

Smoking Behavior 1 Year after Computed Tomography Screening for Lung Cancer: Effect of Physician Referral for Abnormal CT Findings

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Abstract

Background: Computed tomography (CT) lung cancer screening offers a unique clinical setting in which to promote smoking cessation. Focusing on outcomes related to the reporting of CT abnormality, we examined the natural history of smoking in the Pittsburgh Lung Screening Study.

Methods: Pittsburgh Lung Screening Study recruited 50- to 79-year-old current and former cigarette smokers living in the Pittsburgh area. We examined self-reported smoking outcomes 1 year after study entry in a subgroup that contained 2,094 active cigarette smokers without interval lung cancer diagnosis (50.7% women; median age, 57 years; 40-year median duration of cigarette smoking; and 65.2% ≥ 20 cigarettes/d). Analyses compared efforts to quit in relation to physician referral for abnormal CT.

Results: Since study entry, 58.5% [95% confidence interval (95% CI), 56.3-60.6%] reported any quit attempt and 27.2% (95% CI, 25.3-29.1%) reported any quit interval >30 days. One year after study entry, 15.5% (95% CI, 14.0-17.1%) reported not smoking for >30 days. Comparing persons referred because of CT abnormalities creating moderate or high lung cancer suspicion ($n = 156$; 7.4%) to persons not referred for any reason ($n = 1145$; 54.7%), propensity score-adjusted fractions with any quit attempt and with any quit interval >30 days increased 18.8% (95% CI, 11.1-26.5%) and 17.7% (95% CI, 9.4-26.0%), respectively. The fraction quit >30 days at 1 year increased 12.2% (95% CI, 4.9-19.5%).

Conclusions: Persons who experienced referral because of abnormal CT reported more smoking cessation. (Cancer Epidemiol Biomarkers Prev 2009;18(12):3484-9)

Introduction

In 2007, according to the National Health Interview Survey, 47.9% of adult (≥ 18 -year-old) ever smokers still smoked (1). According to the 2003 Tobacco Use Supplement to the Current Population Survey, 64%, 36%, and 5.1% of 35- to 64-year-old recent (in past year) smokers seriously tried to quit, quit for at least 1 day, and quit for at least 6 months in the past year, respectively (2).

Research groups internationally continue to evaluate low-dose computed tomography (CT) screening for detecting early lung cancer in at-risk current and former cigarette smokers (3-9). CT screening may offer a unique clinical setting that is, a teachable moment, particularly conducive to quit smoking intervention (6, 10). In this context, investigators question the effects of CT screening on smoking behavior (11). A negative CT screening result could dampen a smoker's motivation to quit, whereas a positive result could stimulate quitting. To explore this phenomenon, we compared the subsequent quit behaviors of smokers with and without abnormal results on an initial CT screening.

Materials and Methods

Study Population. Between January 2002 and April 2005, the Pittsburgh Lung Screening Study (PLuSS), a research-based low-dose helical CT lung cancer screening program, used mass media, physician referral, and mass mailings to recruit 50- to 79-year-old current and former cigarette smokers without a personal history of lung cancer (12). PLuSS eligibility criteria included a history of cigarette smoking, at least one-half pack per day for at least 25 years, and, if quit, quit for no more than 10 years. All subjects signed written informed consent.

PLuSS subjects completed a standardized, self-administered baseline questionnaire. In addition to screening CT, the baseline assessment included a pulmonary function test (PFT; forced expiratory spirometry conducted according to the American Thoracic Society standards and analyzed according to Global Initiative for Chronic Obstructive Lung Disease categories).⁷ PLuSS mailed PFT and CT results to every subject and his/her personal physician. Subjects with clinically important CT findings were referred to their personal physicians. Using the most

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⁷ Global Initiative for Chronic Obstructive Pulmonary Disease: pocket guide to COPD diagnosis, management, and prevention. Medical Communications Resources, 2008. Accessed 2009 Aug 29. <http://www.goldcopd.com/download.asp?intId=505>.

important CT finding, we classified subjects into four referral categories, including referral for moderate or high suspicion CT (>5% predicted probability of lung cancer), referral for low suspicion CT (<5% predicted probability of lung cancer), referral for other reason (important CT finding not usually associated with lung cancer), and no referral. In addition to mailed reports, a nurse practitioner telephoned subjects placed in a physician referral category. During the PFT completed on the day of study enrollment, PLSUSS encouraged active smokers to quit and recommended a hospital-based small group quit smoking program. During subsequent telephone contacts, the nurse practitioner updated smoking status and informally encouraged smoking cessation.

Subjects eligible for the current analysis included the 2,157 baseline current smokers who survived the first year after CT screening without receiving a lung cancer diagnosis. A brief 1-year follow-up telephone interview of 2,142 (99.3%) subjects supplied information about cigarette smoking behavior since study entry. Responses to one questionnaire item ("Are you currently smoking cigarettes?") were used to distinguish ex-smokers (who then reported the duration of the current quit attempt) from active smokers (who then reported the duration of the longest quit attempt, if any, since study entry). Lacking information about earlier quit attempts, we excluded 48

persons reporting on the day of follow-up interview that they had not smoked for ≥ 30 days. Analyses characterized the remaining 2,094 subjects according to three smoking outcomes, including any quit attempt, regardless of duration, since study entry, any ≥ 30 days quit interval since study entry, and quit on 1-year follow-up date for >30 days. The CT screening occurred a median 29 days (interquartile range, 17-39 days) after the assessment of baseline smoking status and the follow-up telephone interview occurred a median 353 days (interquartile range, 340-366 days) after the CT screening.

To evaluate self-reports of smoking, we measured exhaled air carbon monoxide in a convenience sample of PLSUSS subjects returning for follow-up CT screening between August 2005 and January 2006. Carbon monoxide measurements were consistent with self-reported abstinence (≤ 8 ppm) in 95 of 108 (88.0%) self-reported ex-smokers, suggesting reasonably reliable self-report of smoking status.

Statistical Analysis. Primary analyses compared the frequency of a study outcome among subjects with physician referral for abnormal CT (moderate or high suspicion, low suspicion, and other reason) relative to subjects without referral. We used propensity scores (predicted odds of referral) to control for confounding (13). Using

Table 1. Subjects in a lung cancer CT screening program, *n* (%) according to baseline characteristic and smoking outcome

Characteristic	<i>n</i>	Column %	No quit attempt (<i>n</i> = 870)	Quit ≤ 30 d (<i>n</i> = 655)	Quit >30 d		<i>P</i> *
					Relapsed at 1 y (<i>n</i> = 244)	Quit at 1 y (<i>n</i> = 325)	
					Row %	Row %	
Overall	2,094	100.0	41.5	31.3	11.7	15.5	
Demographic factors							
Sex							0.0075
Men	1,032	49.3	45.0	29.2	10.3	15.6	
Women	1,062	50.7	38.2	33.3	13.0	15.4	
Baseline age (y)							0.4386
50-59	1,292	61.7	43.0	30.1	11.8	15.0	
60-69	625	29.8	39.8	33.6	11.0	15.5	
≥ 70	177	8.5	36.7	31.6	12.4	19.2	
Race							0.0028
White, not Hispanic	1,918	91.7	42.4	30.3	11.4	15.8	
Other	174	8.3	31.6	42.0	14.4	12.1	
Education							0.1743
High school or less	518	24.7	40.3	30.9	13.9	14.9	
Post-high school	859	41.0	40.0	33.9	10.7	15.4	
College graduate	717	34.2	44.2	28.5	11.2	16.2	
Baseline smoking behavior							
Cigarettes/d							0.0411
1-19	729	34.8	39.1	31.1	11.4	18.4	
20-29	921	44.0	40.9	32.6	11.7	14.8	
30-39	306	14.6	49.0	28.8	9.8	12.4	
≥ 40	138	6.6	42.0	29.0	16.7	12.3	
Medical factors							
No. symptoms [†]							0.0002
0	418	20.0	45.5	25.6	9.3	19.6	
1	604	28.8	41.4	30.1	10.8	17.7	
2	495	23.6	42.2	33.3	10.7	13.7	
>2	577	27.6	38.3	34.8	15.1	11.8	
No. diagnoses [‡]							0.0097
0	1,599	76.4	42.8	30.2	10.8	16.3	
1	370	17.7	39.7	32.2	14.6	13.5	
>1	125	6.0	31.2	42.4	14.4	12.0	

NOTE: Referral outcome from screening CT.

* χ^2 test of independence between baseline characteristic and smoking outcome.

[†]Baseline symptoms, including phlegm, wheezing, shortness of breath, and ankle swelling.

[‡]Baseline physician diagnoses, including chronic bronchitis, emphysema, and asthma.

Table 2. Smoking outcomes according to physician referral category

Smoking outcome	No referral (n = 1,145)	Other referral (n = 49)	Low suspicion (n = 744)	Moderate or high suspicion (n = 156)
Quit attempt, %	54.1	69.4	61.2	73.7
Quit >30 d, %	23.8	30.6	29.0	41.7
Quit >30 d at 1 y, %	13.8	26.5	15.3	25.6

subjects without physician referral as a common control group, we fit three logistic regression models (one for each referral category). Independent variables included (a) sex, (b) age, (c) race, (d) education, (e) marital status, (f) age started smoking, (g) years smoking, (h) cigarettes smoked per day, (i) cancer family history, (j) personal cancer history, (k) number of symptoms (phlegm, wheezing, shortness of breath, and ankle swelling), (l) number of physician diagnoses (chronic bronchitis, emphysema, and asthma), (m) time since most recent chest X-ray before study entry, (n) time since most recent chest CT before study entry, (o) severity of airflow obstruction on study PFT, and (p) coronary calcification reported on screening CT. We used subject-level risk factor values and parameters estimated from logistic regression to calculate for each subject the expected odds (propensity score) of physician referral. We verified that control for propensity score quartile eliminated risk factor differences between subjects with and without physician referral. Using subjects not referred as a common reference, we then fit separate general linear models (ref. 14; binomial distribution with identity link executed in PROC GENMOD, SAS System for Windows Release 9.2) to estimate the effect, adjusted for propensity score quartile, of a physician referral category (e.g., moderate or high suspicion) on a smoking outcome (e.g., any quit interval >30 days since study entry). We fit separate models to subgroups defined according to risk factor level (e.g., ages 50-59, 60-69, and ≥70 years) to estimate stratum-specific effects and then added a term to represent the interaction between risk factor and referral category to evaluate the statistical significance (Wald test) of different effects (effect modification) according to risk factor level.

Results

The study group included 50.7% women, median age 57 years (interquartile range, 53-63 years), 8.5% ages ≥70 years, 8.3% minority race or ethnicity, and 34.2% college educated (Table 1). Subjects smoked cigarettes a me-

dian 40 years (interquartile range, 36-45 years) and 65.2% smoked ≥20 cigarettes per day (Table 1). Eighty percent had baseline symptoms (phlegm, wheezing, shortness of breath, or ankle swelling) and 23.7% a physician diagnosis of lung disease (chronic bronchitis, emphysema, or asthma; Table 1). Finally, CT screening prompted physician referral for 45.3%, including 2.3% referred for reasons not related to a lung cancer suspicion, 35.5% referred for low lung cancer suspicion, and 7.4% referred for moderate to high lung cancer suspicion (Table 2). Time intervals between study entry and 1-year follow were independent of physician referral category ($P = 0.30$, Wilcoxon rank-sum test).

Overall, 58.5% [95% confidence interval (95% CI), 56.3-60.6%] reported any quit attempt since study entry, 27.2% (95% CI, 25.3-29.1%) any quit interval >30 days, and 15.5% (95% CI, 14.0-17.1%) quit on 1-year follow-up date for >30 days. Baseline factors related to cigarette smoking outcomes ($P < 0.05$) included sex, race, cigarettes smoked per day, number of symptoms, number of physician diagnoses, and CT referral category (Table 1). Quit attempt, long quit interval, and long quit interval without relapse at 1 year were more frequent among persons referred for CT abnormalities relative to persons not referred (Table 2). Propensity score-adjusted, the fraction of subjects attempting to quit increased, in absolute terms, 15.9% (95% CI, 2.2-29.5%), 7.2% (95% CI, 2.6-11.8%), and 18.8% (95% CI, 11.1-26.5%) among persons with other referral, low suspicion referral, and moderate or high suspicion referral, respectively (Table 3). The fraction of subjects able to quit for >30 days increased 6.0% (95% CI, -7.4% to 19.4%), 5.6% (95% CI, 1.5-9.7%), and 17.7% (95% CI, 9.4-26.0%). Finally, the fraction of subjects quit for >30 days without relapse at 1 year increased 13.7% (95% CI, 1.1-26.4%), 1.6% (95% CI, -1.7% to 4.9%), and 12.2% (95% CI, 4.9-19.5%).

As shown in Table 4, higher suspicion CT referral categories contained higher proportions of subjects with newly discovered chronic lung disease, defined by PFT airflow obstruction in persons without history of emphysema, chronic bronchitis, or asthma. Higher suspicion CT

Table 3. Differences in smoking outcome (expressed as percent of subjects who experience the outcome) between groups with and without physician referral after lung cancer CT screening, unadjusted and adjusted for the predicted odds of referral (propensity score quartile)

Smoking outcome	Other referral vs no referral Δ (95% CI)	Low suspicion vs no referral Δ (95% CI)	Moderate or high suspicion vs no referral Δ (95% CI)
Quit attempt			
Unadjusted	15.2 (2.0-28.5)	7.0 (2.5-11.6)	19.6 (12.1-27.1)
Adjusted	15.9 (2.2-29.5)	7.2 (2.6-11.8)	18.8 (11.1-26.5)
Quit >30 d			
Unadjusted	6.8 (-6.4 to 19.9)	5.2 (1.1-9.3)	17.8 (9.7-25.9)
Adjusted	6.0 (-7.4 to 19.4)	5.6 (1.5-9.7)	17.7 (9.4-26.0)
Quit >30 d at 1 y			
Unadjusted	12.7 (0.2-25.3)	1.5 (-1.8 to 4.8)	11.8 (4.7-19.0)
Adjusted	13.7 (1.1-26.4)	1.6 (-1.7 to 4.9)	12.2 (4.9-19.5)

NOTE: Δ = smoking outcome in group with physician referral minus smoking outcome in group without referral.

Table 4. Subjects in CT referral categories distributed (%) according to baseline history of lung disease (emphysema, chronic bronchitis, or asthma) and entry PFT result

History of lung disease	PFT result, airflow obstruction*	No referral (n = 1,145)	Low suspicion (n = 744)	Moderate or high suspicion (n = 156)
No	None	50.7	46.0	34.6
	Mild	10.2	12.8	13.5
	Moderate-severe	15.9	18.0	25.6
Yes	None	10.0	7.5	7.1
	Mild	2.6	2.2	3.8
	Moderate-severe	10.5	13.6	15.4

NOTE: Excludes n = 49 subjects in the other CT referral category. P = 0.0009.

*Mild and moderate-severe airflow obstruction defined by Global Initiative for Chronic Obstructive Lung Disease I and II-IV, respectively.

referral categories also contained higher proportions of subjects with confirmed chronic lung disease, defined by PFT airflow obstruction in persons with history of lung disease (Table 4). Communicating PFT results plausibly stimulated smoking cessation. This consideration motivated closer evaluation of smoking outcomes associated with PFT abnormality, particularly in subjects reporting no history of chronic lung disease at baseline. In analyses restricted to subjects with no baseline history of lung disease and no CT referral, the quit attempt outcome occurred more frequently among subjects referred because of moderate-severe airflow obstruction than among subjects without airflow obstruction ($\Delta = 8.8\%$; 95% CI, 0.6-17.0%; $P = 0.04$; Table 5). Adjustments for sex, age, race, cigarettes smoked per day, and number of symptoms partially attenuated this difference ($\Delta = 7.4\%$; 95% CI, -1.2% to 16.0%; $P = 0.10$). Neither the quit >30 days nor the quit >30 days at 1 year outcomes differed statistically according to PFT result (Table 5).

Comparing persons referred for moderate or high suspicion to persons without referral, the frequency of a quit interval >30 days increased in 50- to 59-year-old persons (propensity score-adjusted difference, 18.0%; 95% CI, 7.5-28.5%) and 60- to 69-year-old persons (propensity score-adjusted difference, 30.8%; 95% CI, 13.8-47.7%) but not in ≥ 70 -year-old persons (propensity score-adjusted difference, -2.7%; 95% CI, -23.3% to 18.0%; $P_{\text{interaction}} = 0.03$; Fig. 1). No other risk factor statistically modified the effect of a moderate or high suspicion referral on any smoking outcome.

Discussion

Over the 1-year period after CT screening, 58.5% of PLuSS baseline smokers tried to quit and 27.2% quit for >30 days. At the time of the 1-year follow-up, 15.5% had not smoked for >30 days. Compared with smokers not referred, these favorable smoking-related outcomes occurred more

frequently among smokers referred because of abnormalities found on screening CT (Table 2). The smoking cessation effects attributed to referral were more dramatic when the CT report indicated a moderate or high as opposed to low lung cancer suspicion (Table 3). Although consistent with the notion that knowledge of a smoking-related health problem may spur personal smoking cessation efforts, the associations between CT referral and smoking outcomes may also have occurred as a consequence of more intensive interactions with the health-care system. In addition to CT, abnormal PFT could induce medical follow-up. CT referral occurred more often in subjects with abnormal PFT (Table 4). Meaningful association between CT referral and smoking outcome persisted after propensity score adjustments that included factors for severity of airflow obstruction. By comparison, only limited statistical evidence emerged for association between PFT abnormality and smoking outcome (Table 5). These disparate associations involving CT and PFT suggest smoking effects specific to the CT referral process.

Several studies have described changes in smoking behaviors after CT screening and the effects of positive as opposed to negative CT screen results. Contacted a median 6 months after screening, 66 of 134 (49%) baseline smokers from the Early Lung Cancer Action Program stopped or decreased smoking (9). Twenty-one of 34 (62%) and 45 of 100 (45%) with positive and negative CT results, respectively, stopped or decreased smoking ($P < 0.10$). In a Mayo Clinic study, 129 of 901 (14%) baseline smokers self-reported not smoking 1 year after an initial CT screening (6). Rates of smoking cessation did not vary according to the CT follow-up recommendation. However, a Mayo Clinic reanalysis examining outcomes from a sequence of three annual CT screenings showed a significant 1.37-fold (95% CI, 1.12-1.67; $P = 0.002$) increase in the multivariable-adjusted odds of smoking cessation at a next follow-up visit among subjects who received a recommendation for additional follow-up because of an abnormal screening result (15). In the Danish Lung Cancer Screening Trial,

Table 5. Smoking outcomes according to entry PFT result among subjects with no baseline history of lung disease (emphysema, chronic bronchitis, or emphysema) and no CT referral

PFT result, airflow obstruction*	n	Quit attempt		Quit >30 d		Quit >30 d at 1 y	
		n (%)	Δ (95% CI)	n (%)	Δ (95% CI)	n (%)	Δ (95% CI)
None	581	297 (51.1)	Reference	136 (23.4)	Reference	83 (14.3)	Reference
Mild	117	60 (51.3)	0.2 (-9.8 to 10.1)	26 (22.2)	-1.2 (-9.5 to 7.1)	20 (17.1)	2.8 (-4.6 to 10.2)
Moderate-severe	182	109 (59.9)	8.8 (0.6- 17.0)	38 (20.9)	-2.5 (-9.4 to 4.3)	24 (13.2)	-1.1 (-6.8 to 4.6)

NOTE: Δ = difference from percentage for reference category.

*Mild and moderate-severe airflow obstruction defined by Global Initiative for Chronic Obstructive Lung Disease I and II-IV, respectively.

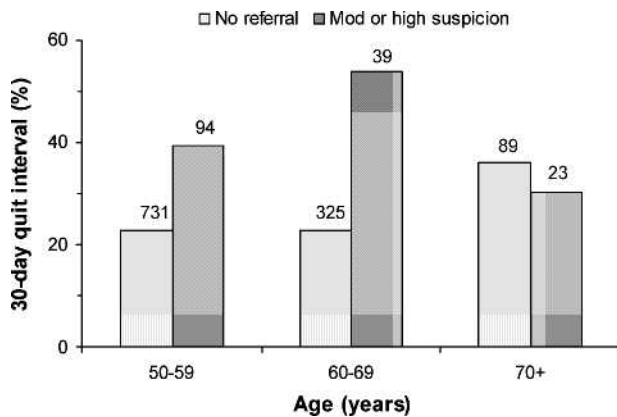


Figure 1. Frequency of a quit smoking interval >30 d since study entry according to physician referral category and age at study entry. The number above each bar indicates the number of subjects.

174 of 1,462 (11.9%) baseline smokers were not smoking (for at least 4 weeks, exhaled carbon monoxide-verified) 1 year after CT screening (16). Quit rates differed between subjects with and without significant CT findings (17.7% versus 11.4%; $P = 0.04$).

In the view of most authors (3, 6, 9, 15, 16), smoking cessation rates after CT screening are favorable when judged against the natural history of smoking in the general population (2) or the response of smokers to physicians' advice to quit (17). Any favorable outcome could reflect either preferential selection of smokers predisposed to quit or specific behavioral effects from CT screening (or associated quit smoking intervention). The current study adjusted findings for many covariates commonly related to quitting activity, suggesting that baseline factors were not responsible for differences in quitting. Also, suggesting a direct effect from CT screening, Taylor et al. compared responses to questionnaires administered before and 1 month after a second (Lung Screening Study) or first (National Lung Screening Trial) CT screening and detected a greater readiness to quit in 12 of 66 (18.2%) Lung Screening Study smokers and 23 of 73 (31.5%) National Lung Screening Trial smokers (18). Dispelling the notion that participation in an organized CT screening program, as such, promotes smoking cessation, the Danish Lung Cancer Screening Trial observed identical 1-year quit rates among smokers "randomly" exposed versus not exposed to CT screening (11.9% of 1,462 versus 11.8% of 1,395; ref. 16). Whatever the explanation, evidence of favorable smoking outcomes may distinguish CT screening as a clinical opportunity, a teachable moment (10, 18), particularly conducive to quit smoking intervention.

Confirming other studies (9, 15, 16), we observed more favorable smoking outcomes in persons informed about significant CT screen abnormality. Explanations include (a) diminished motivation to quit in screen-negative smokers, (b) intensified motivation to quit in screen-positive smokers, (c) quit smoking cointervention targeting screen-positive smokers, and (d) greater tendency for screen-positive smokers to misrepresent quit smoking outcomes. In PLUSS, active smokers were advised to quit and referred to quit smoking programs. To facilitate and document diagnostic follow-up, the nurse practitioner contacted subjects

with abnormal CT results specifically, thereby providing unique opportunity for informal quit smoking cointervention. Referred subjects received more intensive diagnostic follow-up (12), thereby providing more opportunity for cointervention by nonstudy health-care providers. Whatever the explanation, strong associations observed between CT results and quit smoking outcomes reinforce the need for quit smoking interventions that respond to the unique behavioral effects of participation in CT screening. However, our observation that CT referral was associated with quitting among younger (<70 years) but not older persons (Fig. 1) suggests that older smokers resist a referral-induced motivation to quit. Our finding is consistent with Taylor et al. (18) who reported that receiving an abnormal CT report appeared to boost readiness to quit among 55- to 64-year-old, but not necessarily older, smokers in the Lung Screening Study. Thus, use of CT referral, as a teachable moment, may be limited to smokers who perceive significant long-term health gains from quitting. Accumulated experiences with medical screening or diagnostic tests may have immunized older smokers emotionally against disturbing CT results. Other interventions may be necessary to promote quitting in older smokers.

Study strengths included large sample size ($n = 2,094$), nearly complete (99.3%) follow-up for smoking outcomes at 1 year, ability to examine smoking outcomes according to level (low versus moderate or high lung cancer suspicion) of CT abnormality, and use of propensity score methods to control for 16 demographic, smoking-related, and health-related factors that could possibly confound associations between CT abnormality and smoking behavior. Single addition of any one of these 16 risk factors to propensity quartile-adjusted general linear models did not materially change estimated associations between physician referral category and smoking outcome (data not shown). Study weaknesses included lack of information about smoking cessation treatments used by subjects in the year after lung cancer screening and reliance on self-report measures of smoking behavior, although the concordance of self-reported quitting with biochemical validation of abstinence was reasonably high.

In conclusion, referral because of an abnormal CT affected smoking cessation. Quit smoking interventions coupled to CT screening should accommodate, anticipate, or leverage effects of CT results on smoking behavior.

Disclosure of Potential Conflicts of Interest

K.A. Perkins has consulted with Glaxo with regard to developing new smoking cessation medications. Pfizer is providing K.A. Perkins with medications for an active NIH-funded study.

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