Brief report

Does the Magnitude of Reduction in Cigarettes Per Day Predict Smoking Cessation? A Qualitative Review

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Abstract

Introduction: Reduction in cigarettes per day (CPD) aided by nicotine replacement therapy (NRT) increases cessation in smokers; however, it is unclear whether this is due to use of NRT or reduction per se. If the latter, a greater magnitude of reduction in CPD should increase the odds of cessation.

Methods: The authors searched PubMed, Cochrane, PsychINFO, <http://clinicaltrials.gov> and their personal libraries for studies on smoking reduction. Seven of the 76 (9%) identified intervention trials and four of 28 naturalistic studies (14%) reported on the magnitude of reduction in relation to the odds of cessation.

Results: Five of the seven intervention trials and three of the four naturalistic observational (cohort) studies found that increased reduction in CPD was associated with increased cessation. The intervention trials that reported effect sizes found that every 1% decrease in CPD or carbon monoxide was associated with a 3% to 4% increase in the odds of cessation. The naturalistic studies found that ordinal (eg, quartile) increases in participants' magnitude of reduction in CPD were associated with 50% to 290% increases in the odds of cessation. All of the naturalistic studies and four of the intervention trials included covariates; however, reduction's association with cessation could still be due to its association with NRT use or motivation.

Conclusion: Although prospective prediction does not necessarily indicate causality, our findings suggest reduction in CPD is a mechanism of increased cessation in prior NRT-aided reduction studies.

Introduction

Nicotine replacement therapy (NRT) aided reduction increases cessation in cigarette smokers^{1–3}; however, it is unclear whether the pretreatment with NRT, the reduction in cigarettes per day (CPD), or both are responsible for the effectiveness of these interventions. Pretreatment NRT without instruction to reduce CPD increases cessation in many, but not all studies.^{4–7} Further, there is limited research on the efficacy of smoking reduction without NRT.^{8–13} Prior studies indicate that

interventions without NRT effectively reduce CPD.¹⁴ Most of the studies that examined quitting as an outcome found that interventions to reduce CPD increase cessation but were limited by small sample sizes and other confounders.^{8,12} None examined the magnitude of reduction in CPD per se as a predictor of the odds of cessation.

If reduction in CPD per se is a mechanism responsible for increased cessation, then a dose-response relationship between reduction and cessation should occur. If this is the case, reduction

could be a cause itself, could mediate the effect of other variables (eg, NRT), or could influence cessation independent of other variables. The one prior review of this found that magnitude of reduction predicted abstinence but only examined three studies.¹⁵ The current review more systematically examines published intervention trials and naturalistic (observational or cohort) studies of smoking reduction to better test the hypothesis that a greater reduction in CPD prospectively predicts a greater probability of cessation.

Methods

We searched PubMed, Cochrane, PsychINFO, <http://clinicaltrials.gov>, our personal libraries and submitted a request to the Society for Research on Nicotine and Tobacco list serve for intervention trials and naturalistic studies that tested reduction as a means to cessation. We examined intervention trials that collected data on participants before and after an intervention. We examined naturalistic studies that collected longitudinal data on participants from convenience or population based samples without an intervention. Trials and studies were included if they (1) used a sample of smokers who were either actively trying or not trying to quit, (2) measured reduction in CPD continuously or in an ordinal manner, and (3) analyzed whether the magnitude of reduction prospectively predicted the odds of cessation. We did not include trials and studies that measured reduction in CPD dichotomously or compared participants who reduced from daily to nondaily smoking to those who remained daily smokers because a dose-response analysis requires at least three levels of the independent variable. We contacted the authors of trials and studies for clarification on their methodologies as needed. We examined abstinence at the studies' longest reported follow-up. We did not assess study quality because quality assessment scales have not been reliably associated with different outcomes.¹⁶ A meta-analysis was not possible due to the diverse reporting and study methods.

Results

Intervention Trials

We identified 76 intervention trials that tested the effect of reduction in CPD on cessation. All were randomized trials. Seven of these trials (9%) reported on the relationship between the magnitude of reduction in CPD and cessation (Table 1).^{17–23} See [Supplementary Material \(www.uvm.edu/medicine/behaviorandhealth/?Page=Klempner2014.html#naturalisticstudies\)](http://www.uvm.edu/medicine/behaviorandhealth/?Page=Klempner2014.html#naturalisticstudies) for a list of excluded intervention trials. Sample sizes varied from 57 to 1722 participants (median = 212) and mean CPD varied from 21 to 35. Six trials included interventions with cessation as a goal for participants who wanted to quit. One trial included an intervention with reduction as a goal for participants who did not want to quit. Four trials reported findings solely within conditions that received medication and three combined results across conditions that both received and did not receive medication. Treatment length varied from 2 to 10 weeks (median = 2 weeks) and time to follow-up varied from 6 to 260 weeks (median = 13 weeks). Five trials measured reduction continuously, one in an ordinal manner, and one in both a continuous and ordinal manner. Six trials measured reduction during treatment and one¹⁸ measured reduction over the course of 5 years after treatment. Six of seven trials biochemically verified cessation and reduction in CPD with carbon monoxide (CO) levels.

Five of the seven intervention trials found that a greater magnitude of reduction in CPD or CO prospectively predicted a greater odds of cessation (Table 1).^{17,19–22} Two trials reported effect sizes.

One trial of varenicline and bupropion as adaptive treatments for participants who did not respond to NRT found that every 1% decrease in CO was associated with a 4% increase in the odds of cessation (ie, a reduction of 25% of CO should increase the odds of cessation by 100%).¹⁹ A trial of NRT and counseling for participants who were not ready or not able to quit found that every 1% decrease in CPD was associated with a 3% increase in the odds of cessation (ie, a reduction of 25% should increase odds of cessation by 75%) and marginally associated with a 2% increase in the odds of a quit attempt.¹⁷ Two of the four intervention trials that included covariates did not find a significant relationship between participants' magnitude of reduction in CPD and their odds of cessation.^{18,23}

Naturalistic Studies

We identified 28 naturalistic studies that examined the effect of participants' reduction in CPD on cessation. Four of these studies (14%) reported on the relationship between the magnitude of reduction in CPD and cessation (Table 2).^{24–27} See [Supplementary Material \(www.uvm.edu/medicine/behaviorandhealth/?Page=Klempner2014.html#naturalisticstudies\)](http://www.uvm.edu/medicine/behaviorandhealth/?Page=Klempner2014.html#naturalisticstudies) for a list of excluded naturalistic studies. The included studies varied from 1159 to 2443 participants (median = 1873). They examined either true population based samples of smokers^{25,26} or large samples that are essentially comparable to population based samples.^{24,27} In all likelihood, very few of smokers in these studies were actively trying to quit.²⁸ The identified studies varied widely in their measurement of CPD smoked and time to follow-up (Table 2). All of the studies measured reduction in an ordinal manner, included covariates, and relied solely on participants' self-report as a measure of abstinence.

Three of the four identified naturalistic studies found that a greater magnitude of reduction predicted cessation. A Finnish twin cohort study found that those who reduced by 25%–49% were more likely to quit than nonreducers while those that reduced by 50%–74% were even more likely to quit, and those that reduced by more than 75% were the most likely to quit smoking.²⁴ Data from the Health and Retirement Survey yielded a similar dose-responsivity.²⁵ However, a study of smokers in California found a threshold effect where smokers were only more likely to quit successfully if they reduced by more than 67%.²⁶ Finally, among smokers in the International Tobacco Control Four-Country Survey who had failed in a quit attempt, the magnitude of reduction in CPD did not predict cessation or future quit attempts.²⁷

Discussion

NRT aided reduction in CPD increases cessation in smokers.¹ The extent to which this is due to reduction per se rather than pretreatment with NRT^{5,7} has been discussed in a prior review¹⁵ but not clarified. If reduction is a mechanism responsible for increased cessation, then greater reduction in CPD should prospectively predict greater probability of cessation.

In the current analysis, five of seven intervention trials and three of four naturalistic studies found that increased reduction in CPD is associated with increased cessation. The only two intervention trials that reported effect sizes found dose response relationships that indicate that participants who reduce CPD or CO by 1% increase the odds that they will achieve abstinence by 3% to 4% (ie, a reduction of 25% should increase the odds of cessation by 75% to 100%).^{17,22} The two naturalistic studies that tested dose response relationships found effect sizes increase with each quartile reduction in participants' CPD.^{24,25} One of these studies measured reduction before (1975–1981) and cessation after (1990) NRT was

Table 1. Intervention Trials That Examined the Relationship Between the Magnitude of Reduction in CPD and Cessation

First author, year	N	Ss ready to quit?	Conditions examined	Tx length (weeks)	Follow-up from baseline (weeks)	Reduction predicts abstinence	Comments
Intervention trials that reported unadjusted findings							
Carpenter, 2004	212	No	Various NRT	6	24	Yes	Participants had a mean reduction in CPD of 30%. OR = 1.03; 95% CI = 1.02% to 1.05% (ie, a reduction of 25% of CPD should increase the odds of cessation by 75%)
Rose, 1998	80	Yes	Combined NRT, mecamylamine & placebo	4	13	Yes	Reported CO as an indication of CPD.
Rose, 2009	379	Yes	Combined NRT & placebo and usual & low tar/nicotine cigarettes	2	10	Yes	Post-hoc analyses found that reduction only predicted cessation in participants that received NRT. ¹⁴
Intervention trials that included covariates							
Hughes, 2004	1722	Yes	NRT gum	10	260	No	Participants had a mean reduction in CPD of 29%. All participants had a failed quit attempt during treatment. Analyses controlled for all variables that differed across treatment groups. The magnitude of reduction in CPD was a marginal predictor of cessation at 2 years but not a predictor at 5 years. This was the only trial to measure reduction in CPD 9 to 12 months after Tx. All other trials measured reduction during Tx. This trial did not biochemically verify the number of CPD smoked. This analysis used an ordinal measure of reduction in CPD.
Rose, 2006	96	Yes	Combined NRT & placebo and usual & low tar/nicotine cigarettes	2	24	Yes	Magnitude of reduction in CPD was a significant predictor of cessation as a univariate predictor and, after including covariates, as it was measured on the FTND.
Rose, 2013	606	Yes	NRT patch and rescue varenicline & bupropion	2	13	Yes	Reduction was measured during the participants' first week of NRT patch Tx. Rescue Tx (bupropion, varenicline, or none) were made for nonresponders after 1 week of NRT patch Tx. Ordinal and continuous measures of reduction in CPD and CO were found to predict cessation. OR = 1.04, 95% CI = 1.03% to 106% (ie, a reduction of 25% of CO should increase the odds of cessation by 100%)
Schuz, 2014	57	Yes	NRT patch	2	6	No	Analyses controlled for baseline CPD.

CI = confidence interval; CO = carbon monoxide; CPD = cigarettes per day; N = number of subjects; *ns* = not significant; FTND = Fagerstrom Test for Nicotine Dependence; NRT = nicotine replacement therapy; OR = odds ratio; Ss = subjects; Tx = treatment.

publically available to its Finnish participants.²⁴ Another naturalistic study reported a threshold that suggests that only smokers who reduce by 67% or more have an increased odds of cessation²⁶ but we

found no other evidence of a threshold to reduction's effect on cessation. Whether the association of reduction magnitude and abstinence is due to increased quit attempts is unclear. One intervention

Table 2. Naturalistic Studies That Examined the Relationship Between the Magnitude of Reduction in CPD and Cessation^a

First author, year	N	Sample characteristics	Smoking at baseline	Period of reduction	Follow-up (years)	Magnitude of reduction (%)	% of participants that reduced	Reduction's effect on abstinence adjusted effect size (95% CI) compared to participants that did not reduce
Broms, 2008	2443	Population based cohort of same-sex twins born in Finland before 1958	>100 cigarettes in lifetime	1975–1981	9	1–24	4.1	OR = 0.8 (0.4–1.5) <i>ns</i>
						25–49	11.3	OR = 1.5 (1.1–1.5)
						50–74	4.4	OR = 1.6 (1.0–2.5)
						>75	1.8	OR = 2.6 (1.4–4.9)
Falba, 2004	2064	Representative sample born between 1931 and 1941 in the United States	21 CPD	1992–1994	2	1–25	9.2	OR = 1.42 (0.9–2.2) <i>ns</i>
						25–50	18.4	OR = 1.7 (1.2–2.3)
						>50	5.4	OR = 2.7 (1.7–4.3)
Farkas, 1999	1682	Representative sample of smokers in California	<15 CPD = 22%;	1989–1990	2	1–33	6.0	OR = 0.8 (0.2–2.6) <i>ns</i>
			15 to 24			34–49	2.0	OR = 0.2 (0.02–2.6) <i>ns</i>
			CPD = 48%; >25			50–66	7.0	OR = 1.34 (0.6–3.0) <i>ns</i>
			CPD = 31%			>67	3.9	OR = 3.9 (1.5–10.2)
Yong, 2008	1159	Sample of UK, US, Canada, and Australia smokers who made a quit attempt during the period that reduction was measured	≥5 CPD	2002–2003	1	—	—	<i>ns</i>

CI = confidence interval; CPD = cigarettes per day; *ns* = not significant; N = number of participants; OR = odds ratio.

^aAll studies included covariates in their analyses.

trial found that increased reduction is associated with a subsequent increase in quit attempts¹⁷ but one trial and one study did not.^{18,27}

Two of the five intervention trials and three of the three naturalistic studies that found that increased reduction is associated with increased cessation included covariates. Common covariates were participants' baseline CPD, age, gender, and race/ethnicity; however, none of the trials or studies included more plausible confounders such as amount of use of NRT or motivation as covariates.

Two intervention trials and one naturalistic study did not find that increased reduction was associated with increased odds of cessation. Two of these (one intervention trial and one naturalistic study) were also the only studies that examined smokers who had a failed quit attempt during the trial or study.^{18,27} Thus, magnitude of reduction might not predict cessation in smokers who recently attempted to quit. Also, the intervention trial of smokers who had a failed quit attempt found that reduction marginally predicted cessation at a 2-year follow-up but this effect was not apparent at a 5-year follow-up.¹⁸ This was the only trial that measured reduction after, rather than during, treatment and abstinence at a long-term follow-up (5 years); thus, the effects of a reduction intervention could diminish over time.¹⁸ The other trial that did not find this effect found a large but nonsignificant positive effect of reduction but used a small sample size ($n = 57$)²³; thus, the trial may have lacked adequate power.

Reduction's effect on cessation could be due to other variables associated with reduction, such as medication use. None of the trials or studies directly tested this possibility by including NRT as a covariate. If reduction effects are due to NRT use, then reduction should predict cessation when active medication is used but not when placebo is used. In fact, a post-hoc analyses of one placebo controlled intervention trial found this interaction.¹⁵ On the other hand, another intervention trial found that reduction predicted cessation independent of whether smokers received active or placebo patch.²¹ In addition among naturalistic studies of all smokers (including those not trying to quit), one found reduction prior to the availability of medications predicted cessation.²⁴ Among the other three, two found reduction predicted cessation^{25,26} and it is likely that the incidence of NRT use in these two studies is small; probably around 10%–20%.^{29,30} Finally, we know of no trials or studies

that examined whether the effect of magnitude of reduction is due to its association with other covariates such as prereduction motivation to quit, self-efficacy, or other plausible predictors of cessation.

Our results suggest further experimental tests of reduction in CPD without medication are needed to more directly test whether reduction per se causes cessation. Prior studies on interventions to reduce CPD without medication demonstrate feasibility¹⁴ and suggest reduction in CPD per se can increase cessation.^{8,12} However, most were limited by a small sample sizes or other confounders, and none examined magnitude of reduction in CPD as a predictor of cessation.

Limitations

One limitation of this qualitative review is that the majority of intervention trials (91%) and naturalistic studies (86%) did not report on the relationship between participants' magnitude of reduction in CPD and the odds of cessation. Thus, our findings could have been influenced by a publication bias in which negative studies were not described. Another potential bias is that participants self-selected the extent that they reduced. Three of five intervention trials that supported our hypothesis did not include covariates in their analyses; therefore findings from intervention trials should be interpreted with caution. In contrast, all of the naturalistic studies included covariates. Finally, reduction was measured over the course of 1–10 weeks in intervention trials and 1–6 years in naturalistic studies. Unfortunately, intervention trials and naturalistic studies did not report on the rapidity with which participants reduced, which could be a crucial factor.

Conclusion

NRT aided reduction in CPD is an effective intervention to increase cessation but prior research does not address the role of reduction per se as it relates to cessation. We examined the hypothesis that a greater reduction in CPD prospectively predicts a greater probability of cessation. Our results support the hypothesis and, thus, suggest that reduction per se is a mechanism responsible for increasing the odds of cessation. Although none of the studies adequately controlled for confounders, our finding that magnitude of reduction predicted

cessation is consistent with the hypothesis that reduction in CPD per se leads to cessation. However, prospective prediction cannot prove causality; thus, better experimental trials testing reduction without NRT are needed to determine the extent to which reduction per se is causally related to later cessation.

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Declaration of Interests

EMK has nothing to disclose. JRH has received consulting fees from several companies that develop or market behavioral and pharmacological smoking cessation treatments, including nicotine replacement therapies.

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Supplementary Material

Supplementary Material can be found online at <http://www.ntr.oxfordjournals.org>.

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