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Investigating interventions for increasing colorectal cancer screening: Insights from a simulation model

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ABSTRACT

We develop a discrete-event-continuous simulation model of colorectal cancer screening in North Carolina to examine the impact of six different interventions on the fraction of eligible patients receiving the clinically recommended screening. We find that demand side interventions alone are less effective than using only supply side interventions or a combination of both; the single most effective intervention is implementing a patient reminder system to reduce the number of no-show patients; and that all interventions studied are subject to significant diminishing returns.

1. Introduction

Colorectal cancer (CRC), commonly referred to as colon cancer, has a major impact on the US population [1]. Although colon cancer is often fatal, it can be prevented by early detection through screening, and it is estimated that tens of thousands of lives could be saved through proper screening and treatment [17]. Increased use of CRC screening is believed to be a major reason for the decline in the number of colon cancer deaths in the US over the past 15 to 25 years [17]. However, the screening level – the fraction of the eligible population actually receiving screening – remains below desired levels, since it is estimated that only 40% of colon cancers are detected at an early stage [20].

A number of barriers to colon cancer screening have been identified by health services researchers [1,18], including lack of awareness, lack of health insurance, general healthcare costs, inadequate healthcare delivery, fear and other emotional barriers, a low level of education, and lack of communication between healthcare providers and patients. Not only does each of these barriers have its own role in hindering access to colon cancer screening and care, but mutually reinforcing interactions between these barriers can create additional difficulty in accessing colon cancer prevention, detection, and care.

Barriers to colon cancer screening can be broadly classified into two categories. *Supply side* barriers, such as lack of screening capacity and the distance a patient must travel for screening, limit the availability of screening to members of the public who are actively seeking it [24]. *Demand side* barriers, on the other hand, prevent patients who should be screened from seeking screening. Lack of communication between patients and providers, fear, and lack of awareness are examples of demand side barriers.

We develop a combined discrete-event continuous system dynamics model of the CRC screening system in North Carolina that can be used to examine the impact of different interventions on the population screening level. The model combines continuous time representations of fast moving phenomena such as population growth with discrete events representing phenomena occurring at much longer time intervals, such as the installation of new screening facilities.

This type of systems dynamics modeling in healthcare is not novel; there have been a variety of other studies which model system wide performance. Ref. [15] gives a good introductory reference for the use of systems dynamics in healthcare, while ref. [9] discusses a variety of system dynamics models of healthcare delivery systems in Europe. Ref. [2] describes a system dynamics model of a city-wide emergency care system. Some of the chronic diseases modeled in healthcare using systems dynamics are breast cancer screening [13], chlamydia control and prevention [12], and mental health treatment [22]. This paper follows the widely accepted approach of modeling a complex healthcare system via

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systems dynamics, and then experimenting on the model to derive insights into the effects of different policy interventions.

Data for the model comes from state-wide information in North Carolina and numerous federal sources. The system dynamics approach allows us to model many different aspects of the CRC screening system and their interactions while maintaining a flexible framework for inexpensive experimentation.

Our paper addresses the following questions:

1. What interventions will lead to meaningful increases in the final screening level?
2. Which of these interventions are most effective when employed individually? What are the limitations of each intervention when employed alone?
3. What is the nature of the interactions between interventions – which are mutually reinforcing, or mutually inhibiting?

In the next section we present the modeling methodology used to address these questions. We then describe the experiments carried out with the model, and discuss the policy implications of the results.

2. Modeling approach

The methodology in this paper can be summarized as follows:

1. Model the CRC screening system as a system of stocks and flows;
2. Identify factors affecting the screening rate;
3. Identify and model potential interventions to increase the screening level;
4. Verify and validate the model; and
5. Analyze interventions with emphasis on their interactions.

Although the description implies that each stage is investigated serially, there was considerable iteration between stages as new information became available. Details of each step are given below.

2.1. Modeling the CRC screening system using stocks and flows

The continuous or system dynamics portion of our model is best described as a system of interlinked linear differential equations, representing a network of stocks and the flows between them as shown in Fig. 1. The equations are given in detail in Appendices A and B. There are some discrete elements that model events occurring on a significantly longer time scale which we describe in more detail in Section 2.4. While the simulation model is best described as a continuous-discrete hybrid, the continuous elements constitute the dominant components of the model. The primary quantity of interest is the fraction of North Carolina adults aged between 50–75 years who receive the clinically recommended screening for CRC, given by the ratio of the screened population to the total population presented in Fig. 1. Current clinical guidelines [26] recommend that these adults be screened via colonoscopy once every 10 years beginning at age 50, assuming there is no family history or other concerns. Thus the focus of the model is the evolution of the size of this population over time in response to different interventions. This evolution is addressed by considering changes in the population over very short time intervals, which in our case is a day. The different interventions change the values of auxiliary variables that affect the rate at which individuals flow into and out of the screened population through the inflows and outflows represented in Fig. 1. These flows can be summarized as follows:

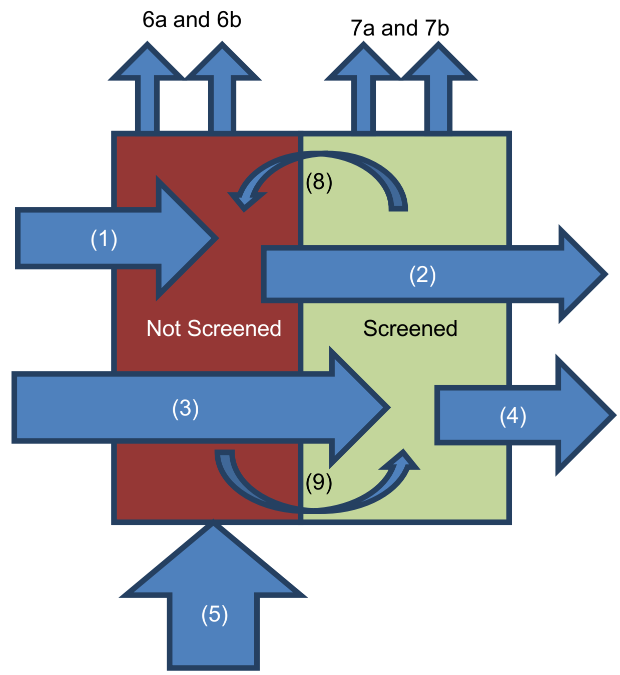

Fig. 1. Tank model of CRC screening levels.

- Flows 1 and 3 represent daily immigration into the screened and unscreened populations from outside the state; we assume that the mix of screened and unscreened individuals in the daily immigration is the same as that in the general state population.
- Flows 2 and 4 represent emigration from each population out of the state; again we assume that the mix of screened and unscreened individuals matches that of the general population.
- Flow 5 denotes the rate at which persons enter the target age group (50–75 years of age) due to aging. We assume these new entrants have not been screened, so they enter the unscreened population.
- Flows 6a and 7a represent the rates at which people leave the target populations because they exceed the upper age limit of 75 years. We again assume that the distribution of screened and unscreened individuals follows that in the general population.
- Flows 6b and 7b represent the rates at which people exit the target age group due to death from any cause. These can be combined with (6a) and (7a) for their respective populations.
- Flow 8 denotes the rate at which the screening an individual has received "expires" due to the passing of more than ten years, causing them to move from the screened to the unscreened population.
- Flow 9 represents the rate at which people get screened, which is the primary focus of the model and is elaborated on in more detail below.

Our model assumes that all populations are homogeneously mixed in status with respect to age, clinical history, and other relevant factors. This assumption may be a cause for concern, but is made for two reasons. First, reliable data at the level of detail needed to model subcategories based on age and past history were not available. Second, modeling subpopulations based on age and history would require significantly more complex modeling structures, complicating both the structure of the model and the analysis of its results, without adding much benefit given the limited data availability.

2.2. Determining the factors affecting the screening rate

A variety of factors that influence a person's decision to get screened for CRC have been identified in the health services literature [3,11,14,27]. In this paper screening *level* refers to the proportion of the target population whose screening is current. The screening *rate* is the number of the target population (adults aged 50–75 years) getting screened each day. These definitions will help clarify the discussion throughout the paper.

The causal loop diagram shown in Fig. 2 was constructed based on literature review and interviews with domain experts, and describes the feedback structure of the CRC screening system. Boxes representing variables are connected by arrows that represent hypothesized causal links and are directed from the cause to the effect [23]. A positive link indicates that when the cause variable increases, the effect variable increases. Similarly, if the cause variable decreases, the effect variable decreases. A negative link indicates that if the cause variable increases, the effect variable decreases, and if the cause variable decreases the effect variable increases. This causal loop representation provides a graphical means of tracing the effects of individual cause variables on each other and on the entire system. A brief description of each link and a justification for its orientation are given in Table 1.

We now give a high-level description of the operation of the screening system using the variables and links in Table 1 and Fig. 2. Patients may seek screening by referral from their primary care physicians during regular primary care physician visits. Thus the *Frequency of Visits to a Physician* (Link 1 in Fig. 2) and the *Quality of Physician–Patient Communication* increase the number of patients seeking screening (*Demand for Screening*), which is also increased by *Public Awareness* that causes some patients to self-refer themselves for screening. The *Number of Screeners* (Link 4) and the *Demand for Screening* (Link 9) jointly determine the *Congestion Level*, which determines the number of patients who will be deterred from actually making appointments and getting screened due to the long wait involved (*No-Show Level*, Link 7). The No-Show level is also affected by the *Average Distance to Screening*, (Link 5) which, in turn, is determined by the *Number of Screening Facilities* (Link 6) under the assumption that screening facilities will tend to be distributed by population over the state. In reality, the effect of new facilities on the congestion level will depend on where those facilities are located relative to the population seeking care. This type of healthcare facility location decision has been addressed extensively as an optimization problem [10,28]. The *Demand for Screening* (Link 10), net of the *No-Show Level* (Link 8), determines the *Screening Level*, the size of the eligible population receiving screening (Link 11). The *Screening Level*, in turn, reduces the *Demand for Screening* (Link 12) since patients who are screened will not need screening for ten years, and increases *Public Awareness* (Link 13), since patients who have been screened are likely to recommend it to others. Detailed functional forms and justifications for the equations are given in Appendix B.

Observing the loops present in the system as seen in Fig. 2 can give some hints about what to expect from system behavior. A loop is defined as any sequence of links which form a closed, directed cycle. Positive loops have either zero or an even number of negative links, while negative loops have an odd number of negative links. Positive links represent reinforcing behavior in the system, where an increase in a variable along the cycle will cause additional increase, leading to exponential growth or decline in the quantity of interest. A negative loop, on the other hand, displays behavior in which an increase in one variable is offset by opposing changes in other variables along the cycle, causing the system to tend towards an equilibrium.

Examination of Fig. 2 yields two positive and two negative loops. The first positive loop, consisting of links 3-10-11-13, represents the reinforcing interaction between Public Awareness and Demand for Screening; increased Public Awareness leads to Increased Demand for Screening, increasing the Screening Level and further increasing Public Awareness. Note that this loop represents relationships between demand-side variables. The second positive loop, consisting of links 9-7-8-11-12, in contrast, also relates to demand variables. Increased Demand for Screening increases the Congestion Level, increasing the No-Show Rate which reduces the Use of Screening. Reduced Use of Screening, in turn, reduces the Screening Level, increasing Demand for Screening. This loop represents the fact that at any point in time there is a fixed population that is eligible for screening, and that a reduction in the Screening Level implies a corresponding increase in the unscreened population, increasing Demand for Screening. This relationship is also represented in the first of the negative cycles, links 10-11-12, which indicate that an increase in Demand for Screening will increase the Use of Screening, increasing the Screening Level and reducing the Demand for Screening. Thus these three loops represent the fact that the system operates in a fixed population at any point in time.

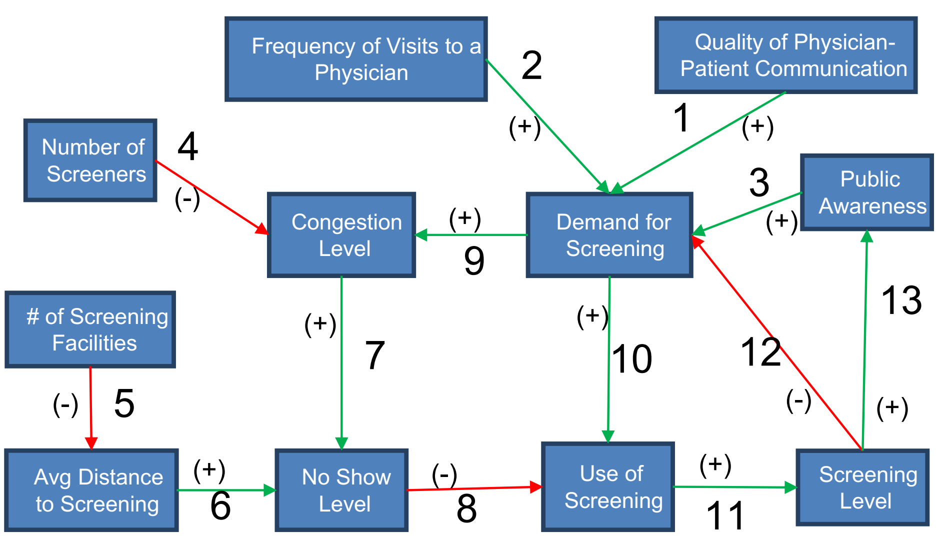

Fig. 2. Causal loop diagram of CRC screening adherence.

Table 1
Causal loop diagram link justifications.

Link No.	Cause variable	Effect variable	Link type	Justification
1	Quality of physician–patient communication	Demand for screening	Positive	More communication of benefits of/reasons for screening increases the desire for/reduces the proportion declining screening
2	Frequency of visits to a physician	Demand for screening	Positive	More interactions with physicians increases likelihood of being referred for screening
3	Public awareness	Demand for screening	Positive	More people knowing of the need for screening causes them to refer themselves for screening and ask about it
4	Number of screeners	Congestion level	Negative	If there is more capacity for screening, there will be less wait to be screened
5	# of screening facilities	Avg. distance to screening	Negative	Facilities will spread out around the state, hence patients can choose to go to closer offices
6	Avg. distance to screening	No-show level	Positive	Longer distances to screening imply greater effort to get screened, hence lower turnout rates for the screening
7	Congestion level	No-show level	Positive	Longer waits for service create lower turnout rates [11]
8	No-show level	Use of screening	Negative	Use = demand × (1 − no show rate)
9	Demand for screening	Congestion level	Positive	More demand results in longer waiting times for service as utilization level of existing resources increases
10	Demand for screening	Use of screening	Positive	Use = demand × (1 − no show rate)
11	Use of screening	Screening level	Positive	By definition
12	Screening level	Demand for screening	Negative	More people being screened means fewer people need to get screened, since screening is only needed once every 10 years.
13	Screening level	Public awareness	Positive	People who are screened are likely to tell others

The second negative loop, links 9-7-8-11-13-3, is of considerable interest. This loop suggests that increasing Demand for Screening will increase the Congestion Level, causing longer waits for screening that will increase the No-Show Level. This will, in turn, reduce the Use of Screening, reducing the Screening Level, Public Awareness and thus Demand for Screening. This loop suggests that any supply-side intervention aimed at reducing either the Congestion Level or the No-Show Level via links 4, 5 or 6 will be offset by an increase in Demand for Screening that will raise both the Congestion Level and the No-Show Level and thus reduce the Screening Level. Similarly, any demand-side intervention aimed at increasing Demand for Screening via links 1, 2 or 3 will result in increased Congestion level and No-Show Level, negating at least some of the benefits of the intervention. These observations suggest that the use of supply-side interventions unaccompanied by demand side intervention, or vice versa, may not yield major improvements in Screening Level, and that for given levels of any intervention the Screening Level will achieve an equilibrium reflecting the balance between the positive and negative links on this cycle.

2.3. Identification and modeling of potential interventions to increase the screening level

We identified the following six potential interventions that can be implemented through policy and process initiatives:

1. Increasing the number of providers who perform screening;
2. Increasing the number of facilities where screening can be performed;
3. Reducing the no show/late cancellation rate via a patient reminder system;
4. Increasing public awareness of the need for CRC screening via a media information campaign;
5. Improving the communication of primary care physicians in explaining the importance of screening to patients; and
6. Directing more screening capacity to rural Health Professional Shortage Areas [8].

These interventions are motivated by the classification of barriers to screening into supply side and demand side barriers. Demand side barriers arise because individuals in the target population are unwilling to seek screening, either because they don't understand the importance and value of screening, or because they are reluctant to be screened for personal reasons such as fear or discomfort. Supply side barriers, such as the limited number of professionals or facilities providing screening, manifest themselves in lengthy waiting times to get screened, and long, expensive trips to obtain screening, which make adherence to screening less likely. Table 2 summarizes how each of the six interventions affects the screening rate through the lens of Fig. 2.

The software used in this study was ARENA by Rockwell Software (www.arenasimulation.com), which provides the capability for simultaneous discrete − continuous simulation. As is the case for most system dynamics software, ARENA archives continuous variables and solves the underlying differential equations by numerically integrating the equations given by the user, while discrete events are processed through an event calendar. This means that the elements in ARENA are processed on very different time scales. Hence every element of the model had to be given a time scale: continuous and (potentially) evaluated many times a day, discrete and frequent evaluated a least once a week, or discrete and infrequent evaluated less than once a month. For example, the public awareness of the need for CRC screening and

Table 2
Explanation of how interventions increase screening.

Intervention	Which side	Location in CL diagram (Fig. 2)
1. Increasing the capacity for screening	Supply side	4–7–8, reduce no-show level
2. Increasing the number of facilities where screening can be performed	Supply side	5–6–8, reduce no-show level
3. Reducing the no show/late cancellation rate via a patient reminder system	Supply side	8, reduces impact
4. Increasing public awareness of the need for CRC screening via a media information campaign	Demand side	3–10, increase demand
5. Improving the communication of primary care physicians in explaining the importance of screening to patients	Demand side	1–10, increase demand
6. Directing more capacity to rural areas to address Health Professional Shortage Areas	Supply side	4–7–8, reduces no-show level

the demand level for colonoscopies are treated as continuous variables, because they are central to the simulation and can change quickly. The NC population, the wait for screening, and the proportion of patients complying with referral for screening are updated discretely and frequently. In contrast, the number of facilities which do screenings and the travel distance to facilities (an associated variable per Fig. 2) evolve discretely and slowly (once or only a few times per year). Details of the equations governing the evolution of the variables over time and their associated time scales are given in Appendix A.

The decisions about how to model each intervention are crucial to the purpose of this study, and so receive some special attention here. The first (more screening capacity) and second (more screening locations) interventions are discrete and infrequent since these changes occur at long intervals, as when a new facility starts to perform colonoscopies regularly. The third intervention (reducing the no-show rate) is simply a one-time change that means more of the potential demand is realized. The fourth intervention (raising public awareness of the need to be screened) could be modeled in a variety of ways. We choose to treat it as a discrete effect occurring on a short time scale, as if there was a sustained media campaign across multiple platforms over time to reach citizens. The fifth intervention (improving PCP-patient communication) was a discrete and infrequent effect, as if there were a series of attempts to raise the education levels of current doctors on how to get their patients to follow through with screening for CRC. The sixth intervention (adding more screening capacity to rural areas) was modeled as a discrete and infrequent effect, since it is directly linked to the first intervention. These interventions' effects on the model are described in Table 3.

2.4. Verification and validation of the model

The model was implemented in ARENA ver. 12.0, with input from and output to Microsoft EXCEL. ARENA was selected for its simplicity and versatility in modeling the variety of phenomena present in the system. Also, a previous model [19] used ARENA, which allowed for simple cross validation. The computations were carried out on a Lenovo T60p laptop.

To ensure that the modeling of this system is useful, the model must be verified and validated. Verification is the process of ensuring that the model behaves in the way it was intended. In this paper, a combination of testing the system with extreme parameter values and examining the system's evolution gave evidence that the model behaved as expected. This was another instance where ARENA's discrete-event capabilities proved valuable, because it was easy to set up discrete shocks that would stress the system. Observing the behavior of the model after these shocks proved very useful in debugging.

Next, validation was performed. To validate the inputs of the model (i.e., parameter values), first account sources were used wherever possible. An extensive list of the sources used is given in Appendix C. To test the importance of each parameter in the system, sensitivity analysis was performed on the screening level over time, which is the primary output of interest. When the screening level was found to be highly sensitive to a parameter, every effort was made to ensure maximum accuracy of that parameter. For example, the frequency of visits to the primary care doctor is very important. The final value for this parameter was based on figures from the CDC, and confirmed by examining the predictions from the model [4,6].

Using data from the CDC's Behavioral Risk Factor Surveillance System, the historical screening level in North Carolina was estimated over time [5]. We then plotted the screening level predicted by the model when initialized with the same data at the beginning of the time period. Fig. 3 shows that the model's predicted screening levels closely match the screening level observed over past history.

There are three data series shown in Fig. 3. The first is the observed screening level in North Carolina [5] over time. The second is the model's prediction of the screening level when it is initialized with rudimentary data. The third data series is the model's prediction of screening level given an intervention which increased the effectiveness of doctor–patient communication from 2000–2008. This intervention required lowering the initial doctor–patient communication level, which caused rapid initial rise in the screening level when the rudimentary data is used. Clearly the projections with the intervention active provide a much better fit. A good deal of tuning went into the creation of this intervention, and the model generally to create an excellent fit. We adopted this approach to tuning the parameters of our model because there was a significant intervention over the 2000–2005 period, increasing public awareness of the importance of CRC screening. This intervention took the form of news and personal interest stories, including Katie Couric of the *Today Show* having a colonoscopy on air [25]. The reason for this intervention being modeled over a long period (9 years) is twofold. First, this resulted in a very close agreement between predicted and observed screening rates. Second, it seems logical that there would be a significant delay between the increased interest in screening and the accumulation of sufficient resources for physicians to meet the resulting demand effectively. Fig. 4 shows the residuals for each series relative the data source and the confidence limits provided by the source [7]. The model with the intervention stays within the confidence limits provided by the data source, giving us reassurance that the model is sufficiently accurate.

Like all system dynamics models, our model may well be sensitive to the estimates of the different parameter values used in the equations, as well as to the form of the equations themselves. However, the large number of parameters and equations precludes a complete sensitivity analysis on each and every parameter. Instead, in the interest of economizing on modeling effort, we have

Table 3
Explanation of how interventions operate in the model to increase screening.

Intervention	Effect in the model	Intervention run time (dates)
More screening capacity	Ten additional procedures per day (in addition to natural increase). This corresponds to approximately one additional person performing screenings.	1/1/2011–12/31/2020
More screening facilities and staff	Makes screening about half as difficult to receive.	1/1/2011–12/31/2020
Patient reminder system (reduce no-shows)	20% of no-show patients actually show up instead. This is a constant effect, which continues until 2030.	1/1/2011–12/31/2030
Raising public awareness	90% of the target population will be reached each year by the intervention (whether they follow through or not is still up to them).	1/1/2011–12/31/2030
Improving PCP communication with patients	Doctor–patient communication improves each year. Five percent of doctor visits which did not result in a referral now do. Cumulative through the years.	1/1/2011–12/31/2020
Increasing proportion of screening capacity in rural areas	Instead of 40% of new capacity going to rural areas, 76% goes to rural areas.	1/1/2011–12/31/2030

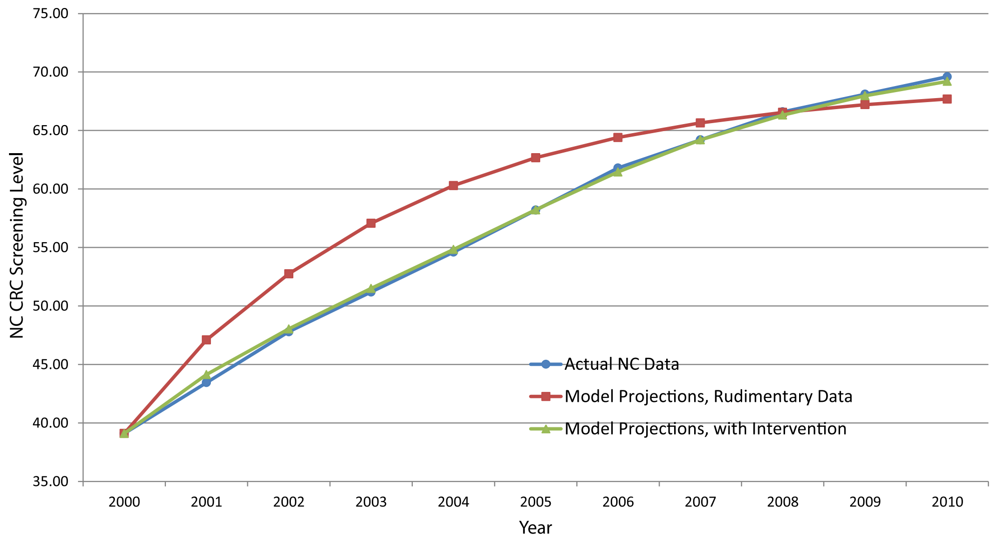

Fig. 3. Comparison of predicted and observed screening levels.

focused on manipulating one important parameter, the increase in public awareness, to obtain the best possible match between the model's predictions and the observed North Carolina data. However, the possible sensitivity of our results to different parameter estimates remains as a limitation of this study.

2.5. Analysis of interventions

After verification and validation we used the model to examine the effects of the different interventions both individually and in combinations. Our analysis of the various interventions is based on a 2^6 experimental design, with each intervention at a high and a low level (the latter generally representing no intervention). This design allowed us to determine whether each intervention was significant (statistically and practically) in raising the screening levels. Since the simulation is deterministic, if all the interaction terms (first order through fifth) were included, we would have a perfect fit (64 terms for 64 design points). To allow for statistical interpretation of the results, we excluded orders of interaction terms sequentially (fifth through first) and checked the resultant fit. This also allowed us to determine what order interactions between the various interventions were significant.

We examined whether there were limits on the maximum improvement that could be obtained by deploying that intervention at a very high level with no regard to cost. This analysis is of interest to policymakers in terms of setting reasonable expectations for the benefits from specific interventions. We also examined how the interactions behaved. Specifically, we considered three

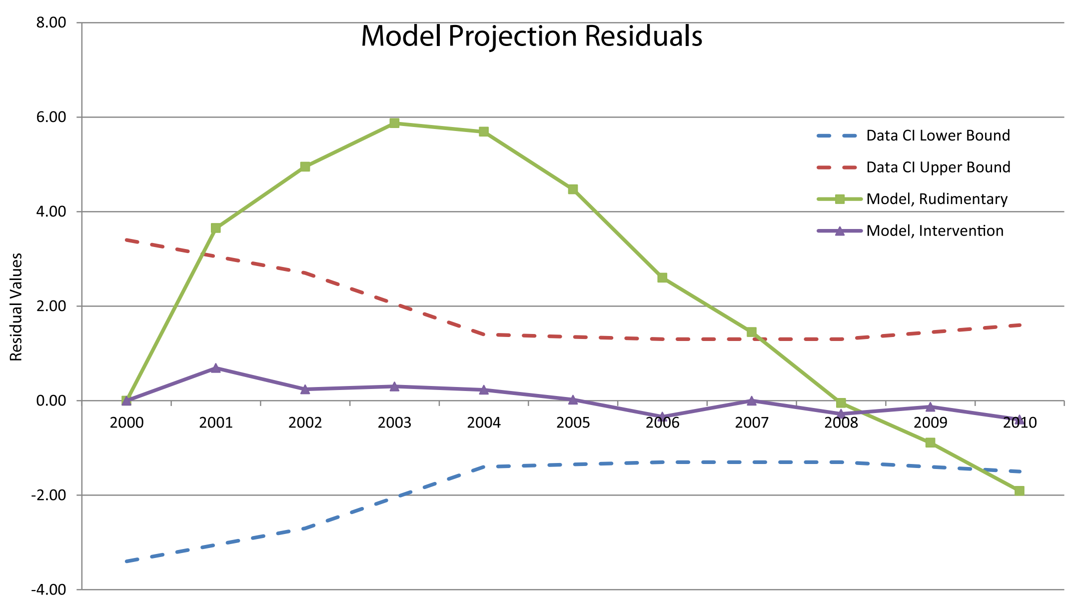

Fig. 4. Model projection residuals.

Table 4
Important intervention and interactions of interventions.

$\|\beta\|\rangle.02$	$\|\beta\|\rangle 1.00$
0, 1, 2, 3, 4, 5, 6, (1,3), (1,4), (1,5), (1,6), (2,3), (2,4), (2,5), (3,4), (3,5), (3,6), (4,5), (4,6), (1,3,4), (2,4,5)	0, 1, 2, 3, 4, 5

different classes of interactions: Supply side/Supply side, Demand side/Demand side, and Supply side/Demand side. To perform this analysis we looked at the relative "efficiencies" of each interaction, i.e., how the individual intervention benefits compare to those realized when combined with other interventions. Simple two-sample *t*-tests were used to complete the analysis.

3. Results

In order to address the questions of interest, a baseline performance level was established from which the effects of the interventions can be measured. All interventions are measured by their effect on the screening level at the end of the 30 year period, relative to the accepted model with intervention as discussed in Section 2.4. The first ten years of the simulation constitutes the second data series in Fig. 3. When that circumstance is simulated to 2030, the screening level reaches 73.74% of the target population. The interventions were implemented relative to this baseline starting in 2011 and maintained over time as stated in Table 3.

The results of the full 2^6 DOE results are available from the authors upon request. In Table 4, we summarize the results. In this table two levels of statistical significance and two levels of practical significance are identified, admittedly arbitrarily, to facilitate the discussion of results. The level of statistical significance of a coefficient is classified as moderately significant ($\alpha < .10$) or strongly significant ($\alpha < .001$). The level of practical significance of coefficients is classified as slight ($|\beta|\rangle 0.02$) and very strong ($|\beta|\rangle 1.00$). These β values represent the magnitude of change in the final screening level caused by an intervention. A change of .02% (slight practical significance threshold) in the screening level in NC would correspond to about 500 people in the target age group being up-to-date on their screening. Based on standard incidence rates [16], this corresponds to early detection of approximately one case of CRC across the state. We find that any term which achieves even slight practical significance will have strong statistical significance. Table 4 shows which terms have practical significance at each level. An entry X (e.g., 1) indicates that the coefficient related to intervention X (as numbered in Table 2) is significant. The (X, Y) entry indicates that the coefficient related to the combination of interventions X and Y is significant. We now use these results to examine the research questions motivating this study.

We found that no 3rd order or higher interactions (>3 interventions being mixed) exceeded our threshold for practical significance. However, four other 2nd order interactions did come close: (1,4,5), (2,3,4), (2,3,5), and (3,4,5) all had absolute beta values between .01 and .02.

> *First Question*: What interventions will yield improvements in the final screening level?

All six interventions examined had the desired result of raising screening levels. However, one of the interventions, the percentage of new capacity going to rural areas, had very small positive effects. This limited effect was because the average discrepancy in availability of capacity between rural and urban areas is not sufficiently large when weighted by the number of patients who are affected. It also is limited because medical procedures like a colonoscopy are sufficiently significant that many of the rural barriers to care do not strongly affect adherence to screening – people are willing to travel for a procedure of this importance.

> *Second Question*: Which of these interventions are most effective when employed individually? What are the limitations on each intervention when employed alone?

In addition to the percentage of new capacity going to rural areas, increasing the number of screening facilities also had limited impact because there are substantially diminished returns on further investment. The simple reality is that for a procedure as important as a colonoscopy that is undergone once every ten years, the difference between a 30 min trip and a 60 min trip is likely to be negligible. Furthermore, the distance to screening only drops approximately in proportion to the inverse of the square root of the number of facilities [21].

In contrast, implementing a patient reminder system reducing the proportion of no-shows is the most effective single intervention. Directing more physicians to rural areas to address Health Professional Shortage Areas is the least effective. Increasing the number of screening facilities is also limited in its effectiveness because there is only limited room for improvement.

We have already noted that both directing more PCPs to rural areas and increasing the number of facilities have limited effectiveness. All interventions have limitations on their effectiveness in the form of diminishing returns on intervention level. To clarify this issue, we found the level of each intervention needed to produce a 1% increase in final screening levels for the four most effective interventions. We then doubled the magnitudes of each intervention. The resulting increases in screening levels did not double, but increased between 37% and 99%. We then increased the magnitude of each intervention to three times the original magnitude, and again observed diminishing returns. This behavior is summarized in Table 5, which shows the percent effectiveness of each intervention when scaled relative to its effectiveness at the original "1x level".

> *Third Question*: What are the interactions between interventions – are they mutually reinforcing, or mutually detrimental?

Table 5
Marginal returns of increased interventions.

Intervention	% Improvement in final screening level over that from 1% increase in intervention level				
	1×	2×	3×	5×	10×
More capacity	100.00%	187.22%	263.14%	386.85%	584.91%
More facilities	100.00%	137.04%	158.03%	182.26%	209.89%
Patient reminder system	100.00%	198.78%	296.12%	485.82%	926.98%
Media to incr. public awareness	100.00%	154.23%	183.52%	218.22%	261.81%
Doctor–patient communication	100.00%	183.47%	253.75%	364.11%	529.11%

Table 6
Summary of major interactions (only 2nd order).

Coefficient absolute value	Positive interaction	Negative interaction
>0.25		More capacity + patient reminder system, Raising public awareness + improving communication
<0.25 and >0.10		More capacity + raising public awareness, More facilities + patient reminder system, Patient reminder system + raising public awareness
<0.10 and >0.04	More screening facilities + patient reminder system	More capacity + improving communication, More facilities + improving communication, Patient reminder system + raising public awareness
<0.04 and >0.02	More capacity + more rural capacity	Patient reminder system + improving communication

This question can be first investigated by examining the signs of the coefficients of the interaction terms in the DOE. Table 6 shows the importance level of various interaction terms and whether the interaction is positive or negative.

From this table we see that the strongest positive interaction is between the increased number of screening facilities and an effective patient reminder system. This is understandable, since if both were achieved, we should observe an additive reduction in no-shows. When either of these interventions is employed individually, the negative effect of the lack of the other intervention (difficulty getting to screening or long waits for service) reduces the effectiveness of the intervention employed. This result is visualized in Fig. 5. The small box at the center of the larger figure on the right is labeled "Int", which stands for interaction. It shows how these two effects work together better than they do separately. With either intervention by itself we do not gain the "Int" portion, we only get the "More Facilities Effect" or the "Patient Reminder Effect." However, when we have both interventions together we get both of their individual effects, as well as the interaction effect, which is positive in this case.

The strongest negative interactions from Table 6 were (1) more capacity + patient reminder system and (2) raising public awareness + improving communication. The fact that these two interactions were strongly negative suggests that adding supply without demand (1) or demand without supply (2) does not improve the screening level as much as might be expected.

However, Table 6 does not paint a fully accurate picture. Since we know that there are diminishing returns on investment in interventions, we would expect there to be diminishing returns on a combination of interventions. To get a better understanding of how interventions work in combination, we examined the performance of several combinations.

We chose seven levels each of public awareness measures and improving communication, to give us 14 demand side interventions. We picked four levels each for a patient reminder system, increased capacity, and increased new screening facilities, for a total of 12 supply side interventions. The interventions are of varying magnitudes ranging from +.415% to +2.527%.

Next, we used our model to evaluate 49 possible pair-wise combinations of demand side interventions (7×7) and 48 possible pair-wise combinations of supply side interventions ($3 \times 4 \times 4$). We then used the model to evaluate all 168 possible pair-wise combinations of a supply side intervention and a demand side intervention (14×12).

To evaluate the interactions between these pair-wise combinations we consider the "efficiency" of the interaction measured by the ratio of the combined effect of both interventions when deployed together to the sum of their individual effects.

We calculated the mean and variance of the efficiencies of each class of interactions (supply/supply, demand/demand, and supply/

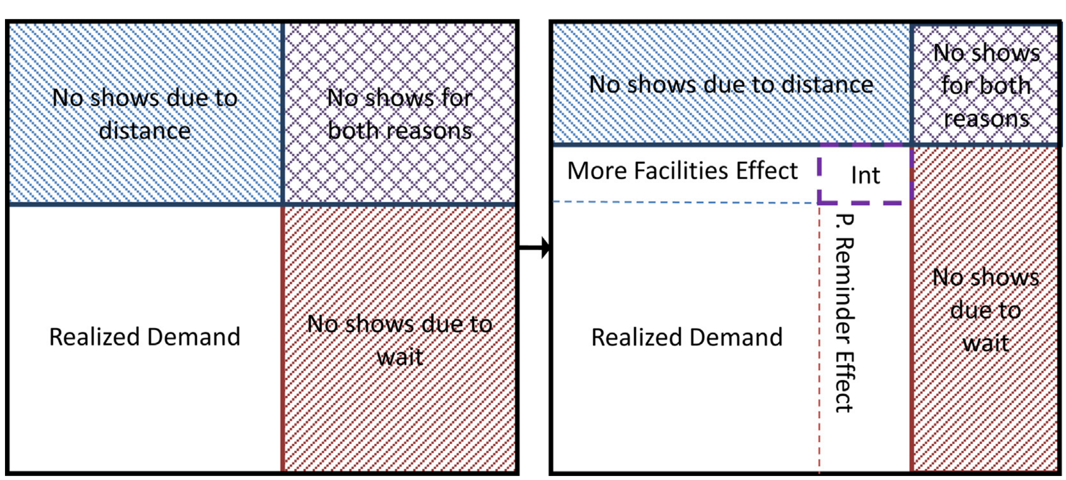

Fig. 5. More facilities + patient reminder system interaction.

Table 7
Summary of efficiencies for different classes of intervention interactions.

	Demand/Demand	Supply/Supply	Supply/Demand
Mean	0.9486	0.9841	0.9810
Variance	0.000374	0.001048	0.000266

Table 8
Comparison of different classes of intervention interactions.

Intervention classes	Difference of means	*t*-statistic	*p*-value
Sup/Sup–Dem/Dem	0.0355	6.543	<0.001
Dem/Sup–Dem/Dem	0.0325	10.69	<0.001
Dem/Sup–Sup/Sup	−0.0031	−0.631	0.531

demand). The variance is computed to give a sense of how much the effect of each class of intervention varied over the set of all such interventions, and not in the usual statistical sense. This information is shown in Table 7.

Finally, we compute independent two sample *t*-statistics (Welch's t-test) comparing the efficiencies of each group. This information is summarized in Table 8.

In summary, we find a statistically significant difference between combinations of only supply side interventions over those addressing only demand. We also find that combining demand and supply interventions is superior to combinations of only demand interventions. However, we do not find a significant difference between combinations using both supply and demand and those using only supply side interventions. These results suggest that if we are to employ multiple interventions, we would do best to use a combination of supply and demand side interventions or focus on supply side interventions.

It is important to keep these results in perspective. The estimated differences in efficiencies are only about 0.03 to 0.04. This means that the difference in real returns from the sum of individual returns is only 95% versus 98%–99%. Since most interventions have effects from .5% to 5% this difference corresponds to between .015% and .2% difference in final screening level. So these effects are worth considering, but do not produce dramatic changes.

4. Discussion

Our six proposed policy interventions – increasing the capacity for CRC screening in the system, increasing the number of screening facilities, reducing the no show/late cancellation rate via a patient reminder system, increasing public awareness of the need for CRC screening via a media information campaign, improving the communication between primary care physicians and patients, and directing more screening capacity to rural areas to address Health Professional Shortage Areas – all raised screening levels. However, directing more physicians to rural areas to address health professional shortage areas was severely limited in effectiveness. We also found that increasing the number of screening facilities is limited in effect because the difficulties in receiving screening are not restrictive. There are diminishing marginal returns on investment in each intervention. These diminishing returns may in some cases even be accompanied by increasing marginal costs, which are not reflected in the analysis of this paper but must be considered in real-world policy.

The interactions between various interventions are of particular interest. We found that when interventions were used in combination, it was beneficial to combine interventions from both the supply and demand sides. If interventions were to be picked from only one side, supply side interventions were most effective. This effect is likely to become more pronounced as more adults age into the target age group (50–75), since we consistently found that the biggest barrier to screening is getting patients to actually adhere to the recommended screening guidelines.

Appendix A. Model variables

Table A.1 contains all the variables used in the simulation model. The model contains fifty-one real-valued variables, of which ten are one-dimensional arrays. It also has seven "levels" that compose the basic state variables. The Arena software uses "levels" and "rates" to describe the simultaneous differential equations. In the definitions, NC is an abbreviation for North Carolina.

Table A.1
Variables in simulation model.

Name	Type	Size	Meaning
Year	Variable		Current year of simulation, used for intervention implementation
Inflow for age array	Variable array	31	Data on inflow rates of people aging into the target population
Outflow for age array	Variable array	31	Data on outflow rates of people aging out of the target population
Outflow for death array	Variable array	31	Data on the outflow of people aging in the target population
Net migration array	Variable array	31	Data on the rate people migrate into NC
Inflow for age	Variable		The number of people who age into the target population each day
Inflow for migration	Variable		The net number of people who migrate into the target population each day
Outflow for age	Variable		The number of people who age out of the population each day
Outflow for death	Variable		The number of people in the target population who die each day
Urban prop screened	Variable		The proportion of the urban population who are screened
Rural prop screened	Variable		The proportion of the rural population who are screened
Prop rural	Variable		The proportion of the total population who live in "rural" NC
Tot prop screened	Variable		The overall proportion of the target age group which is screened
Rural prop complying	Variable		The proportion of rural patient who when offered a screening, accept and follow though
Urban prop complying	Variable		The proportion of urban patients who when offered a screening, accept and follow though
Total pop	Variable		Total size of the target population
Rural NS due to wait	Variable		The proportion of rural patients who refuse a screening or no show due to the length of the wait for said screening

Table A.1 (*continued*)

Name	Type	Size	Meaning
Urban NS due to wait	Variable		The proportion of urban patients who refuse a screening or no show due to the length of the wait for said screening
Rural NS due to distance	Variable		The proportion of rural patients who refuse a screening or no show due to the distance to or cost of said screening
Urban NS due to distance	Variable		The proportion of urban patients who refuse a screening or no show due to the distance to or cost of said screening
Doctor communication	Variable		
Rural capacity	Variable		The daily capacity to screen rural people in the target population (not a fixed number, like might be imagined in a queuing model, but a surrogate for that idea) used in congestion calculations
Urban capacity	Variable		The daily capacity to screen urban people in the target population (not a fixed number like might be imagined in a queuing model, but a surrogate for that idea) used in congestion calculations
Rural congestion	Variable		A measure of how long the average wait for screening is, for rural people
Urban congestion	Variable		A measure of how long the average wait for screening is, for urban people
Number of screening facilities	Variable		The number of facilities offering screening in NC, used to estimate the average distance traveled to get screened
Urban dist to screening	Variable		The average distance to screening for urban people, surrogate for cost and inconvenience
Rural dist to screening	Variable		The average distance to screening for rural people, surrogate for cost and inconvenience
Intervention awareness	Variable array	3	Controls the intervention based on raising public awareness (start year, end year, magnitude)
Intervention capacity	Variable array	3	Controls the intervention based on increasing screening capacity, reducing congestions (start year, end year, magnitude)
Intervention facilities	Variable array	3	Controls the intervention based on increasing the number of screening facilities, reducing distance to screening (start year, end year, magnitude)
Intervention patient reminder	Variable array	3	Controls the intervention based on reducing no shows due to wait (start year, end year, magnitude)
Intervention doctor education	Variable array	3	Controls the intervention based on improving adherence to screening guidelines, so more patients are referred for screening (start year, end year, magnitude)
Intervention HPSA	Variable array	3	Controls the intervention based on directing more screening capacity the HPSA, reducing health outcomes inequality (start year, end year, magnitude)
Prop urban cap increase	Variable		The proportion of the annual capacity increase which goes to urban patients
Prop rural cap increase	Variable		The proportion of the annual capacity increase which goes to rural patients
Doc visits	Variable		The proportion of the target population who have at least 1 interaction with a medical professional which may result in referral for screening (e.g. annual physical)
Rural daily screening rate	Variable		The number of urban people in the target population who undergo screening in a given day
Urban daily screening rate	Variable		The number of urban people in the target population who undergo screening in a given day
Daily rural rescreens	Variable		The number of rural people who renew their screening when it expires (happens at higher chance than normal unscreened people) otherwise they reenter the general rural unscreened pop
Daily urban rescreens	Variable		The number of urban people who renew their screening when it expires (happens at higher chance than normal unscreened people) otherwise they reenter the general urban unscreened pop
Daily rural doc referrals	Variable		The number of rural people referred for screening by doctors (primary care physicians)
Daily urban doc referrals	Variable		The number of urban people referred for screening by doctors (primary care physicians)
Daily rural self referrals	Variable		The number of rural people referred for screening by themselves due either to word of mouth or a general awareness intervention (media)
Daily urban self referrals	Variable		The number of urban people referred for screening by themselves due either to word of mouth or a general awareness intervention (media)
SM expo	Variable		This is for the “peer pressure” effect in word of mouth screening, an abbreviation for screening momentum exponent
Tot cap increase	Variable		The total increase in capacity, sum of natural economic growth and capacity intervention
Tot prop screened 100	Variable		This shows the final screening proportion as a percentage
Daily self referrals due to word of mouth	Variable		This is the number of referrals for screening due to unscreened people interacting with screened people
Daily self referrals due to intervention	Variable		This the number of people who refer themselves for screening due to some kind of media intervention or directed information campaign
Rural unscreened	Level		Number of unscreened rural people in the target population
Rural screened	Level		Number of screened rural people in the target population
Urban unscreened	Level		Number of unscreened urban people in the target population
Urban screened	Level		Number of screened urban people in the target population
Fast screening momentum	Level		This is a measure of the number of people who might interact with others and communicate getting screened recently
Medium screening momentum	Level		This is a measure of the number of people who might volunteer this CRC screening experience/information when discussed by others
Slow screening momentum	Level		This is a measure of the number of people who might answer questions about CRC screening but not be quick to volunteer information

Appendix B. Model equations

Forty-four equations describe the model, thirty-five of which are evaluated daily, while the remainder are evaluated annually. Twenty-two equations are “state” equations while thirteen are “rate” equations that may daily change the state of the simulation. The remaining equations are annual values. The Arena software employs these as simultaneous simple, first-order questions, which are solved (in this case) by Euler approximations. Some are treated as discrete events.

The set of equations are described in three interrelated figures/tables. The equations are presented in mathematical form, so they can be translated into whatever software is used to perform the systems dynamics simulation (the Arena model is available upon request).

Table B.1 lists the equations, and includes an equation identification number, the equation left-hand side (LHS), the frequency of update, and the equation right-hand side (RHS). Variables are defined previously in Appendix A: Table A.1.

Table B.1
Model equations.

Eqn ID number	LHS	Frequency	RHS
D1	Doctor communication	Daily	Doctor communication + .0001*(Year ≤ 3)*(Year ≥ 1) + .00005*(Year ≤ 6)*(Year ≥ 4) + .00003*(Year ≤ 9)*(Year ≥ 7)
D2.1	Rural NS due to distance	Daily	.05 + .35*(1 − Exp(−3*Rural dist to screening/100))
D2.2	Urban NS due to distance	Daily	.05 + .35*(1 − Exp(−3*Urban dist to screening/100))
D3.1	Rural congestion	Daily	20*(Rural daily screening rate/rural capacity)**2
D3.2	Urban congestion	Daily	20*(Urban daily screening rate/urban capacity)**2
D4.1	Rural NS due to wait	Daily	.05 + .45*(1 − exp(−rural congestion/25))
D4.2	Urban NS due to wait	Daily	.05 + .45*(1 − exp(−urban congestion/25))
D5.1	Rural NS due to wait	Daily	Rural NS due to wait*(1 − (Year ≤ intervention patient reminder(1,1))*(Year ≤ intervention patient reminder(2,1))*intervention patient reminder(3,1))
D5.2	Urban NS due to wait	Daily	Urban NS due to wait*(1 − (Year ≥ intervention patient reminder(1,1))*(Year ≤ intervention patient reminder(2,1))*intervention patient reminder(3,1))
D6.1	Rural prop complying	Daily	(1 − Rural NS due to wait)*(1 − Rural NS due to distance)
D6.2	Urban prop complying	Daily	(1 − Urban NS due to wait)*(1 − Urban NS due to distance)
D7.1	Daily rural rescreens	Daily	(.1/365)*((1 + Doc visits)/2)*Rural screened
D7.2	Daily urban rescreens	Daily	(.1/365)*((1 + Doc visits)/2)*Urban screened
D8.1	Daily rural doc referrals	Daily	(Doc visits/365)*(doctor communication)*rural unscreened
D8.2	Daily urban doc referrals	Daily	(Doc visits/365)*(doctor communication)*urban unscreened
D9	Daily self referrals due to word of mouth	Daily	(Fast Screening momentum/2.5 + medium screening momentum/122 + slow screening momentum/365)
D10	Daily self referrals due to intervention	Daily	(Year ≥ intervention awareness(1,1))*(Year ≤ intervention awareness(2,1))*intervention awareness(3,1)*((doctor communication + 1)/2)*total pop
D11.1	Daily rural self referrals	Daily	Prop rural*(1 − rural prop screened)*(daily self referrals due to word of mouth + daily self referrals due to intervention)
D11.2	Daily urban self referrals	Daily	(1 − prop rural)*(1 − urban prop screened)*(daily self referrals due to word of mouth + daily self referrals due to intervention)
D12.1	Daily rural self referrals	Daily	(Daily rural self referrals)*(((1 − rural prop screened)*(rural prop screened))**SM expo)
D12.2	Daily urban self referrals	Daily	(Daily urban self referrals)*(((1 − urban prop screened)*(urban prop screened))**SM expo)
R1.1	Rural unscreened rate	Daily	(Prop rural)*(inflow for age − (1 − rural prop screened)*(outflow for age + outflow for death)) + (1/3)*(1 − rural prop screened)*inflow for migration
R1.2	Rural screened rate	Daily	(Prop rural)*(−(rural prop screened)*(outflow for age + outflow for death)) + (1/3)*(rural prop screened)*inflow for migration
R1.3	Urban unscreened rate	Daily	(1 − prop rural)*(inflow for age − (1 − urban prop screened)*(outflow for age + outflow for death)) + (2/3)*(1 − urban prop screened)*inflow for migration
R1.4	Urban screened rate	Daily	(1 − prop rural)*(− (urban prop screened)*(outflow for age + outflow for death)) + (2/3)*(urban prop screened)*inflow for migration
R2.1	Rural unscreened rate	Daily	Rural unscreened rate − (daily rural rescreens + daily rural doc referrals + daily rural self referrals)*(rural prop complying) + (.1/365)*rural screened
R2.2	Rural screened rate	Daily	Rural screened rate + (daily rural rescreens + daily rural doc referrals + daily rural self referrals)*(rural prop complying) − (.1/365)*rural screened
R2.3	Urban unscreened rate	Daily	Urban unscreened rate − (daily urban rescreens + daily urban doc referrals + daily urban self referrals)*(urban prop complying) + (.1/365)*urban screened
R2.4	Urban screened rate	Daily	Urban screened rate + (daily urban rescreens + daily urban doc referrals + daily urban self referrals)*(urban prop complying) − (.1/365)*urban screened
R3.1	Rural daily screening rate	Daily	(Daily rural rescreens + daily rural doc referrals + daily rural self referrals)*(rural prop complying)
R3.2	Urban daily screening rate	Daily	(Daily urban rescreens + daily urban doc referrals + daily urban self referrals)*(urban prop complying)
R4.1	F screening momentum rate	Daily	(Rural daily screening rate + urban daily screening rate) − (.2)*fast screening momentum
R4.2	S screening momentum rate	Daily	(Rural daily screening rate + urban daily screening rate) − (.000274)*slow screening momentum
R4.3	M screening momentum rate	Daily	(Rural daily screening rate + urban daily screening rate) − (.00274)*medium screening momentum
A1.1	Tot cap increase	Annual	(Urban capacity + rural capacity)*.01 + (year ≥ intervention capacity(1,1))*(year ≤ intervention capacity(2,1))*intervention capacity(3,1)
A1.2.1	Prop rural cap increase	Annual	.4 + .6*(year ≥ intervention HPSA(1,1))*(year ≤ intervention HPSA(2,1))*intervention HPSA(3,1)
A1.2.2	Prop urban cap increase	Annual	.6*(1 − (year ≥ intervention HPSA(1,1))*(year ≤ intervention HPSA(2,1))*intervention HPSA(3,1))
A1.3.1	Rural capacity	Annual	Rural capacity + tot cap increase*prop rural cap increase
A1.3.2	Urban capacity	Annual	Urban capacity + tot cap increase*prop urban cap increase
A2.1	Number of screening facilities	Annual	Number of screening facilities + (1/3) + (year ≥ intervention facilities(1,1))*(year ≤ intervention facilities(2,1))*intervention facilities(3,1)
A2.2.1	Rural dist to screening	Annual	120/Sqrt(Number of screening facilities)
A2.2.2	Urban dist to screening	Annual	30/Sqrt(Number of screening facilities)
A3	Doctor communication	Annual	1 − ((1 − Doctor communication)*(1 − (year ≥ intervention doctor education(1,1))*(year ≤ intervention doctor education(2,1))*intervention doctor education(3,1)))

The relationship among the equations can be displayed in an equation tree, given in Fig. B.1. This equation tree inter-relates the state variables, the rates, and the interventions. The numbers in the symbols refer to the equation numbers in Table B.1. The rectangular symbol represents an equation (or set of equations), while the rounded corner rectangle refers to the interventions described in the paper. The circle refers to basic data and includes the inflow/outflow for age, inflow/outflow for migration, rural/urban population proportion, the rural/urban/total proportion of screening population, and the rural/urban daily screening rate. Wildcard extensions (* and **) imply that there are multiple equations being represented.

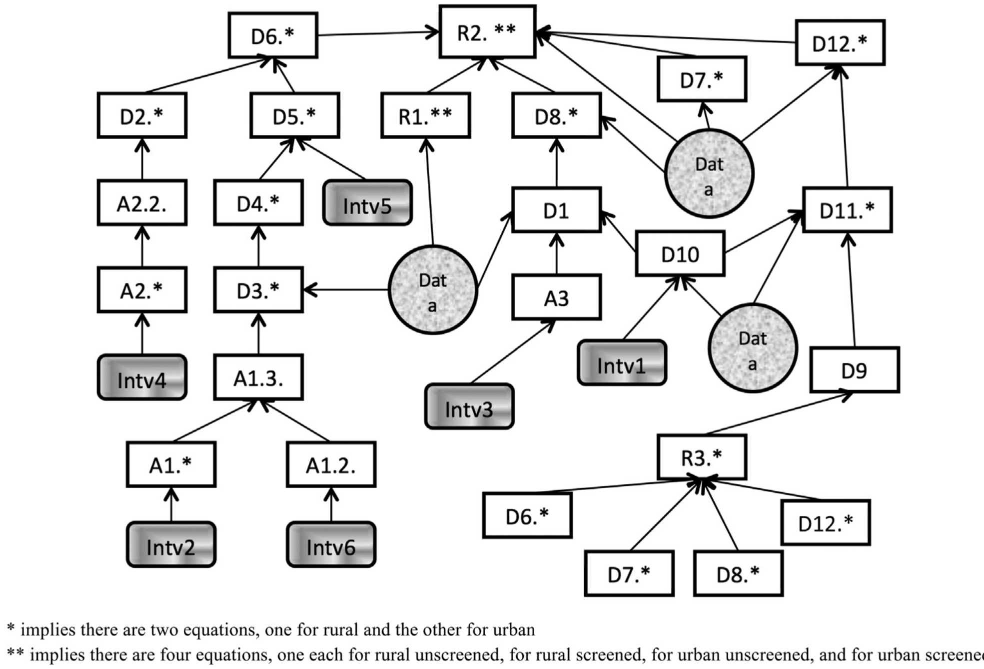

Fig. B.1. Equation tree.

In Table B.2 a brief justification is given for each equation. More details on the development of the equations are found in Murray [19]. A blank line means the equation is self-explanatory.

Table B.2
Justification of equations.

Eqn ID number	Justification (blank means equation is self-explanatory)
D1	There was a significant increase in the effectiveness of doctor visits over the time period from 2000–2008
D2.1	This accounts for both the distance to screening, and is a general surrogate for costs/difficulties in following through with screening
D2.2	
D3.1	This is an estimate of how capacity, demand, and congestion relate. We do not use a queuing formula because capacity will adapt to demand
D3.2	
D4.1	People who have long waits for screening tend to not to actually get screened (forget to go, make conflicting plans, balk at length, etc.)
D4.2	
D5.1	This is for if we utilize an intervention to reduce the effect of long wait on no shows
D5.2	
D6.1	This a shorthand for what proportion of "referred" patient go through with screening
D6.2	
D7.1	Of those for whom screening is expiring, a high proportion simply go through another screening
D7.2	
D8.1	This is the flow of people who have never been screened or are lapsed on their screening getting referred for screening
D8.2	
D9	This calculates what we call screening momentum. It is a measure of word of mouth spread of screening. It can also be furthered by interventions increasing the chances people will go for screening without need of referral from their doctor
D10	This is the flow of people self referring for screening because of a media intervention or a directed information campaign
D11.1	This breaks the self referral group up by rural/urban
D11.2	
D12.1	The first two terms of this equation should be self explanatory, only people who are currently not screened, may be referred this way. The second part of the expression accounts for what we are calling "peer pressure". This peer pressure (PP) accounts for the idea that word of mouth spread is mainly effective when many people know about being screened, but also only works with a small proportion of the unscreened population. If you plot $(x \times (1 - x))^2$ from 0 to 1, you get a bell curve representing the likelihood that peer referral will be effective as a function of the current proportion screened. If few people are screened, PP is unlikely to work since it is not a common enough. If many are screened, the people who are not currently screened are unlikely to be influenced by PP, because there are a few who choose not to change. But if the right number is screened, around half, then this can be a powerful force.
D12.2	
R1.1	This accounts for the "natural" population flows: age in, age out, immigration, and death
R1.2	
R1.3	
R1.4	
R2.1	This moves the people from unscreened to screened and vice-versa
R2.2	This moves the people from unscreened to screened and vice-versa

(*continued on next page*)

Table B.2 (*continued*)

Eqn ID number	Justification (blank means equation is self-explanatory)
R2.3	This moves the people from unscreened to screened and vice-versa
R2.4	This moves the people from unscreened to screened and vice-versa
R3.1	This is needed for the screening momentum calculation
R3.2	This is needed for the screening momentum calculation
R4.1	This is the rate at which screening momentum grows from each day's new group of people being screened. It also decays exponentially, if people are not getting screened
R4.2	
R4.3	
A1.1	The .01 is the average annual economic growth in screening capacity, be it technological improvement or simply more qualified individuals
A1.2.1	
A1.2.2	This divides the capacity increase for rural/urban. It allows for the intervention which sends more capacity to HPSA areas, helping reduce the health outcome inequality between the rural and urban populations
A1.3.1	
A1.3.2	
A2.1	Here is our natural screening facility growth, as well as our intervention to increase screening availability. Don't be concerned by the no integer number of screening facilities, this is a surrogate for availability and ease of screening. Hence an increase of 1/3 might mean a new endoscopy suite, and so lower prices somewhere, or better procedures such that more patients follow through with the preoperative prep
A2.2.1	
A2.2.2	
A3	This is to implement the intervention improving doctor communication with patients. It can take many forms including, but not limited to: better adherence to screening guidelines, better methods of explaining the benefits of screening, better ways to reduce fear of the procedure

Appendix C. References for model construction

In no particular order, the sources used to estimate the parameters and equations in our model are listed below.

- Kaiser State Health Facts; www.stathealthfacts.org
  - Number of Physicians
  - Health Professional Shortage Areas
- Centers for Disease Control; http://www.cdc.gov/
  - CRC screening levels
- Social Security Administration; www.socialsecurity.gov
  - Actuarial Life Tables
- US Census; www.census.gov
  - NC population, by age
- NC Office of State Budget and Management; http://www.osbm.state.nc.us/index.shtm
  - State population projections
  - NC population by age
  - Rural/Urban population breakdowns
- NC Speed; http://www.ncspeed.org/resources
  - Colorectal Cancer Screening Toolkit
- Enhancing the Use and Quality of Colorectal Cancer Screening; Evidence Reports/Technology Assessments, No. 190
  - http://www.ahrq.gov/downloads/pub/evidence/pdf/crcuse/crcuse.pdf
  - Factors influencing CRC Screening quality and quantity
- National Cancer Institute; http://www.cancer.gov/
  - CRC Screening guidelines
  - Cancer statistics
- American Cancer Society; http://www.cancer.org/
  - CRC Statistics, fact and figures
- South Florida Radiation Oncology; http://www.sfrollc.com/
  - Effect of patient reminder system
- National Center for Biotechnology Information; www.ncbi.nlm.nih.gov
  - Predictors of Non-adherence to Screening Colonoscopy

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