

CREATING COMMON PATIENTS AND EVALUATING INDIVIDUAL RESULTS: ISSUES IN INDIVIDUAL SIMULATION FOR HEALTH POLICY ANALYSIS

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ABSTRACT

The research direction in modeling complex, chronic conditions for health policy evaluation has been to incorporate individual heterogeneity. This detail makes our models more powerful and relevant. In implementing an individual simulation model of colorectal cancer we have recognized two considerations related to incorporating individual heterogeneity that have not been adequately discussed in the literature. First, there are substantial computational gains and interpretation benefits if an individual's life courses are identical except when differences are directly induced by an intervention. Achieving this is not trivial. We have developed the notion of a "common patient" who is the same between scenarios except for intervention-induced changes. We create the common patient using a careful application of Common Random Numbers (CRN). Second, when we model differentiated individuals we can examine differing impacts of policies on specific sub-groups. This leverages the detail in individual attributes to produce useful results for policy makers.

1 INTRODUCTION

1.1 Simulation for Health Policy Analysis

Over the last several decades, the simulation community has developed techniques and modeling frameworks that have enabled simulation models to contribute to health policy decision-making by creating accurate representations of disease progression and individuals' response to treatment regimes. With these detailed models, policy makers are able to make comparisons regarding the cost-effectiveness of various policies proposed for implementation and to understand the impact of uncertainty on the robustness of the benefits of various policy options.

To accept a model as valid for the purpose of evaluating policies on the population being analyzed, policy makers have demanded a high degree of fidelity, ensuring the modeled population matches the evaluated population and ensuring that the dynamics of disease are captured accurately by the model. For

chronic disease modeling, discrete event natural history models of disease have become the gold standard by which to evaluate policies. These models, often called individual (or micro-) simulation models, incorporate heterogeneity of individuals through differing disease progression.

Utilizing fixed populations of individuals for evaluating health policies has an intuitive appeal, since comparability between individuals in different interventions is assured; an individual in a population dataset will have the same life course over all intervention scenarios except when changes are directly caused by that intervention's impacts. Since individuals in this line of research represent patients in health care settings, we call the person represented by this data a "common patient". The common patient is created using careful synchronization of events in an individual's life course through the implementation of Common Random Numbers on significant event streams. While this concept may appear simple, implementation in complex individual simulation models requires careful design decisions. Using common patients for analyzing interventions is a variance reduction technique that significantly reduces the computational requirements necessary to determine the dominance of interventions under uncertainty. When individual's life courses are comparable, we do not need to "simulate out", via more replications, the stochastic differences in individual life courses when analyzing interventions. The need for such variance reduction techniques becomes particularly apparent when the interventions analyzed have only small effects on individuals. In our model of colorectal cancer, we analyze public health campaign interventions that "nudge" individuals to comply with screening. We demonstrate how using common patients serves as a variance reduction technique.

The fixed population datasets that define our population incorporate a multitude of attributes. Since the simulated individuals defined by this data set are comparable between interventions, we propose that calculating cost-effectiveness at an individual level and calculating individual cost-effectiveness ratios for specific subgroups are beneficial ways of analyzing the distribution of the benefit of an intervention across a population. With this information it is also possible to make qualitative statements about the equity of particular interventions.

2 LITERATURE REVIEW

The concept of Common Random Numbers (see Law (2014)) is a well-known and accepted variance reduction technique that has long been applied in various simulation applications. Leveraging the variance reduction and interpretability of CRN in individual simulation has only recently been recognized as an important methodology in health policy simulations. Shechter et al. (2006) demonstrated that efficiency gains could be achieved by using CRN in a Monte-Carlo simulation of individuals. In their cohort-based, Monte Carlo simulation, they showed that using common random numbers in an individual's event generators produced smaller confidence intervals for any fixed-size cohort. The authors' results also demonstrate that the confidence intervals produced by fairly small cohorts simulated using common random numbers were essentially the same as those produced by cohorts whose size was orders of magnitude larger (large size being an alternative variance reduction technique); thus substantial computational savings may be achieved by using CRN. Murphy et al. (2013) contributed to the literature relating to CRN in Monte Carlo simulation by investigating the effect of degrees of integration of Common Random Numbers within a simulation model. In their study, fully integrating CRN led to a 93.7% reduction in variance, while partial CRN provided a 5.6% reduction in variance. Additionally, using CRN with Probabilistic Sensitivity Analysis (PSA), the authors demonstrate that these CRN techniques produce substantially tighter dispersions of results from the PSA compared to no CRN, and this results in better identification of the true effects of risk and uncertainty in the model.

The literature presented so far demonstrates the effectiveness of using CRN in Monte Carlo simulation only. These papers, with their focus on Monte Carlo simulation, have not dealt with the details of implementing CRN in more complex discrete event models. Despite the history of CRN as a variance reduction technique (VRT) in discrete event simulation and this support for its effectiveness, CRN is rarely discussed or known to be applied in individual discrete event models of disease progression. A few of the

major discrete event models of disease have noted the use of separate random number streams for different life course events (see Roberts et al. (2007) and Goldhaber-Fiebert et al. (2007)). The main work that attempts to provide guidance on how to implement CRN in a discrete event individual simulation model is by Stout and Goldie (2008). Stout and Goldie provide a good overview of important issues faced when implementing CRN in a discrete event model. Particularly, they highlight the need to have multiple random number streams driving the different event streams in a discrete event individual simulation model. Additionally, they recognize the benefits of interpretability of individual level results when CRNs are applied to a detailed model of an individual.

Our work builds directly on Stout and Goldie. Our particular application of disease modeling, however, which models how individual choice affects colorectal cancer progression and hence outcomes, has raised issues beyond those addressed in Stout and Goldie. These new issues require additional approaches to fully implement CRN within a simulation model. Additionally, we extend Stout and Goldie by demonstrating the utility of individual comparability generated by applying CRN in our simulation model.

Having comparable individuals in our simulation model generated by CRN is most useful in that it allows us to make comparisons across groups in our simulated cohort. Subgroup analysis is particularly common in the analysis of medical clinical trials and observational studies. Particularly, there has been a line of work that has highlighted looking at individual cost-effectiveness between subgroups of individuals as the best approach for identifying policy impacts. Ioannidis and Garber (2011) present the notion of an individual cost-effectiveness ratio. They utilize this ratio to highlight differences in impacts to different groups across the population. Differences in impacts should inform our decision making. Pauly (2014) highlights the difficulty in determining the cost effectiveness of an intervention when the benefit is heterogeneous across the population. We intend to show that individual cost-effectiveness is a qualitative tool for making decisions on the cost-effectiveness of interventions even when those effects are heterogeneous.

3 NATURAL HISTORY MODEL OF COLORECTAL CANCER WITH INDIVIDUAL CHOICE

3.1 Description of Model

We have developed an individual-level simulation model of Colorectal Cancer (CRC) which we use to evaluate interventions that affect users' decisions to screen for colorectal cancer. Their choices can be affected either through their mode choice (between invasive colonoscopy and less invasive Fecal Occult Blood Test (FOBT)) or through their probability of compliance with their chosen mode. The core disease progression model is based on a discrete event, natural history model of colon cancer progression that represents the polyp/adenoma process of colon cancer development. Our discrete event representation is based on the MISCAN-Colon implementation of the polyp-adenoma process (Loeve et al. 1999). In this representation; `Lesion` objects are generated based on incidence rates within the population. The lesions either start out as polyps or precancerous objects, then depending on the rate of progression and testing choices, they progress to later stages (or can be removed) as time goes on.

The user choice component of our model is represented by a logistic regression model estimated using claims data from individuals in a state-supported health plan. This includes full information on Medicare, Medicaid and Dually insured populations, as well as individuals covered by the private insurer Blue Cross and Blue Shield of NC (Cornejo, Mayorga, and Hassmiller Lich 2014).

3.2 Population Evaluated

The population analyzed by this model is a representative synthetic population of individuals in the State of North Carolina in the year 2007. This population is based on data from the non-public, micro-level files of the US Census American Community Survey ("American Community Survey" 2012) completed in 2007. Using appropriate sample weights, a full size population is generated from these non-public samples

(Wheaton et al. 2014). This “smart shuffling” process enables public access and use of the resulting population size files. The census data contains demographic information, including gender, race, income and geographic locational information. Information about insurance status is added by using a logistic regression model (Brown 2012).

3.3 Interventions to be Evaluated

Using our models of choice and colorectal cancer progression, we intend to evaluate two interventions that affect individual compliance or modality choices. We wish to understand how each of these interventions affects the number of patients up-to-date with screening over time and how these increased screening rates affect individual downstream outcomes like life years lost to cancer (lifelost) and the number of cancer deaths. The two interventions that we evaluate are: A program of mailed reminders to Medicaid and Dually-insured patients and a mass media campaign targeted to African Americans. Each of these interventions will be compared to a baseline scenario of “compliance as usual” in which individual compliance with screening is determined by the baseline statistical models estimated from the data. These interventions change outcomes by changing the probability of compliance with assigned modality. Detailed information about the structure of the interventions can be found in Lich et al.(2014).

4 CREATING A “COMMON PATIENT” USING COMMON RANDOM NUMBERS

In order to make meaningful comparisons of policies, we want to ensure that the individuals we are simulating have the same life course between interventions, except as altered by the intervention policy. We call the individuals who have identical life course between interventions, except for events induced by interventions, “common patients”. By creating a common patient, we are separating the stochastic noise created by the dynamic, stochastic events in an individual’s life course from the uncertainty in the effects of applying the intervention to a particular individual. Eliminating stochastic noise in life courses between interventions reduces the computational effort required to evaluate intervention policies that affect individuals and it also enables the individual analysis presented in the next section. Individual analysis, as previously stated, allows meaningful comparison of individual’s outcomes between intervention policies.

Creating the common patient requires synchronization of simulation events between interventions. Synchronization implies that between interventions in a given replication (replications are differentiated by different random number seeds) individuals will have the same set of events such as cancer onset, screening choices, screening results and death age except as those events are directly affected by the intervention. The well-known variance reduction technique of Common Random Numbers (CRN) is the fundamental way of synchronizing simulation events; it uses identical streams of pseudo-random numbers between interventions (same initial seed in our pseudo-random number generator) to generate the same stream of random variates (draws from a statistical distribution) that then determine simulation events. However, our application of CRN to our colorectal cancer simulation shows that the complexities of discrete event simulation models require more than just a synchronization of the model’s overall random number streams. Many discrete event models of individuals, ours included, are composite models of several discrete event or stochastic systems. For example, in our model of colon cancer, the Disease Progression process consists of two separate event generators, Cancer Creation and Cancer Progression, that must be synchronized. Each of these composite stochastic systems, must be synchronized in order for the individual’s life courses to be comparable. Additionally, some of these event generators interact during the dynamic progression of time in the model. Changes in one process can generate a change in another process, and this can change the path of sampling from its random number stream.

To address the issues discussed above, we have developed a multi-pronged approach to synchronize events in order to create a common patient. First, we classify the events streams that generate events in an individual’s life course and put these event streams on separate streams of Common Random Numbers (CRN). Secondly, we do as much pre-calculation of events in an individual’s life course as possible. This is accomplished either outside the model in a pre-processing step and/or at the beginning of the model run

for other events. In the remaining subsections, we provide insight regarding the necessity of synchronizing event streams and address practical considerations in the synchronization of events. Finally, we more fully discuss the advantages of common patients in dealing with uncertainty and in the comparing of results.

4.1 Visualizing the Issues in Synchronizing Event Streams

We have highlighted the issues related to synchronizing life courses to create common patients. We emphasized that it is the multiple event streams in a discrete event model that cause difficulties. In this section, we provide a visual comparison of different levels of event synchronization with CRN using our CRC model under two different scenarios: 1) no CRN, and 2) CRN for each event stream (the common patient). Referencing our model of colorectal cancer described in Section 2, there are several event streams modeled as objects in our Object Oriented simulation framework. The `Person` objects encapsulate the health states of individuals. Individual health states are primarily determined by the existence of `Lesion` objects which represent cancers. `Lesion` objects only exist when a person has cancer and are generated when a polyp/cancer develops. These polyps are generated and assigned to patients by a `LesionGenerator` object that exists over a person's life course and generates Lesions based on incidence rate tables. Thus `LesionGenerators` exist throughout the whole life course, but lesions only exist when they are created. For this model, lesions can also be removed if the cancer is cured. Each of these objects `Person`, `LesionGenerator` and `Lesion` encapsulate dynamic events that need to be synchronized, thus they will each need an independent random number stream. Figure 1 illustrates the impacts of event synchronization by comparing the No CRN scenario with the Common Patient implementation. This highlights the differences in events in a single individual's life course between interventions. Most notable, it is seen that when no CRN (Figure 1, top two panels) was used we can neither guarantee identical cancer progression nor can we equate estimated lifetimes. This stands in contrast to the common patients model (Figure 1, bottom two panels) where cancer progression and estimated lifetimes are the same except when the patient is influenced by the interventions to pursue more screenings, thus effecting a change in the progression of the disease process.

4.2 Methods for Creating Common Patients

Having established the need for synchronizing event streams within the simulation model, we present several techniques that can be applied alone or in combination to synchronize the events of the simulation model to create a common patient. All of these techniques are fundamentally based on using common streams of random numbers for events. The three techniques that we have found useful include: 1) running each event generator on its own random number stream, 2) determining as many events as possible at the beginning of the model run, and 3) pre-computing states/events outside of the model.

4.2.1 Separate Random Number Streams

We have found that there is substantial difficulty synchronizing the events of a simulation model, and hence in creating a common patient, when Common Random Numbers are only used at the model level. Model level random numbers means that the streams between two scenarios (interventions) share the same random number seed, but all random number calls in each of the scenarios use the same random stream. The problem with this design is that if an intervention adds random number calls or causes changes to one or more of the event processes, all future events will be out of sync between the scenarios from that point in time on. For example, in our model, an intervention adds some random number calls to check whether an individual is eligible to receive the intervention which may or may not induce any real change in behavior and hence disease progression. The fact that we have added some random numbers draws causes all future disease progression and decision events for a given patient to be out of sync because we are sampling at different locations in the random number stream.

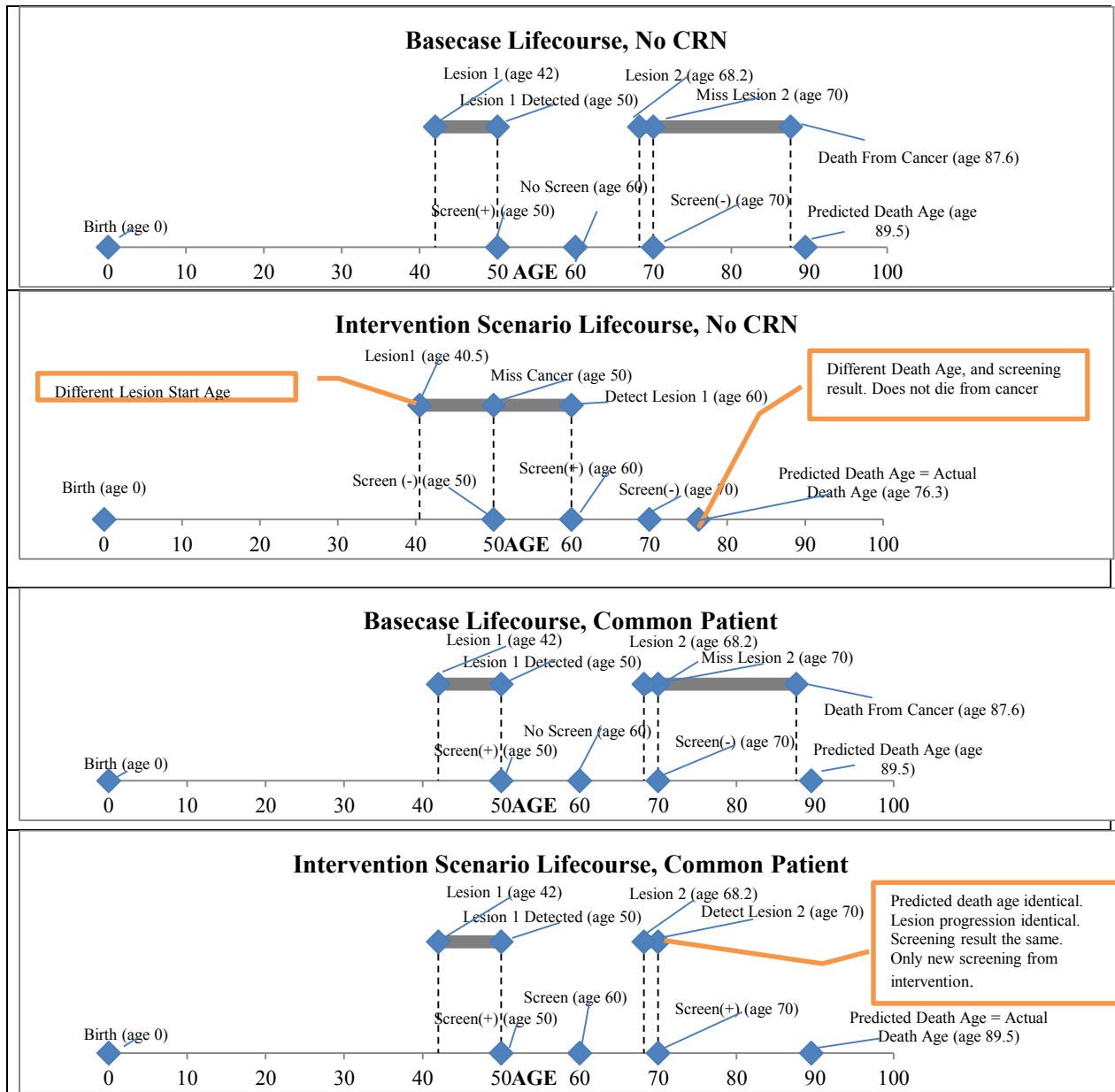


Figure 1: Life courses under different implementations of Common Random Numbers.

Our solution to this difficulty is to have separate random number streams for each major “event-generating process” in the model. We define an important “event-generating process” as a process that we want to progress separately and in sync over time except as it is directly impacted by the intervention. In our model, this meant establishing separate random number streams for our `Person` objects, `LesionGenerator` objects and `Lesion` objects. Additionally, interventions called within the `Person` object were placed on their own random number stream.

In the `Person` object, an individual’s health states are tracked and his/her compliance decisions are made. Within the `Person` object, there are two event streams that need to be coordinated, the compliance decision event stream and the test result event stream. The compliance event stream is synchronized between interventions, ensuring changes in the compliance probabilities from the interventions affects final

compliance decisions made. When synchronized, the same uniform random variate is used to determine the compliance decision. This ensures that we are evaluating the marginal impact on decisions resulting from the changed compliance probability. The separate test result stream ensures that the additional tests generated by the intervention do not change the results of future tests. Since FOBT tests have relatively low sensitivity, this is an important issue; we do not want to change the results of the baseline tests (tests that would have been performed regardless of the intervention) when we sample results from the additional tests.

The `LesionGenerator` and `Lesion` object also have their own event streams. The `LesionGenerator` is entirely independent of the compliance decisions and other events in the model. The `Lesion` object's trajectory should be independent of any other lesion and of the individual's events except when an individual recognizes and removes a precancerous lesion or polyp.

4.2.2 Compute Events at the Beginning of the Model Run

The dynamic, interactive nature of the components of the simulation model is the main source of difficulty in synchronizing the random number streams. We can avoid many possible issues, and simplify our design by computing as many events related to our new interventions as possible at the beginning of the run. This removes the effects that might be generated by events being reordered over time by the intervention. Model intervention events are candidates for this technique if they are independent of a dynamic model state. For example, in our model, an individual's decision to screen or not to screen depends only on states that can be pre-determined at the beginning of the model run, therefore, we can pre-determine the sequence of tests, patient compliance with those tests, and the test results (i.e. whether the cancer is found or not) at the beginning of the model run. Not all events are candidates for this solution. Events that are directly dependent on the state progressions of some model component cannot be computed at the beginning of the model run. Applying this technique carefully can reduce the complexity of applying common random numbers because we can do this processing step with carefully controlled random number streams rather than having to safeguard random number synchronization at every stage.

4.2.3 Pre-compute Events/States Before the Model Run

In a very similar fashion to the process discussed above for computing events at the beginning of the model run, we can pre-compute events/states. When events are computed before the model run in external code, they can be imported into the model by data files as needed during the model run. Almost any event identified as a candidate for pre-computation within the model can be pre-computed outside the model and then imported this way. The main consideration here is a practical one and depends upon the functionality or data structures of the simulation software being used that can make the event computation or storage much easier. For example, we compute individuals' insurance status before and after age 65 and store them in our population input files. This eliminates the need to perform a probabilistic transition between insurance types during the model run.

4.3 Computational Benefits of Common Patients

We have highlighted the issues in event synchronization important for creating a common patient and presented some practical recommendations on how to achieve a truly common patient in a simulation model. In justifying the common patient so far we have focused on comparability of outcomes as the reason for expending this effort in synchronizing simulation events. In this section, we will demonstrate the computational benefits of the common patient using as an example from our individual simulation model of colorectal cancer.

Since we have carefully coordinated the cancer-free lifetimes of individuals between intervention policies, we can confidently isolate the effects of each intervention. To effectively eliminate the stochastic

noise if all events were not coordinated would require repeated random runs for a given individual and would require many (about 100) replications of each individual/population cohort. With the common patient concept implemented, we only need to simulate out the stochastic noise associated with the marginal change in compliance probabilities and how that affects individual marginal choice; for this purpose, it is sufficient to do 10-20 replications of the individual/population cohort to understand the effect of the intervention. This represents a significant decrease in computational effort with no loss of accuracy. For our application this means that simulation experiments can be completed in hours, rather than days, because of the high computation time cost of each replication.

4.4 Numerical Example of Common Patient Concept

In the previous discussion, we argued that the common patient gives us comparability between individuals in different scenarios and that this comparability gives us a substantial computational advantage when simulating heterogeneous cohorts of individuals. We conduct several experiments to analyze the effect of the two interventions on two outcome statistics of interest in our model. The first statistic is a time varying statistic that tracks the number of individuals alive in each of the model years 2014 -2033. The second statistic is an output statistic that calculates the average life lost by each individual. We run the model with common patients implemented. By taking the difference between the baseline scenario and each intervention scenario we calculate the number of cancer deaths averted due to improved screening choices. The results for deaths averted is graphed in Figure 2. This figure shows the cumulative number of cancer deaths averted by the intervention. As expected the differences between the baseline and the interventions scenarios is always non-zero and there is a monotonically increasing total number of deaths averted due to screening.

To demonstrate the difficulty in interpreting the deaths averted statistic when the common patient is not implemented, we graph the common patient result against the results of models where common patients are not implemented. To simplify this comparison, we chose one of our interventions, the All ON (free screening, mailed reminder and mass media applied simultaneously). In Figure 3, we compare the results of the common patient scenario with 1, 20 and 50 replications when common patients is not implemented. As we see there is some erratic behavior in the death averted statistic when common patients is not implemented. For low numbers of replications this value may be negative, implying that the intervention scenario may be worse than baseline. As more replications are performed, we see a convergence toward the common patients scenario, as expected, but it is notable that this convergence required an order of magnitude more replications than the common patient scenario.

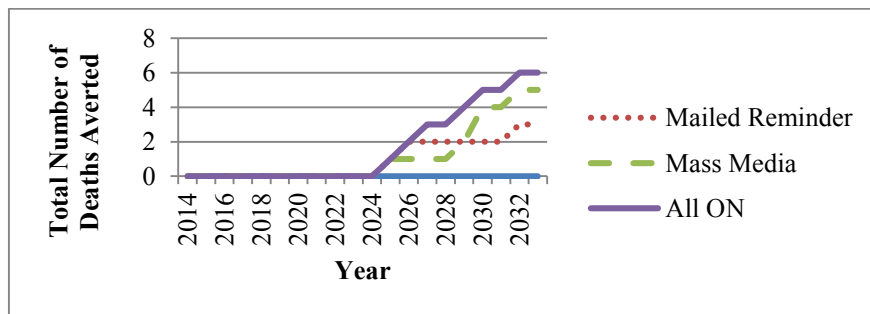


Figure 2: Total Death Averted under each intervention between 2014-2033.

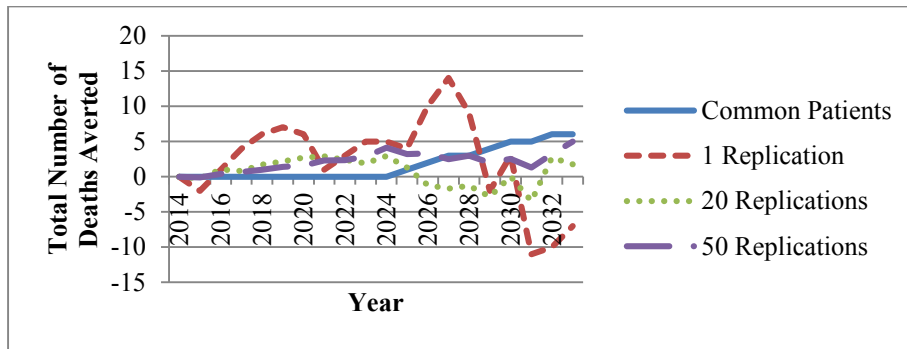


Figure 3: Death Averted for All ON Intervention: Common Patient vs. Standard approach.

In addition to faster convergence of the time varying statistics presented in Figures 2 and 3, the common patient concept also led to faster convergence for output statistics. One output statistic of interest in our model is the number of life years lost to cancer (lifelost). If a person dies from cancer, we compare his death age with his cancer free lifetime determined at the beginning of the model. If there is a difference in their final death age, this is his lifelost. If a person does not die before his natural, cancer-free lifetime due to cancer this value is 0. The individual lifelost values are averaged over the whole population to determine average lifelost at the end of the model run. When the base case and the All ON scenario values of this aggregate lifelost statistic are differenced, we get the life years gained per person. When we compare the results of calculating this statistic using common patients vs. the no CRN approach with 1,20 and 50 replications, we see (Figure 4) a convergence to the common patient produced value as we perform more replications, but again this convergence comes at substantial added computational cost in terms of the number of required replications for convergence when common patient is not used.

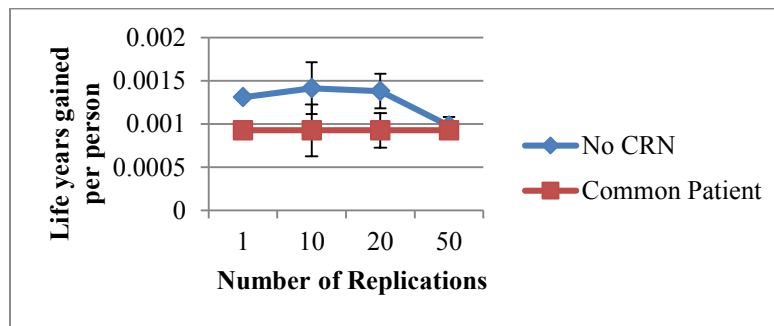


Figure 4: Life years gained convergence: common patient vs. no CRN for the All ON intervention .

These numerical examples clearly demonstrate that implementing common patients is very beneficial from a computational point of view.

5 INDIVIDUAL COST-EFFECTIVENESS FOR EQUITY EVALUATION

In our individual simulation model, an individual’s disease progression, compliance and response to treatment are functions of a large array of individual attributes. Having created the common patient, it is possible to directly compare individuals between two scenarios (interventions). Given the low probability of the events being evaluated here, there is often not a substantial benefit to comparing a single individual between interventions, however, each individual has multiple individual attributes. If we average the outcome effects of the intervention for a subgroup of which the individual is a part, we can get a clearer picture of how much a particular individual in that subgroup would stand to benefit from the intervention

applied. Because of heterogeneity of disease progression and response to interventions by different groups, the magnitude of the improvement in outcomes can vary significantly between subgroups defined by individual attributes. We believe that incorporating individual level cost-effectiveness information for different subgroups is valuable information for policy makers that can aid in understanding potential disparate impacts of the intervention. Providing information on these disparities provides a qualitative tool for promoting equity in the slate of interventions that are applied to a population.

5.1 Performing Subgroup Analysis

We demonstrate the utility of subgroup analysis by presenting a case study utilizing the results from our simulation model of colorectal cancer. Recall from Section 3 that disease progression in our model varies based on age, race and sex and individual choice varies on a range of attributes including race and sex, but is also driven by individual insurance type. In Table 1 we present the results from the lifelost statistics (described in Section 4.4) grouped by insurance type and sex for the base case and for the free screening, mailed reminder and mass media campaigns as well as an “all on” scenario for the age cohort who will turn 50 in 2014 (this is only a portion of our population).

Table 1: Lifelost statistic by insurance type and sex.

Insurance Type	Sex	Count	Life years lost to cancer				
			Baseline	Free Screening	Mailed Reminder	Mass Media	All ON
Medicaid	Female	4843	0.1682	0.1682	0.1558	0.1508	0.1476
Medicaid	Male	2806	0.1460	0.1460	0.1170	0.1189	0.1170
Uninsured	Female	11595	0.2210	0.2198	0.2210	0.2061	0.2049
Uninsured	Male	13650	0.1635	0.1635	0.1635	0.1508	0.1508
Private	Female	49704	0.1687	0.1687	0.1687	0.1625	0.1625
Private	Male	46360	0.0989	0.0989	0.0989	0.0942	0.0942

Table 1 shows that females have greater average life lost than their male counterparts in all scenarios. When examining results by insurance type, the uninsured individuals have significantly worse outcomes compared to the other insured groups. In examining the cost effectiveness of interventions we will look particularly carefully at this group.

To perform cost effectiveness analysis we must have costs of each intervention. We have developed a cost structure for each of the interventions analyzed and described in Hassmiller Lich et al. (2014). Once these costs have been determined, they can be distributed across the population subgroups proportional to the number of individuals in each of these subgroups. Table 2 contains the individual cost effectiveness ratios for each of the subgroups for the mailed reminder, mass media and all on interventions.

Table 2: Individual cost-effectiveness ratios.

Insurance Type	Sex	Count	Individual CER on lifelost statistic	
			Mailed Reminder	Mass Media
Medicaid	Female	4843	\$513.34	\$80.83
Medicaid	Male	2806	\$218.97	\$51.64
Uninsured	Female	11595	N/A	\$93.90
Uninsured	Male	13650	N/A	\$110.15
Private	Female	49704	N/A	\$225.81
Private	Male	46360	N/A	\$299.15

From these cost effectiveness results we can see the relative cost effectiveness of the mass media campaign for all population groups. We can also see that the nature of the effects of the mass media campaign does not make it a particularly cost effective intervention to reach privately insured individuals. When we compare these costs of targeting the mailed reminder program to Medicaid/dual insured patients we do not see a significant difference in cost. This suggest that it may be valuable to spend the additional money on Medicaid/dual patients because there are public policy reasons to improve their outcomes and it is equally cost effective to reach this group as compared to privately insured patients.

6 CONCLUSION

Creating individuals that are comparable across interventions is highly desirable for individual disease simulation models. These comparable individuals are created by carefully identifying the different event processes in the model that generate the health events in an individual's life course and running them on separate random number streams that are comparable between interventions. Since the life course thus generated are the same except for differences specifically induced by the interventions, we describe these individuals as common patients. This is a result of the application of Common Random Numbers. However, because of the complex dynamic nature of many models, achieving full individual life time synchronization requires multiple, careful approaches to synchronization of events. We achieve synchronization both by using different random number streams and by determining as many events as possible at the beginning of the model run or in a preprocessing step. As demonstrated with numerical examples from our model of colorectal cancer, the common patient concept has substantial computational benefits.

The use of the common patient enables comparisons to be made between individuals and this opens up a host of possibilities for performing subgroup cost-effectiveness analyses. We performed some of this analysis for subgroups in our model and demonstrated how these analysis can be used as a qualitative tool for the identification of disparities in outcomes and for evaluating the relative cost effectiveness of interventions across subgroups .

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