Objective
Monte Carlo simulations are driven by the generation of pseudo random numbers (PRN). An effective PRN generator needs to generate random variables that are uniformly distributed between 0 and 1 and mutually independent. Testing the effectiveness of PRN generators is rarely undertaken yet any systematic pattern or bias has implication for simulation run time and simulation accuracy, particularly for rare events. The objective of this study was to compare three commonly used PRN in an applied setting to illustrate potential implications of low performance.

Methods
Three PRN generators were compared inside the framework of the JMS Core Diabetes Model (CDM) to explore their precision in detecting the onset of end stage renal disease (ESRD) in one million repetitive runs being bootstrapped over 1000 times. PRN from the MS-Visual C+ + 2008 build-in random generator (MSG), the Mersenne Twister (MTG) [1], and Wichmann Hill generator (WHG) [2] were compared. One-year probabilities of ESRD for a 65 year old female smoker were calculated for systolic blood pressure (SBP) of 135 mm Hg (p = 0.000363) and 140 mm Hg (p = 0.000444) using a risk equation from UKPDS 68 [3]. The expected one year incidence of ESRD was calculated using a deterministic approach in MS Excel 2007 and compared to probabilistic observations in the CDM for all PRN. PRN were evaluated with respect to their accuracy to predict the expected incidence of ESRD and ability to differentiate risk scores associated with a 5 mm Hg difference in SBP. The frequency distribution of all PRN in the interval between 0 to 0.002 was assessed to interpret the results.

Results
The expected yearly incidence of ESRD was 0.0363 % (SBP 135 mm Hg) > 0.0444 % (SBP 140 mm Hg) > 0.0444 % (SBP 140 mm Hg). With a 22.3% relative increase in ESRD risk associated with a 5 mm Hg increment in SBP (Figure 1) and the relative increase in incidence associated with a 5 mm Hg increase in SBP are presented in Table 1. The incidence of ESRD associated with 135 mm Hg was overestimated (+) or underestimated (−) by +1.02%, −3.28% (significant) and −0.1% using the MSG, MTG, and WHG, respectively. The relative increase in incidence associated with a 5 mm Hg SBP rise was 24.9%, 0%, and 22.1% for the MSG, MTG and WHG, respectively. The frequency distribution of all PRN in the interval between 0 to 0.002 was assessed to interpret the results.

Expected and observed ESRD incidence associated with both SBP levels are presented in Table 1. The incidence of ESRD associated with 135 mm Hg was overestimated (+) or underestimated (−) by +1.02%, −3.28% (significant) and −0.1% using the MSG, MTG, and WHG, respectively. The relative increase in incidence associated with a 5 mm Hg SBP rise was 24.9%, 0%, and 22.1% for the MSG, MTG and WHG, respectively.

Conclusions
The three PRN generators tested in this analysis produced substantially different results. Both WHG and MSG algorithm appeared efficient with uniform distribution of pseudo independent random variables. This was in stark contrast to the MTG which significantly under predicted ESRD incidence.

For the future, accurate algorithm for the simulation of probability distributions over a large sample space is essential. The results of this study suggest that the simulation of probability distributions is not trivial and should be carefully assessed to ensure that the accuracy of the simulation is maintained.

References