PRM50

Random number generators in Monte Carlo simulation

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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 implications 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 IMS Core Diabetes Model (CDM)[1] 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)[2], and Wichmann Hill generator (WHG)[3] 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[4].
- 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)
  - → With a 22.3 % relative increase in ESRD risk associated with a 5 mm Hg increment in SBP (Figure 1)
- Expected and observed ESRD incidence associated with both SBP levels 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 %, -32.8 % (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 22.3 % for the MSG, MTG and WHG, respectively.
- Analysis of the frequency distribution of PRN displayed areas sparsely populated with random variates from MSG and MTG (Figure 2) and a continuous spectrum for WHG.
- Sparsely populated areas were found to be largest in the MTG and accounted for the fact that the risk difference associated with a 5 mm Hg increase in SBP was not detected.
- The minimum detectible probability differences (precision) was 0.00003 and 0.0002 for MSG and MTG, respectively, whereas WHG presented no limitations due to its continuous spectrum of random variates.

Figure 1. Comparison of MSG, MTG and WHG to track ESRD probabilities

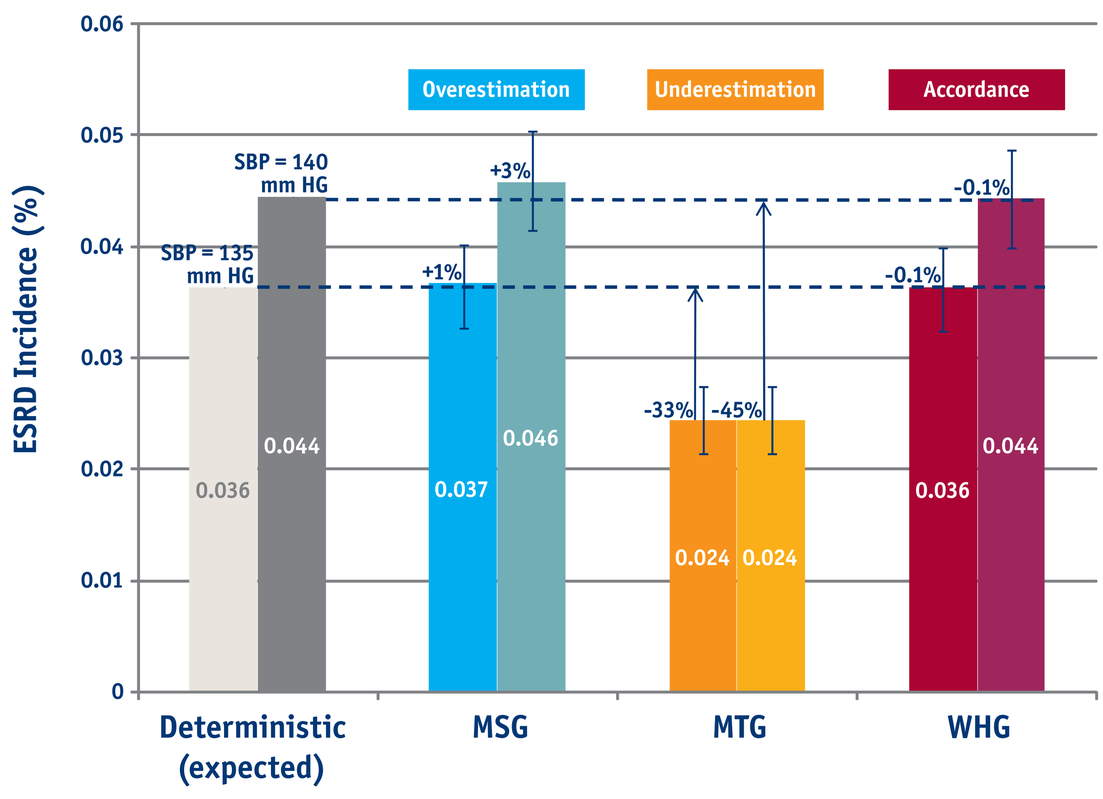

Figure 2. Frequency distribution of 10^8 uniformly distributed random samples generated with MSG, MTG and WHG in a range between 0 and 0.002

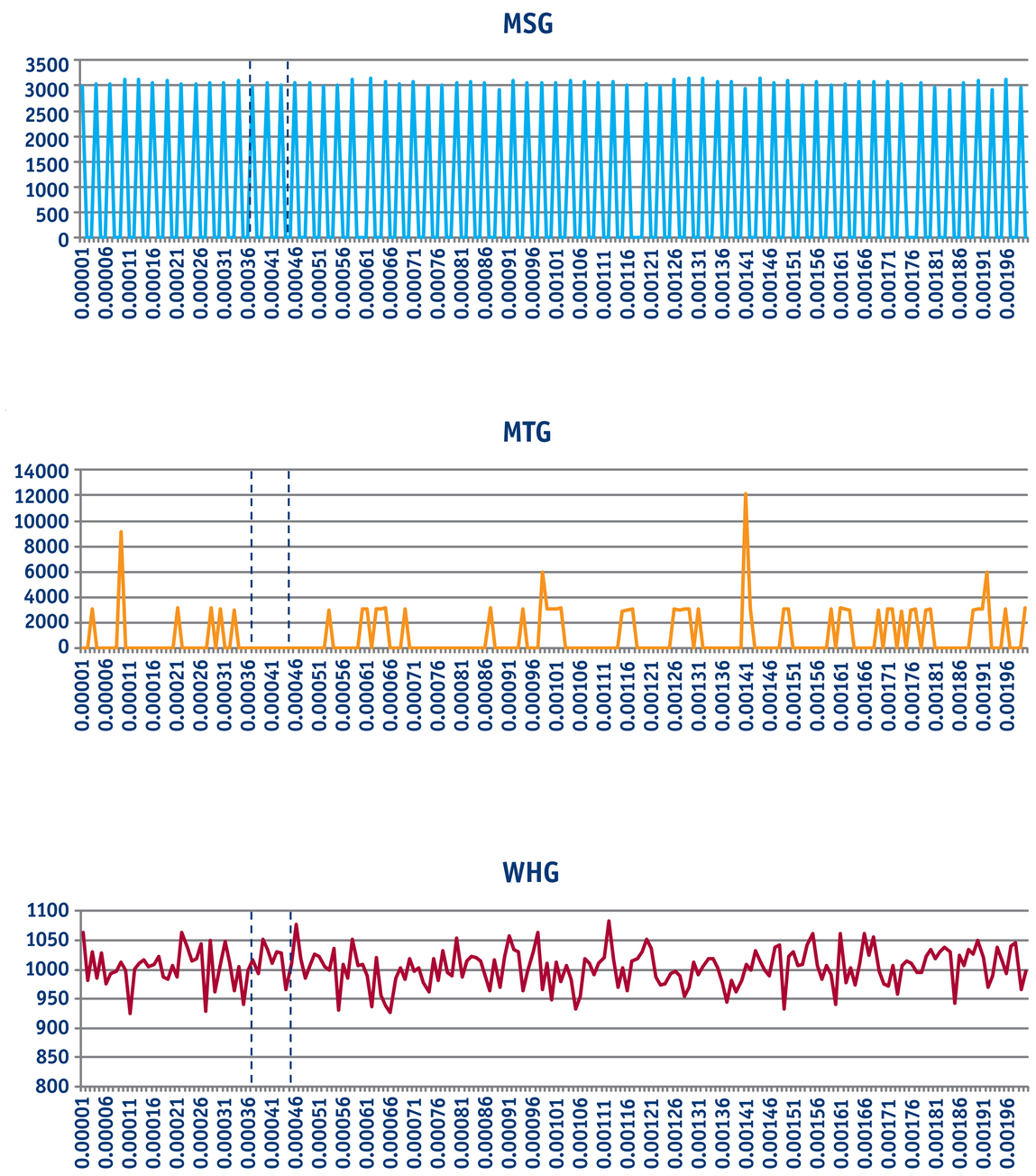

Table 1. Expected vs. observed incidence and ability to track probability change following 5 mm Hg increase in SBP for MSG, MTG and WHG generators

	Expected incidence (EI)	MSG Mean (95 % CI)	Deviation from EI	MTG Mean (95 % CI)	Deviation from EI	WHG Mean (95 % CI)	Deviation from EI
SBP 135 mm Hg	0.0363 %	0.0367 % (0.0327 % — 0.0402 %)	1.02 % (-9.92 % — 10.74 %)	0.0244 % (0.0214 % — 0.0275 %)	-32.80 % (-41.10 % — -24.20 %)	0.0363 % (0.0324 % — 0.0399 %)	-0.06 % (-10.70 % — 10.20 %)
SBP 140 mm Hg	0.0444 %	0.0457 % (0.0415 % — 0.0503 %)	3.10 % (-6.50 % — 13.30 %)	0.0244 % (0.0214 % — 0.0275 %)	-45.03 % (-52.00 % — -38.00 %)	0.0443 % (0.0399 % — 0.0486 %)	-0.13 % (-10.10 % — 9.50 %)
Increase in incidence for 5 mm Hg SBP rise	22.3 %	24.9 % (19.1 % — 31.1 %)	2.60 % (-3.20 % — 8.80 %)	0.0000 % (0.0000 % — 0.0000 %)	100.00 % (100.00 % — 100.00 %)	22.3000 % (17.2000 % — 28.0000 %)	0.00 % (-5.10 % — 5.70 %)

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 variates. This was in stark contrast to the MTG which significantly under predicted ESRD incidence.
- Imbalance of the frequency distributions leads to over- or underestimation of expected incidence whereas areas sparsely distributed with random variates across the sample spectrum limit the ability of PRN generators to detect probability differences.
- These limitations cannot be overcome by increasing run time and hence account for systematic bias in decision models.
- When assessing the internal validity of Monte Carlo simulations the efficiency and robustness of PRN generators should not be assumed.

References

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