For the purpose of this study, only the Household Component, which is administered to single individuals within each sampled household as well as their medical providers, was used. The MEPS Household Component is designed to be nationally representative of the U.S. civilian, non-institutionalized population and collects information about each respondent's demographic and socioeconomic characteristics, health status, medical care use, medical care expenditures, and health insurance coverage.¹² The number of individuals surveyed in the household component of the MEPS for 1997–1998 and 2004–2005 was 120,646.¹² The MEPS uses an overlapping panel design, in which the sample in any given year is followed for a total of 2 calendar years. The survey consists of 5 in-person interviews over 30 months to yield annual use and expenditures for 2 calendar years. The survey data gathered as part of the Household Component is organized into several data files. Our study used the following data files: Full-Year Consolidated Data, Medical Conditions, Prescribed Medications, Hospital Inpatient Stays, Emergency Room Visits, Outpatient Visits, and Office-Based Medical Provider Visits. Within the various data files, MEPS collects key health care utilization measures for asthma, including emergency department visits, hospitalizations, outpatient visits, and asthma medication use based on pharmacy dispensing. An institutional review board (IRB) application (#09-008519) to the Mayo Clinic Foundation IRB was completed, and because of the de-identified nature of the data, was determined exempt.

Participants and definitions

Individuals were included in our analytical sample if they had a Clinical Classification System code for Asthma (128) in any position (1–4) from the Outpatients Visit File or Office-Based Visits File. Individuals 5 to 56 years old were identified and used for the primary analysis to limit diagnostic misclassification, which can be more common in younger and older individuals. Individuals younger than 5 and older than 56 were included in a similar analysis to conduct sensitivity analyses of our findings. Key health care utilization measures of asthma were defined consistent with recent expert recommendations.¹³ For the purposes of this study, an asthma exacerbation was defined as any one of the following

events: (1) inpatient visit for asthma; (2) emergency room visit for asthma; (3) dispensing of a systemic corticosteroid for asthma. An inpatient visit for asthma was defined by an inpatient visit with either a primary or secondary diagnosis (ie, only if the first or second listed diagnosis, not the third or higher) of asthma as indicated by a Clinical Classification System code. An emergency room visit was similarly defined as an emergency room visit with either a primary or secondary diagnosis of asthma as indicated by a Clinical Classification System code. Prescriptions for a systemic corticosteroid were based on pharmacy dispensing and were counted on a monthly basis. Exacerbations were identified on a monthly basis, with multiple events within a single month counting as 1 exacerbation for that month. Ultimately, exacerbations were summed for the year to yield an annual exacerbation rate (with values between 0 and 12). A full year measure of insurance coverage was used and was defined hierarchically as follows: (1) If an individual ever had Medicaid, they were coded as Medicaid; (2) if an individual ever had Medicare they were coded as Medicare; (3) if an individual ever had private insurance (employer-sponsored insurance or direct purchase) they were coded as Private; (4) if an individual indicated that they did not have any type of coverage at any point in the entire year, then they were coded as Uninsured.

Asthma medications were grouped for the purposes of calculating a controller-to-total asthma medication ratio (CR).¹⁴ The CR is defined as a ratio of the number of asthma controller medication prescriptions (based on pharmacy claims data) divided by the total number of asthma medications prescriptions (controller + rescue) over a specified time period. Controller medications included inhaled corticosteroids (ICS), a combination of ICS/long-acting beta-agonist (LABA), leukotriene modifier, mast cell stabilizer, and theophylline. The LABA (when used without ICS) and long-acting anticholinergic medications were not included as controller medication. For the purposes of this study, a combination of ICS/LABA in a single inhaler was counted as 1 controller medication. Rescue asthma medications (included in the denominator of the CR) included short-acting β -agonists, and combination of short-acting β -agonists and short-acting anticholinergic medications.

A CR greater than 0.5 was selected as a proxy measure of pharmacologic adherence to asthma guidelines based on findings from previous studies that find a CR greater than 0.5 correlates with important asthma outcomes.^{15–17} The CR cannot account for inhaler technique or measure medication adherence beyond pharmacy claims data. Adherence to asthma medication guidelines can be considered from the provider and patient perspective. The CR accounts for both by measuring the downstream effects of provider recommendations and patient decisions regarding asthma medications.

Statistical analysis

Two-year averages for 1997–1998 and 2004–2005 are reported to include a large enough sample to produce stable estimates. Demographic data were reported as percentage of the population. Differences between the 1997–1998 and 2004–2005 individuals were analyzed using the Wald χ^2 test. All reported summary statistics use survey weights developed by and as recommended by the Agency for Healthcare Research and Quality to account for the complex survey design of the MEPS. A multinomial logistic regression model was constructed for the controller ratio, which was categorized as greater than 0.5, greater than or equal to 0.5, and no asthma medications and for the exacerbations, which was categorized as none, 1 exacerbation, and 2 or greater. The models controlled for sex, age group (5–17, 18–34, 35–44, 45–56), poverty level (below federal poverty level [FPL], 100–199% of FPL, 200–399% of FPL, 400% or more of FPL), census region (northeast,

Table 1
Demographic characteristic of individuals (5–56 years old) with asthma 1997–1998 and 2004–2005, United States

Variable	1997–1998 Percent (standard error)	2004–2005 Percent (standard error)	Wald chi-squared P value
Age groups			.003
5–17	41.17% (2.03)	41.41% (1.93)	
18–34	28.07% (2.17)	18.44% (1.77)	
35–44	13.19% (1.36)	16.15% (1.60)	
45–56	17.57% (1.59)	24.01% (2.16)	
Sex (female)	58.81% (2.07)	56.84% (2.35)	.52
Ethnicity			.59
White	67.85% (1.77)	65.01% (2.13)	
Black	15.25% (1.55)	15.12% (1.52)	
Hispanic	13.22% (1.24)	14.85% (1.42)	
Other/unknown	3.68% (0.85)	5.02% (0.87)	
Insurance status			<.0001
Private	65.41% (1.98)	61.91% (2.22)	
Medicaid	22.41% (1.26)	29.95% (2.03)	
Medicare	0.63% (0.63)	1.76% (0.52)	
Other	0.67% (0.33)	1.59% (0.66)	
Uninsured	10.88% (1.48)	4.79% (0.85)	
Poverty status (FPL)			.81
Below poverty	19.79% (1.69)	18.78% (1.79)	
100–200% poverty	19.56% (1.80)	18.08% (1.35)	
200–300% poverty	29.11% (2.12)	31.44% (1.99)	
>300% poverty	31.54% (2.37)	31.70% (2.24)	
Metropolitan Statistical Area			.98
Non-MSA	17.31% (1.73)	17.40% (2.29)	
Census region			.85
Northeast	21.02% (1.56)	24.40% (3.21)	
Midwest	22.60% (1.95)	21.53% (2.19)	
South	33.97% (2.11)	32.71% (2.26)	
West	22.41% (1.99)	21.36% (2.05)	
Self-reported health			.68
Fair, poor	22.88% (1.98)	23.91%	
Number of Comorbidities (Mean)	0.09 (0.01)	0.13 (0.02)	.10

Data obtained from Medical Expenditure Panel Survey.

mid-west, south, west), urban versus rural, self-reported health (excellent, very good, or good versus fair or poor), time (1997–1998 vs 2004–2005) and Charlson comorbidity index. To isolate the impact of time, we used recycled predictions, also known as predictive margins, a method that took into account the complex survey data.¹⁸ Recycled predictions were used to estimate the outcome rates by setting first all patients to a time of 1997–1998 and then setting all patients to 2004–2005. This allows us to control for everything else in our model and isolate the impact of time on controller ratios. The predictions were also compared by

time within race. Point estimates were calculated and mean differences for the 1997–1998 and 2004–2005 time points were calculated with 95% confidence intervals for both. The statistical analysis was performed using SAS version 9.1.2 (Cary, North Carolina) and StataSE version 11 (College Station, Texas). The complex survey design of the MEPS was accounted for in all analyses by identifying necessary survey design variables, including the estimation weight, sampling strata, and primary sampling unit, as recommended by the Agency for Health Care Research and Quality.¹⁹

Table 2
Adjusted asthma controller ratio—proportion CR > 0.5 for individuals (5–56 years old) with asthma 1997–1998 and 2004–2005, United States

	1997–1998 % (95% CI)	2004–2005 % (95% CI)	Difference % (95% CI)
Totals			
>0.5	57.8% (53.5%, 62.0%)	73.8% (70.4%, 77.2%)	16.1% (10.8%, 21.3%)
≤0.5	21.1% (17.6%, 24.6%)	13.7% (10.8%, 16.6%)	–7.4% (–12.0%, –2.8%)
No asthma meds	21.2% (17.9%, 24.5%)	12.5% (10.1%, 14.9%)	–8.7% (–12.5%, –4.9%)
White			
>0.5	60.8% (55.9%, 65.7%)	76.2% (72.2%, 80.2%)	15.4% (10.1%, 20.6%)
≤0.5	22.1% (18.1%, 26.2%)	14.1% (10.7%, 17.5%)	–8.0% (–12.7%, –3.3%)
No asthma meds	17.1% (13.5%, 20.6%)	9.7% (7.2%, 12.2%)	–7.4% (–10.7%, –4.0%)
Black			
>0.5	53.6% (46.0%, 61.2%)	70.7% (64.9%, 76.6%)	17.1% (11.5%, 22.8%)
≤0.5	19.6% (13.2%, 26.0%)	13.1% (8.8%, 17.4%)	–6.5% (–11.4%, –1.5%)
No asthma meds	26.8% (19.3%, 34.2%)	16.1% (11.2%, 21.1%)	–10.6% (–15.9%, –5.4%)
Hispanic			
>0.5	52.7% (45.9%, 59.4%)	70.0% (64.3%, 75.6%)	17.3% (11.8%, 22.9%)
≤0.5	18.9% (13.5%, 24.2%)	12.8% (8.5%, 17.0%)	–6.1% (–10.5%, –1.7%)
No asthma meds	28.5% (22.4%, 34.6%)	17.2% (12.7%, 21.8%)	–11.2% (–16.3%, –6.2%)
Other/unknown			
>0.5	42.5% (29.2%, 55.8%)	61.0% (48.1%, 73.9%)	18.5% (12.6%, 24.3%)
≤0.5	16.4% (4.7%, 28.2%)	12.0% (3.3%, 20.7%)	–4.5% (–9.8%, 0.8%)
No asthma meds	41.1% (26.0%, 56.1%)	27.1% (15.2%, 38.9%)	–14.0% (–21.2%, –6.8%)

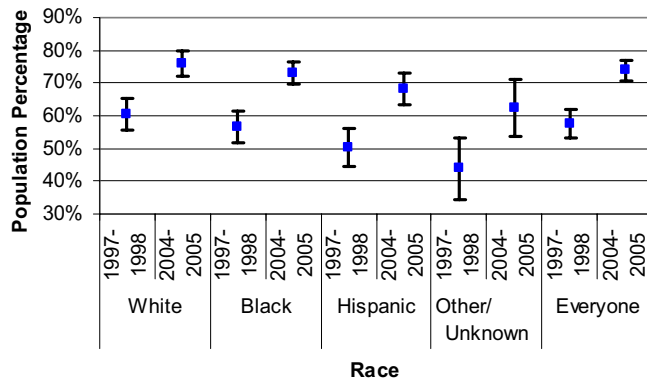


Fig. 2. Proportion of population with a controller-to-total asthma medication ratio greater than 0.5 comparing 1997–1998 and 2004–2005.

Results

Based on inclusion and exclusion criteria, 1,847 individuals aged 5 to 56 years old who met our definition of asthma for this study were identified and included in the analysis (879 individuals in the 1997–1998 timeframe and 968 individuals in the 2004–2005 timeframe). In total, the 1,847 individuals who are included in the analysis represent 15 million non-institutionalized individuals in the United States that meet our criteria for asthma as defined. A summary of the demographic characteristics of the study population is displayed in Table 1. Notable demographic differences between 1997–1998 and 2004–2005 include an older population in 2004–2005 ($P = .0025$) and more individuals with Medicaid in 2004–2005 ($P < .0001$). No significant differences were seen in the distributions of sex, ethnicity, poverty status, metropolitan statistical area, census region, self-reported health, or number of comorbidities between 1997–1998 and 2004–2005.

The controller-to-total asthma medication ratio (CR) was calculated for white, African-American, Hispanic, other/unknown, and total (all groups combined) adjusting for age, sex, insurance status, poverty status, metropolitan statistical area, census region, self-reported health, or number of comorbidities (Table 2). The proportion of individuals with a CR > 0.5 increased by 16.1% from 1997–1998 to 2004–2005. We performed an additional analysis treating CR as a continuous variable and found a similar significant difference between 1997–1998 and 2004–2005 (data not shown). All

racial/ethnic subgroups examined had significant increases in the proportion of individuals with a CR greater than 0.5 in 2004–2005 compared with 1997–1998. The changes in the CR by race/ethnicity and between different study periods (1997–1998 and 2004–2005) are depicted in Figure 2 and demonstrate that all groups had a similar increase in the proportion of individuals with a CR greater than 0.5 and that Black and Hispanic individuals continue to have a lower proportion of individuals with CR greater than 0.5 compared with white individuals.

Overall, the proportion of individuals with no asthma exacerbations did not change from 1997–1998 to 2004–2005, nor did the proportion of individuals with 1 or 2+ asthma exacerbations (Table 3). The asthma exacerbation rates for all study individuals were 0.27/year in 1997–1998 and 0.23/year in 2004–2005. The yearly asthma exacerbation rates by race/ethnicity did not change significantly from 1997–1998 to 2004–2005.

The mean CR value was compared between 1997–1998 and 2004–2005 by number of asthma exacerbations (0, 1, or 2+). Individuals with no asthma exacerbations had the highest mean CR (0.779 in 1997–1998 and 0.817 in 2004–2005 for mean difference of 0.039, 95% CI -0.008 , 0.085), followed by those with 1 asthma exacerbation (0.179 in 1997–1998 and 0.158 in 2004–2005, for a mean difference of -0.020 , 95% CI -0.065 , 0.024), and the lowest mean CR was for those with 2 or more asthma exacerbations (0.042 in 1997–1998 and 0.024 in 2004–2005, for a mean difference of -0.018 , 95% CI -0.037 , 0.00). Therefore, although those with the lowest mean CR tended to have more asthma exacerbations, no trend was found between 1997–1998 and 2004–2005. In fact, individuals in the group with the greatest number of asthma exacerbations (2+) have a slightly lower mean CR value in 2004–2005 that is not statistically significant. In addition, the events that qualified participants for an asthma exacerbation (inpatient visit, emergency visit, or systemic corticosteroid) were not different between 1997–1998 and 2004–2005 (Table 4).

To determine whether restricting our sample by our preselected age limits affected our conclusions, an additional 834 individuals younger than 5 years old or older than 56 years old that met all the other inclusion criteria were included in a separate sensitivity analysis (data not shown). There were no significant differences in any of the endpoints when the analysis included individuals of all ages compared with the data presented for ages 5 to 56 years.

Table 3

Adjusted asthma exacerbation rates for individuals (5–56 years old) with asthma 1997–1998 and 2004–2005, United States

	1997–1998 % (95% CI)	2004–2005 % (95% CI)	Difference % (95% CI)
Overall			
0	77.9% (74.2%, 81.6%)	81.7% (78.7%, 84.8%)	3.9% (–0.8%, 8.5%)
1	17.9% (14.4%, 21.3%)	15.8% (12.9%, 18.7%)	–2.0% (–6.5%, 2.4%)
2+	4.2% (2.6%, 5.9%)	2.4% (1.5%, 3.4%)	–1.8% (–3.7%, 0.0%)
White			
0	78.3% (74.1%, 82.5%)	81.9% (78.4%, 85.4%)	3.6% (–1.1%, 8.3%)
1	18.4% (14.3%, 22.4%)	16.2% (12.8%, 19.6%)	–2.2% (–6.7%, 2.4%)
2+	3.3% (1.8%, 4.8%)	1.9% (1.0%, 2.7%)	–1.4% (–2.9%, 0.1%)
Black			
0	76.6% (72.4%, 80.7%)	80.8% (77.3%, 84.3%)	4.2% (–0.6%, 9.1%)
1	18.1% (14.4%, 21.9%)	16.1% (13.0%, 19.3%)	–2.0% (–6.5%, 2.6%)
2+	5.3% (3.1%, 7.5%)	3.0% (1.8%, 4.3%)	–2.3% (–4.7%, 0.1%)
Hispanic			
0	77.7% (73.0%, 82.3%)	82.1% (78.3%, 85.8%)	4.4% (–0.3%, 9.1%)
1	16.0% (12.0%, 20.1%)	14.3% (10.9%, 17.8%)	–1.7% (–5.8%, 2.4%)
2+	6.3% (3.7%, 9.0%)	3.6% (2.0%, 5.3%)	–2.7% (–5.4%, 0.1%)
Other/unknown			
0	76.5% (69.6%, 83.3%)		
1	15.4% (9.7%, 21.1%)	13.9% (8.6%, 19.2%)	–1.5% (–5.4%, 2.5%)
2+	8.1% (4.0%, 12.2%)	4.8% (2.4%, 7.2%)	–3.3% (–7.0%, 0.3%)

Table 4

Asthma Exacerbations Comparing 1997–1998 with 2004–2005

	Inpatient (95% CI)	ER visit (95% CI)	Systemic corticosteroid prescription (95% CI)
1997–1998	14.6% (10.3%, 18.8%)	46.4% (36.1%, 56.7%)	40.3% (30.7%, 49.8%)
2004–2005	12.9% (9.0%, 16.8%)	43.8% (34.7%, 53.0%)	43.2% (31.8%, 54.7%)

Discussion

There was a statistically significant increase in the proportion of individuals with a controller-to-total asthma medication ratio of greater than 0.5 in 2004–2005 compared with 1997–1998, suggesting an increased adherence to asthma medication guidelines. However, no significant changes occurred in asthma exacerbation rates over the same time period. While African-American and Hispanic individuals with asthma continue to have lower proportions of those with CR greater than 0.5 and higher asthma exacerbation rates than white individuals in both 1997–1998 and 2004–2005; these differences between the 2 time periods were not statistically significant.

Our finding that asthma exacerbation rates using an administrative database have not changed from 1997–1998 to 2004–2005 is consistent with findings from the National Health Interview Survey.² The asthma exacerbation rates in this study (0.27/year in 1997–1998 and 0.23/year in 2004–2005) are slightly lower than multicenter clinical trials, which report asthma exacerbation rates between 0.29 and 0.91/year. This is likely because of inclusion of individuals with intermittent asthma, who have lower exacerbation rates, in our population-level study.^{20,21} The proportion of the population with CR greater than 0.5 in our study (0.58 in 1997–1998 and 0.74 in 2004–2005) is similar to a previous report from a Medicaid population in 2001–2002 (0.73),¹⁷ an adult health maintenance organization population in 2000 (0.53),¹⁵ and an administrative claims database in 2006–2007 (0.74).²²

What are the possible explanations for why asthma exacerbation rates failed to improve with increased adherence to asthma medication guidelines? The increased prescription of controller medications may not have been targeted properly to patients who need them. The increased use of controller medications may have occurred in individuals from the mild intermittent and mild persistent asthma categories, possibly an effect of the newly created separate classes in the 1997 National Asthma Education and Prevention Program update (see Fig 1 for a description of key National Asthma Education and Prevention Program update changes in 1997 and 2002). Even patients with mild persistent asthma may not benefit significantly from regular use of a controller medication.²³ Second, possibly a larger increase in controller medication prescription may be needed to achieve population-level decreases in asthma exacerbation rates. Third, we measured medication possession and not the actual adherence to the prescribed controller medication or the use of proper technique, and this could potentially underestimate the potential benefits of controller medications. Conversely, possibly randomized controlled trials, such as the Gaining Optimal Asthma Control (GOAL) study, may overestimate the population-level impact of asthma exacerbation reduction.²⁴

The findings of this study have important implications for future asthma research. First, the finding that asthma exacerbation rates are not improving should be a cause for concern and encourage research directed at improving this rate. Second, these efforts should be focused in African-American and Hispanic populations, where asthma exacerbation rates are higher than for white individuals. Third, strategies addressing management aspects beyond medication guideline implementation may be necessary to significantly impact asthma population-level exacerbation rates. Fourth,

the findings from this study may be significantly different if we compared 2010–2011 to 2004–2005, as national guidelines released in 2007¹ highlight the need to consider impairment and risk when determining optimal asthma management.

In conclusion, an increase in asthma controller-to-total medication ratio in a sample reflective of the US population was not associated with a decreased asthma exacerbation rate comparing 1997–1998 and 2004–2005.

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