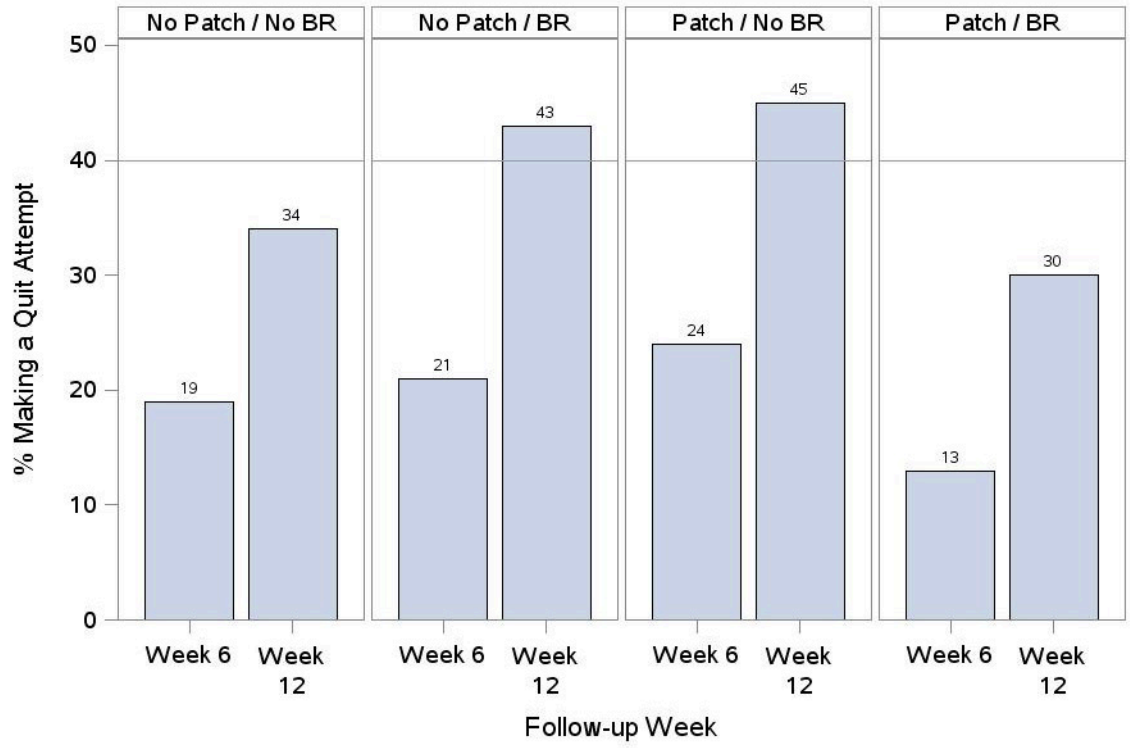
SUPPLEMENTAL TABLE

Supplemental Table 1. Model Generated Coefficients for Main Effects and for Different Numbers of Intervention Components as Related to Quit Attempts at Week 6 in the Motivation Study (N=517)

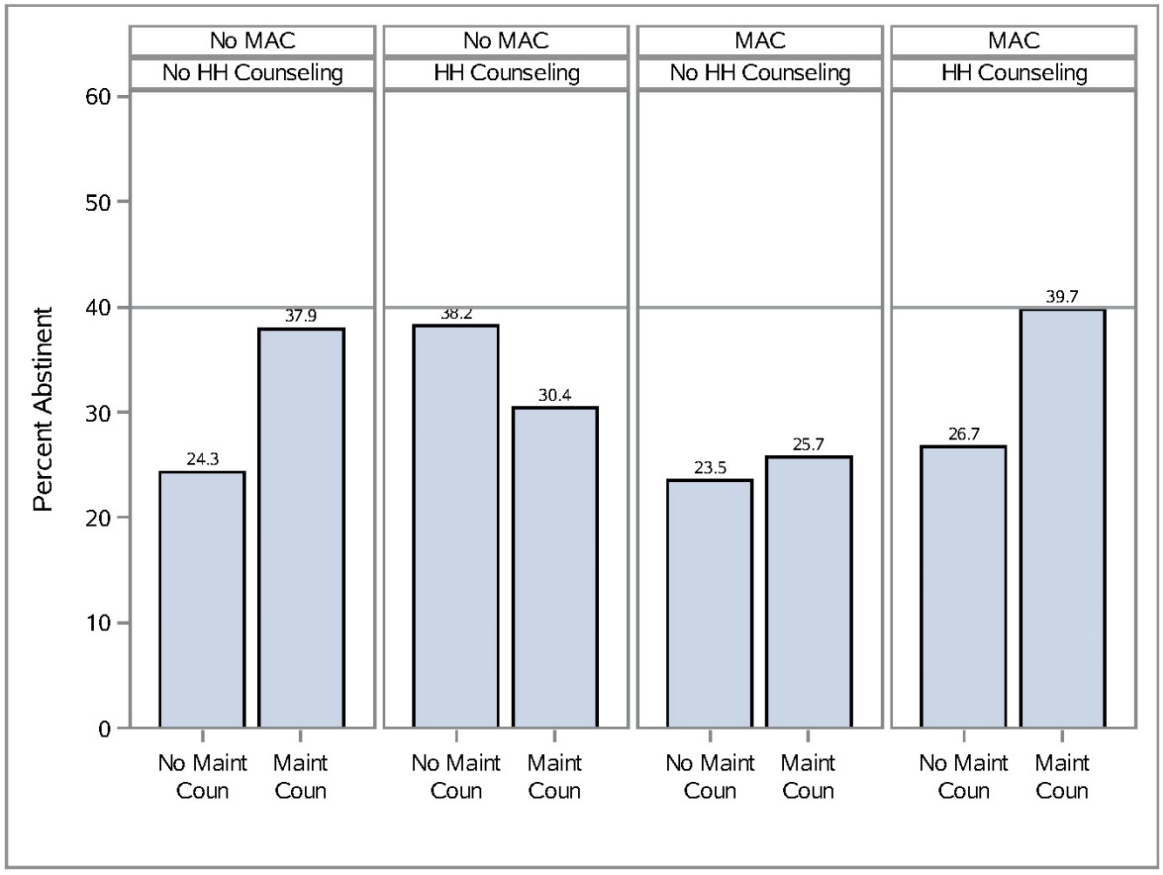
Intervention Component Main Effects	**B**	**SE**	**OR**	**P**	**95% CI for OR**
Constant	-.811	.425	.444	.002	-
Nicotine Patch	.119	.710	1.13	.867	(.280,4.532)
Nicotine Gum	.840	.703	2.32	.232	(.584,9.185)
Behavioral Intervention	.305	.714	1.36	.670	(.335,5.495)
Motivational Interviewing	.867	.703	2.38	.218	(.599,9.443)
2 Components ON	-.501	.836	.606	.549	(.118,3.119)
3 Components ON	-.396	.745	.673	.595	(.156,2.900)
4 Components ON	-.183	.865	.832	.832	(.153,4.534)

SUPPLEMENTAL FIGURES

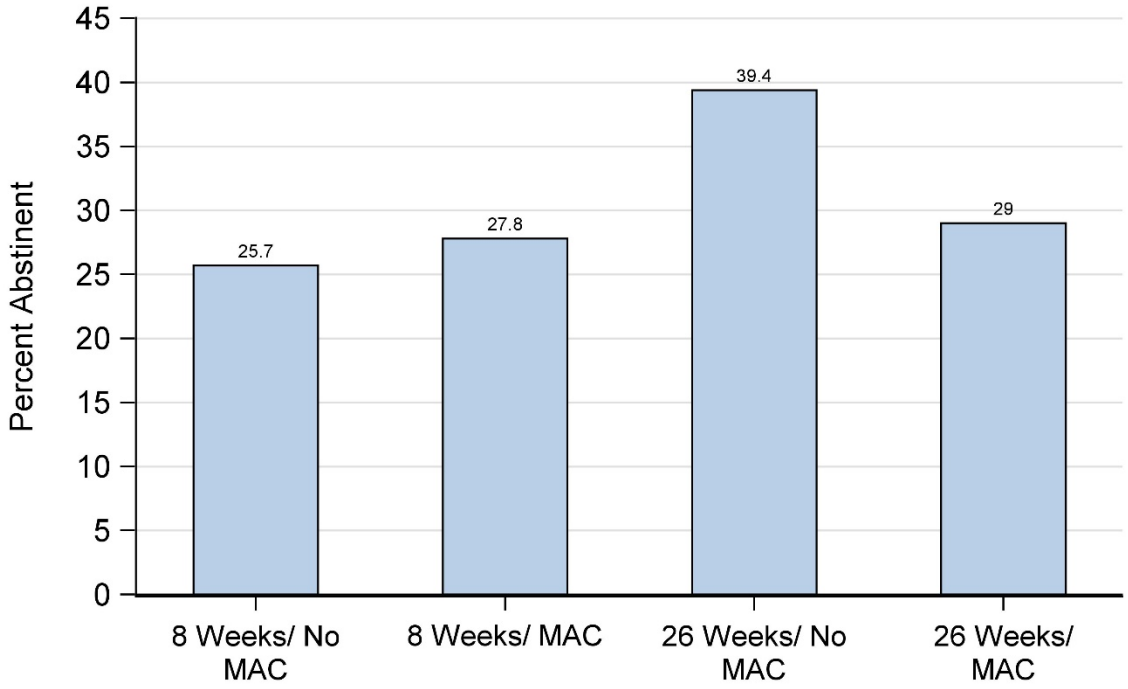
Supplemental Figure 1. Unpackaging Two 2-way Interactions Amongst Behavioral Reduction Counseling and Nicotine Patch Therapy On Quit Attempts at 6 and 12 weeks in the Motivation Study



Supplemental Figure 2. Unpackaging an Interaction Amongst Maintenance Counseling, Medication Adherence Counseling (MAC), and Helping Hand Counseling on 52 Week Abstinence in the Maintenance Study



Supplemental Figure 3. Unpackaging an Interaction Amongst Medication Adherence Counseling (MAC) and Extended Medication on 52 Week Abstinence in the Maintenance Study



SUPPLEMENTARY NOTES

Supplemental Note 1: The Population-Based Intervention

Data from the Population-Based experiment were analyzed to determine whether the same pattern of negative interactions seen in the Motivation and Maintenance Studies was seen in this study. Because this study will be used primarily to confirm some of the results of the Motivation and Maintenance Studies, and because it had relatively few variables that were useful for examining the mechanisms that might account for the negative interactions, we will describe this study in less detail than the other studies.

Participants in the Population-Based experiment (Fraser et al., 2014) were 1,034 adult smokers invited to participate in a research program when they visited a smoking cessation website (*Smokefree.gov*). They were 68% female; had a mean age of 39.3 years (SD = 12.3); 84.8% were White; and they smoked an average of 19.3 cigarettes/day (SD = 8.9) . This was a 2^5 fully crossed factorial experiment; each factor had 2 levels, ON and OFF. The factors were: (1) the National Cancer Institute's (NCI) web site (*www.smokefree.gov* vs a "lite" Web site), (2) telephone quitline counseling (5 sessions vs none), (3) a smoking cessation brochure (36 pages vs a 'lite' brochure), (4) motivational e-mail messages (for 3 months vs none), and (5) a 2-week starter kit of mini-lozenge nicotine replacement therapy (162 lozenges vs none).

Subjects were assessed and screened on-line but made a confirmation call to complete study entry. Randomization occurred immediately after that call and was communicated via an email. There were three follow-up assessments at 1-, 3-, and 7-months post study entry. The primary

outcome for the current analyses is self-reported 7-day point-prevalence abstinence at 1 and 3 months post-quit observing the intent-to-treat principle.

Supplemental Note 2: Motivation Study

Participants in the Motivation Intervention experiment (Cook et al., 2016) were 517 adult smokers recruited from 2010 to 2013 in 11 primary care clinics (also used in the Motivation Study); smokers not willing to try to quit were invited to participate in a research program to help them to reduce their smoking. Mean age=47.0 years old (SD = 14.4); mean cigarettes per day=17.5 (SD = 7.8); 63.4% female; 91.1% White and 4.8% African American; 1% Hispanic; and 61.6% had at least some college. This was a 2^4 fully crossed factorial experiment; each factor had 2 levels ON and OFF. The four factors comprised intervention components that were designed to reduce smoking and increase attempts and abstinence: (1) nicotine patch (14 mg patch for 6 weeks daily) versus none; (2) nicotine gum (2 mg with instruction to use 1 piece/1-2 hours) versus none; (3) motivational interviewing (MI) versus none, and (4) behavioral reduction (BR) counseling versus none. BR involved one initial 20-minute in-person counseling session followed by six weekly 10-minute counseling calls. During these sessions, participants set smoking reduction goals and developed reduction strategies (e.g. delaying smoking, eliminating smoking in specific situations). Participants were also instructed to record daily smoking, which counselors used to identify successes and challenges. MI involved one initial 20-minute in-person MI counseling session (Miller & Rollnick, 2002; Rollnick, Mason, & Butler, 1999) followed by three biweekly, 10-minute counseling calls over the 6-week intervention period. The MI counseling was designed to reinforce intrinsic motivation and to help participants overcome ambivalence about quitting.

There was an initial 6-week motivation-phase treatment period, and participants could choose to extend the same experimentally assigned intervention components for another 6 weeks. Participants could choose to use a cessation treatment (8 weeks of nicotine patch+gum, and two brief phone counseling sessions) at any time in the 6-month study period. Assessments included smoking history questionnaires and as outcomes, smoking reduction quantified as percentage change in cigarettes smoked per day at 12 and 26 weeks post-study enrollment, number of quit attempts made within 6 and 12 weeks post study enrollment, and point-prevalence abstinence at 6, 12, and 26 weeks post study enrollment. For the current paper we examined whether or not participants made a quit attempt (a binary variable) at 6- or 12 weeks after treatment inception.

Supplemental Note 3. Genetics and Tipping Point Phenomena for Disease Risk

This sort of relation between initial status, intervention sensitivity, and change or transition likelihood has considerable precedence. For instance, the Huntington's Disease (HD) phenotype reflects the number of C-A-G codon repeats in the HD gene that a child inherits from his or her parents. The more repeats the child receives from one's parents the closer the child is to a 40-repeat tipping point and the more likely it is that transcription/translation errors will add even more repeats. Thus, the likelihood of a child's developing HD is a function of two factors: 1) a heightened proximity to the 40-repeat tipping point and 2) the number of parental repeats is positively related to adding extra copies of the C-A-G codon during transcription and translation; the greater the number of parental repeats, the more likely that extra copies will be added. Thus, a child's likelihood of tipping over into Huntington's Disease status is a function of distance and responsivity to the change agent (in this case, transcription/translation).

Supplemental Note 4. Appreciation of nonlinear relationships in understanding effects in logistic regression

Interpretations of effects in a logistic regression analysis should recognize the nonlinear relationship between the predictor value and percentages (and percentage change). For example, consider two smokers, one who in the absence of any intervention has a probability of a successful quit of 10% (far from the tipping point), the other a probability of 45% (closer to the tipping point). Under logistic regression, , the two smokers are at values of -2.20 and -.20, respectively without intervention on a standardized predictor metric., A constant effect of an intervention component (say a change of 1.0 when turning only this component ON) will bring the first smoker to a 23% probability of quit (a difference of 13%) while the second smoker's probability is 69% (a difference of 24%). Despite the greater gain seen by the second smoker on the probability metric (which can be attributed to the smoker being closer to the inflection point of the logistic function), this does not reflect a differential effect of the component across smokers as the effect is actually constant in a logistic regression. In general, we expect to see larger changes in the probability of success for smokers close to the inflection point of the logistic curve than for smokers farther away (either in a positive or negative direction from the inflection point) when components are showing the same effect across smokers. The same issue applies to how we think about interactions (or the lack thereof) between treatment components for smokers near the tipping point. If the smoker near the tipping point who is already receiving one component (e.g., producing a change under logistic regression from -.20 to .80) receives a second component with an effect of the same magnitude (e.g., producing a change from .80 to 1.80), in the absence of an interaction we see a smaller difference in the probability of quit

related to the added second component in terms of percentages (from 69% to 86%, a difference of 17%), relative to the 24% change seen when turning only the first component ON.

Supplemental Note 5. Effect vs. Dummy Coding

While effect coding is highly effective for parsing variance so that main effects and lower-order interactions can be estimated relatively discretely, it is less suitable for the present purpose of examining the effects of number of ON components per se. The main virtue of dummy coding in this regard is one of interpretability in relation to a theory suggesting diminishing effects of individual components as more components are ON. The effects of individual components are interpreted, along with other effects in the dummy coding model, as the effect of the component when all other components are OFF, effect that can be understood as first-order effects tests. A dummy coded representation also yields parameter estimates that allow us to specifically evaluate how the effects of individual components tend to change as more ON components are added. We did not use effect coding in the modeling of added component numbers because effect coding main effects are indexed against the means generated across levels of all other factors in the design. Likewise, with effect coding, interaction effects (which occur with multiple components) are interpreted relative to the averaged effects of the other components that are also included in the design. In the presence of negative (sub-additive) interactions, effect coding tends to yield main effect estimates that from the perspective of the theory are diminished because they are estimated in large part under conditions where other components are also ON. However, the analyses we conducted with dummy coding could be similarly conducted using effect-coding, albeit through the construction of non-orthogonal contrasts, to produce equivalent estimates (Kugler et al., 2018) Note, however, that we are not

advocating the use of dummy coding as a standard approach to analyzing data from factorial experiments.

Supplemental Note 6 and Table Correlations of Treatment Contact Data Between Intervention Components

We conducted analyses that addressed the hypothesis that those participants who respond to one intervention component will tend to respond similarly to any of the other components. Conversely, those who do not respond to one type of component will likely not respond positively to any component. Note that this hypothesis is compatible with the treatment redundancy hypothesis. However, the tipping point assumption focuses especially on the notion that there is a strong linkage regarding response to intervention components so as to create a dimension amongst individuals in terms of trans-component response likelihood. In theory, this would allow one to identify populations of responders and nonresponders (i.e., those near and distant from the hypothetical tipping point).

Note, however, that this cannot be evaluated meaningfully with a binary outcome; it therefore cannot meaningfully reflect differential benefit in response to different components on a within-subjects basis (the person would either be abstinent or not). Thus, we chose adherence or treatment contact completion as an index of component response because this variable is strongly related to outcome and can convey likelihood of responding for all components to which an individual is assigned.

The table associated with Supplemental Note 6 shows correlations in attendance/adherence scores (proportion of visits or use episodes completed) for participants who were randomized to the ON conditions of the corresponding pair of intervention components. This analysis showed generally strong associations in attendance or adherence scores across pairs of components.

Thus, adherence is meaningfully linked across most components, which suggests some interchangeability amongst components, consistent with the notion that one component can substitute for another, which we assume is manifested amongst those near the tipping point. Of course, such correlations may reflect person factors, such as conscientiousness, or it may be that treatment failure causes nonadherence.

Table for Supplemental Note 6. Adherence Score Correlations among Intervention Components in the Maintenance Study (N=513)

Intervention Components	**Medication Duration**	**Maintenance Counseling**	**Medication Adherence Counseling**	**Automated Adherence Calls**	**Electronic Medication Monitoring**
Medication Duration (26 versus 8 weeks)	1				
Maintenance Counseling (On versus Off)	r=.604 p<.001 n=128	1			
Medication Adherence Counseling (On versus Off)	r=.523 p<.001 n=138	r=.536 p<.001 n=128	1		
Automated Adherence Calls (On versus Off)	r=.591 p<.001 n=143	r=.334 p<.001 n=128	r=.394 p<.001 n=134	1	
Electronic Medication Monitoring (With versus Without Printouts/Associated Counseling)	r=.756 p<.001 n=132	r=.780 p<.001 n=127	r=.741 p<.001 n=133	r=.392 p<.001 n=136	1

Note: Adherence scores for Medication Duration were computed as follows: 1=attended all medication distribution sessions and 0=attended a reduced number of sessions; for Maintenance Counseling, Medication Adherence Counseling, Automated Adherence Calls, and Electronic Medication Monitoring, adherence scores reflected the proportion (between 0 and 1) of completed treatment contacts.