Economic Risk Analysis of Embryo Transfer Programs through Stochastic Simulation

D. G. Aherin[a], M. D. MacNeil[a,c], J. M. Bormann[a], J. L. Heier Stamm[b], and R. L. Weaber[a]

[a] Department of Animal Science and Industry, Kansas State University, Manhattan, KS 66506 U.S.A.

[b] Industrial & Manufacturing Systems Engineering, Kansas State University, Manhattan, KS 66506 U.S.A.

[c] Delta G, Miles City, MT 59301 U.S.A. and Department of Animal, Wildlife and Grassland Sciences, University Free State, Bloemfontein, South Africa

ABSTRACT

To accomplish the objective of creating an economic risk analysis tool for user-defined embryo transfer (ET) programs, a circumstantial, stochastic prediction model utilizing @Risk© software to generate comparable economic values as an aid in the ET decision making process has been created. More realistic than the use of means in deterministic models, distributions defining the biological uncertainty for a multitude of reproductive outcomes are estimated through extensive literature review and limited industry sources. Applying the Latin Hypercube variation of Monte Carlo simulation, a sample value from the descriptive distribution associated with each stochastic variable is included in an iteration of the simulation. Through large numbers of iterations with dynamic combinations of variables, the process culminates in a distribution of possible values for the net present value (NPV), annuity equivalent net present value (ANPV), and return on investment (ROI) associated with the model described scenario of in-vivo derived (IVD) or in-vitro produced (IVP) embryos. Finally, using the distributions of NPV, ANPV, and ROI a decision maker can assess the economic risk linked to a user-defined ET program.

Cattle producers are presented with a choice between two primary methods of ET: Multiple Ovulation Embryo Transfer (MOET) and IVP. Encompassed within the two methods of ET exist several different sub-techniques, including the use of unsorted or sex-sorted semen in both methods and the exception or inclusion of follicular synchronization and/or stimulation before ovum pick-up (OPU) in IVP procedures. Even more recently, the commercial application of pre-transfer embryo biopsy has entered the marketplace. Ultimately, operators must decide whether ET programs, of any type, serve as an economically viable means to increase rate of genetic improvement or take advantage of marketing opportunities. Ample opportunity exists for the commercial application of in-depth, alternative ET scenario assessment afforded through stochastic simulation methodology that the ET industry has not yet fully exploited.

1. Introduction

Dynamic environments, varying production practices, and biological uncertainty associated with bovine reproduction make informed, strategic decision making regarding implementation of bovine reproductive technology a great challenge for producers. Profitability of an ET program depends on marketability of the end-products (embryos, pregnant recipients, progeny, etc.) and expenses required to produce them. Aherin (2017) describes in detail the many sources of production and economic variation.

Although several economic value predictors for ET programs already exist (Beltrame et al. 2010), the opportunity remains to create more applicable models for *Bos taurus* beef production and varying marketing avenues in the U.S. The host of stochastic factors, decision points, and interactions among them that affect the success of an ET program motivated development of a simulation model for their joint consideration in assessing the economic feasibility of alternative programs.

2. Model

2.1. Model Outline

The model allows for the comparison and analysis of the production and economic factors of ten primary ET protocols.

1. MOET: Unsorted Semen
2. MOET: Sex-Sorted Semen
3. MOET: Frozen Biopsied Embryos
4. MOET: Frozen Non-Biopsied Embryos
5. IVP: No Ovarian Stimulation (NS), Random OPU Interval, Unsorted Semen
6. IVP: No Ovarian Stimulation (NS), 3-4 d or 14 d OPU Interval, Unsorted Semen
7. IVP: Follicular Synchronization and Ovarian Stimulation (SS), Unsorted Semen
8. IVP: NS, Random OPU Interval, Sex-Sorted Semen
9. IVP: NS, 3-4 d or 14 d OPU Interval, Sex-Sorted Semen
10. IVP: SS, Sex-Sorted Semen

2.2. Economic Values

NPV, ANPV, and ROI are used to measure ET program profitability. Each simulation replication for a particular ET protocol produces a value for the NPV, ANPV, and ROI. Since multiple replications are performed, the result is a probability distribution for NPV, ANPV, and ROI under each protocol.

2.3. Assumptions

2.3.1. General Model Assumptions

- No correlation between traits/measurements
- All recipients enter the system as purchased opens
- All purchases occur on d 1 of fiscal year
- All calves weaned same day
- If calf lives to weaning, it lives through development

2.3.2. Reproductive Model Assumptions

- Healthy donors, recipients, and bulls
- 21 d estrous cycles
- ET on d 7 following the onset of estrus
- Recipients synchronized within 24 h of donor
- Normally cycling donors and recipients
- ET program is seasonal, not continuous
- MOET IVD is limited to 3 flushes/breeding season

2.3.3. Embryo Production Model Assumptions

- Recipients that return to estrus on d 21 reenter available recipient population, depending on ET round and time interval between flush/OPU.
- ET recipients that experience pregnancy loss between 21 d and 60 d of pregnancy are eligible for natural service, depending on interval between transfers and length of bull turnout.
- ET bred recipients that experience pregnancy loss between d 60 and term are not eligible for natural service.
- Natural service bred recipients that experience pregnancy loss at any point after d 21 of gestation are not eligible for another natural service conception.

2.3.4. Revenue Model Assumptions

- Bred recipients are sold carrying a minimum 60 d pregnancy with no calf at side.
- Calf development revenue occurs in same fiscal year that calves are born.

2.3.5. Expense Model Assumptions

- Expenses not included:
  - Overhead or whole ranch costs
  - Facilities
  - Non-ET veterinary costs (pulling calves, emergencies, etc)
  - Labor when not applied to ET program
  - Equipment Expense
  - Taxes

2.4. Distributions of Biological Uncertainties

@Risk© is an Excel© add-in that allows for probability distributions to be built into an Excel© workbook and values drawn from said distributions through the simulation of an Excel©-based model. The model includes stochastic variables describing donor superovulation response, embryo production, oocyte production, blastocyst rate, recipient synchrony, pregnancy rates, pregnancy failures, calf survival, and progeny revenue according to each respective ET methodology and/or marketing scenario. Aherin (2017) describes the distributions generated for each of the stochastic variables in further detail.

2.9. Deterministic Variables

Accompanying the stochastic variables characterized by the distributions previously described are user-defined deterministic variables. Deterministic elements include variables describing ET production management strategy and protocols, anticipated calf performance, costs associated with specific factors, and several end-product marketing values (Aherin, 2017).

2.10. Model Simulation

To demonstrate the capability of the stochastic model, analysis for a select few scenarios is presented here. For the scenarios, 100,000 replications of the simulation model are performed using the parameters described previously. The use of 100,000 iterations balances a high confidence in output, while still allowing for a reasonably short simulation run-time. Sections of the model where the numerical outcome is influenced by an estimation of the true probability associated with a binary outcome (i.e., pregnancy rate) are determined using a binomial distribution with *n* number of trials and success probability, *p*. As the true probability of success for such traits is unknown, a sample value from the distribution describing the potential value of the true probability is selected per LHS for each iteration/replication of the model. The distributions describing the range of values for stochastic variables with non-binary outcomes are sampled per LHS without the need for a complementary binomial distribution. The LHS variation of Monte Carlo simulation (Iman and Shortencarier, 1984) culminates in a distribution of possible outcome values through large numbers of iterations with dynamic combinations of variables.

The model may be used to analyze numerous scenarios utilizing sex-sorted or unsorted semen with variations in ownership of donors and recipients and alternative marketing avenues compared simultaneously. The intent of the selected scenarios is to illustrate these possibilities, not to provide a means for industry wide assessment of a specific reproductive technology application or the profitability of a given marketing strategy, in general.

Scenario 1:

- Embryo Production Method: MOET using unsorted semen.

Scenario 2:

- Embryo Production Method: IVP NS, 14 d OPU interval using unsorted semen.

Scenario 3:

- Embryo Production Method: IVP SS using unsorted semen.

All Scenarios:

- Ownership: Own donors and own recipients.
- Marketing: Sell developed bulls and females per the pricing distribution described in the previous chapter. Sell all cull progeny and naturally sired calves by weight, as feeder cattle, per the feeder calf pricing index. Market excess embryos using the user-defined price disclosed in the preceding chapter. Open females are sold at the conclusion of the breeding season, with the corresponding value of an open female.

2.11. Statistical Analysis

Statistical analysis was performed using StatTools 7.5 ©. Using the individual results generated from each simulation replication, a standardized, stepwise regression analysis was executed for each scenario with each stochastic variable serving as an independent variable and ROI as the dependent variable (Iman et al., 1985). Adjusted R-squared values were determined for each regression model (Mendenhall and Sincich, 2012). The assumptions of multivariate linear regression were tested by analyzing the distribution of residuals.

3. Results: Scenario: Unsorted Semen- Owned Donors- Owned Recipients- Market Developed Bulls and Heifers

Figure 1 through Figure 9 and Table 1 display the results of the simulation model according to the example scenario, in terms of ROI.

3.1. Scenario 1: MOET

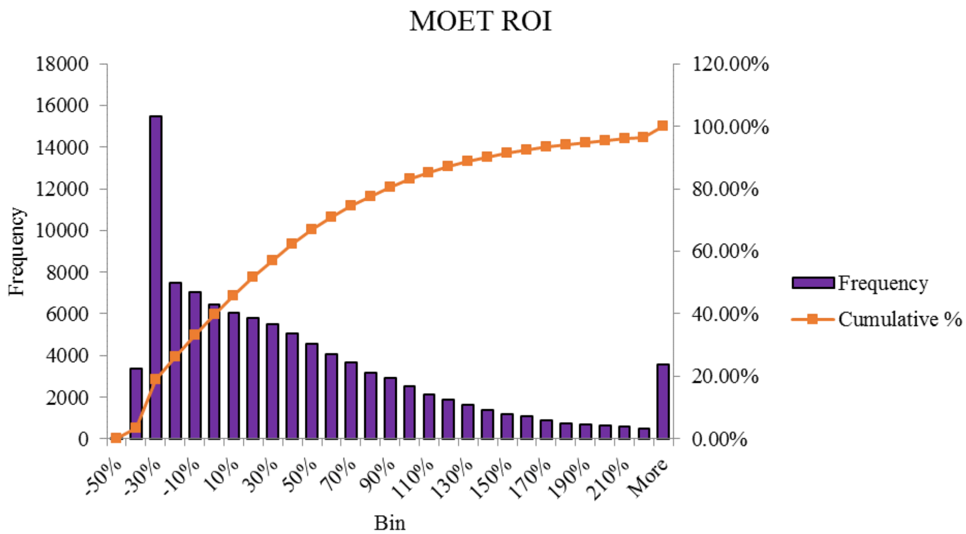

Figure 1. Probability distribution of the ROI resulting from the scenario of MOET- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.

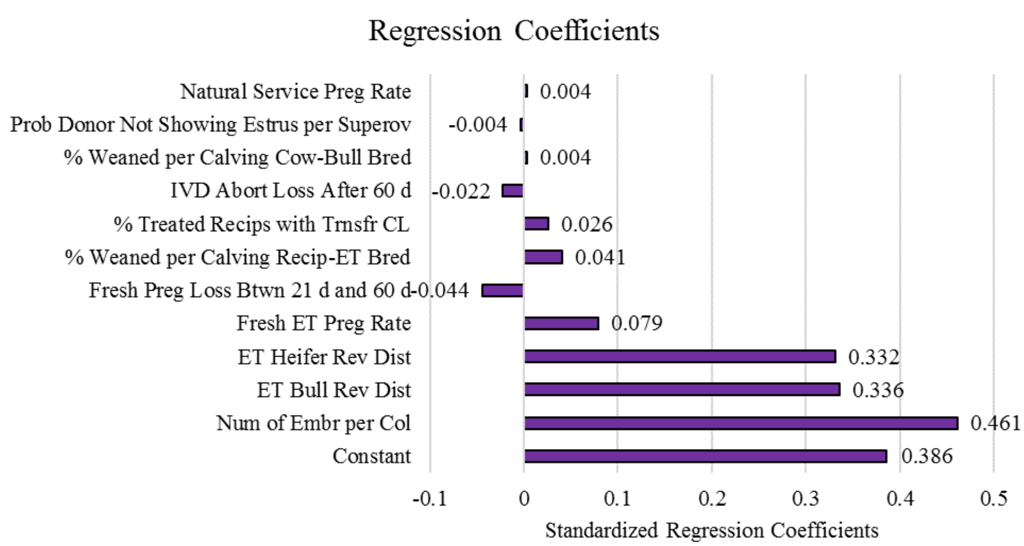

Figure 2. Standardized stepwise regression coefficients for the stochastic variables influencing the scenario of MOET- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.

Num of Embry per Col (number of transferable embryos per collection). Preg Rate (pregnancy rate at 21 days post-ovulation).

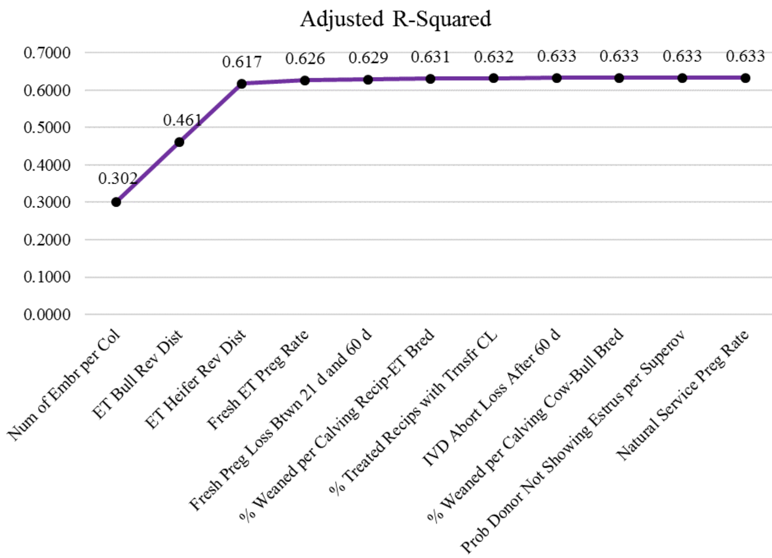

Figure 3. Cumulative distribution of the R-squared value associated with the stochastic variables influencing the scenario of MOET- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.

Num of Embry per Col (number of transferable embryos per collection). Preg Rate (pregnancy rate at 21 days post-ovulation).

3.2. Scenario 2: IVP NS

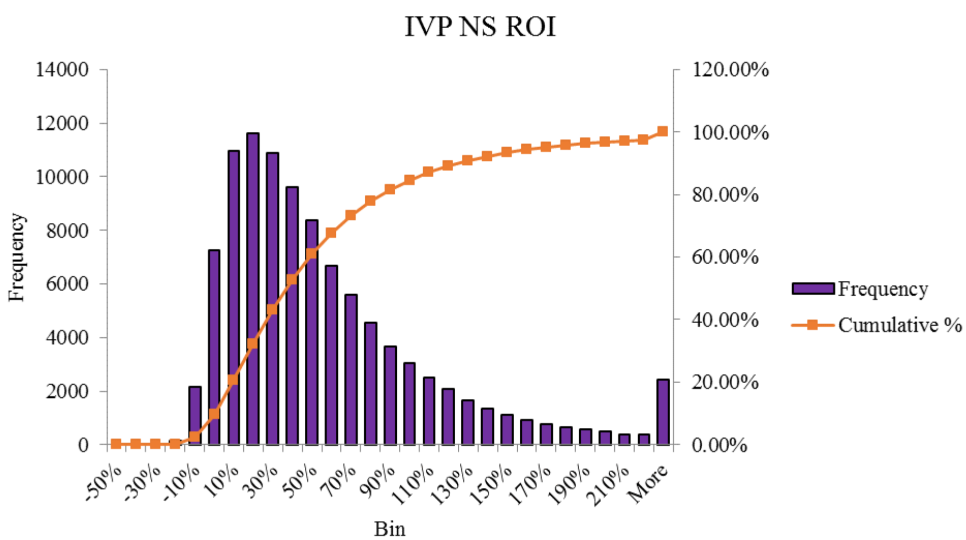

Figure 4. Probability distribution of the ROI resulting from the scenario of IVP NS- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.

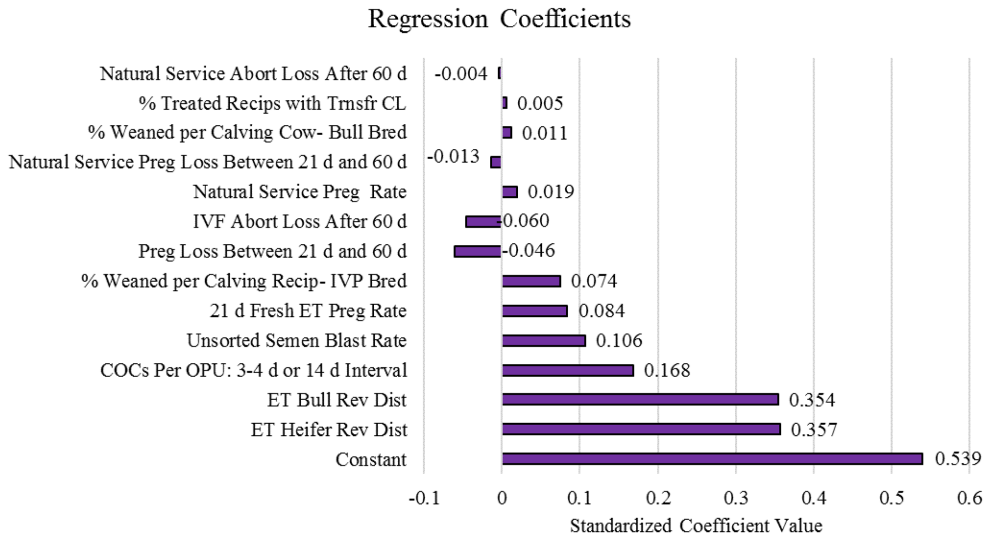

Figure 5. Standardized stepwise regression coefficients for the stochastic variables influencing the scenario of IVP NS- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.
Preg Rate (pregnancy rate 21 d post-ovulation). Blast Rate (blastocyst rate). COCs Per OPU (number of cultured oocytes per OPU).

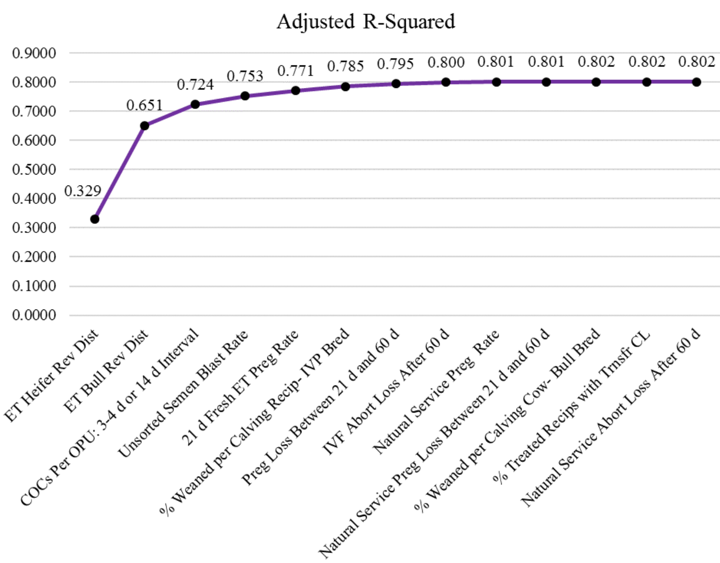

Figure 6. Cumulative distribution of the R-squared value associated with the stochastic variables influencing the scenario of IVP NS- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.
Preg Rate (pregnancy rate 21 d post-ovulation). Blast Rate (blastocyst rate). COCs Per OPU (number of cultured oocytes per OPU).

3.3. Scenario 3: IVP SS

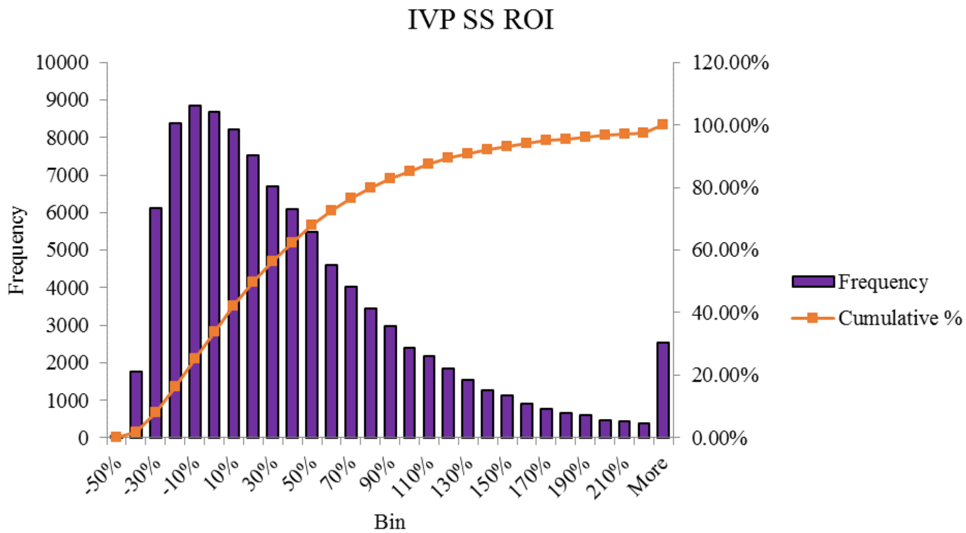

Figure 7. Probability distribution of the ROI resulting from the scenario of IVP SS- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.

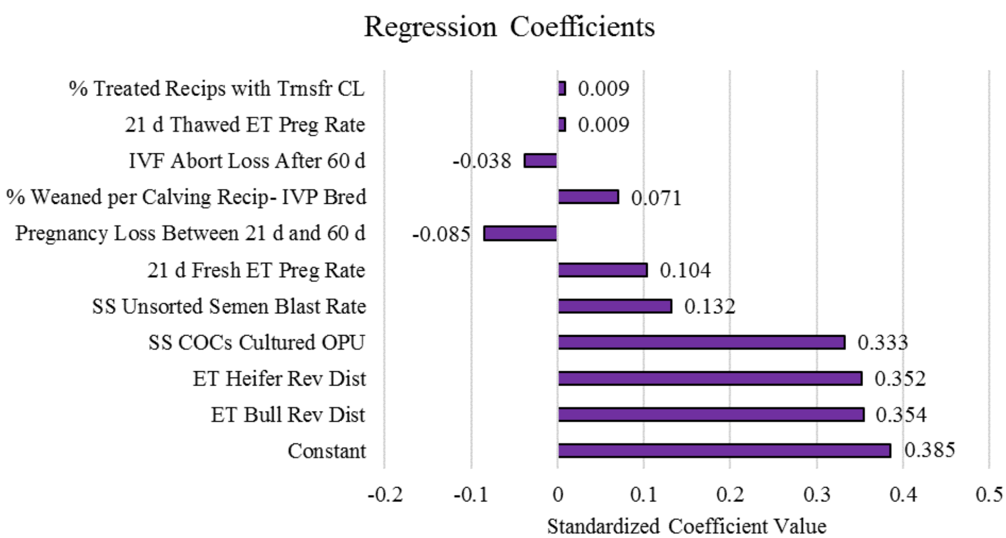

Figure 8. Standardized stepwise regression coefficients for the stochastic variables influencing the scenario of IVP SS- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.
Preg Rate (pregnancy rate 21 d post-ovulation). Blast Rate (blastocyst rate). SS COCs Cultured OPU (number of cultured oocytes per OPU).

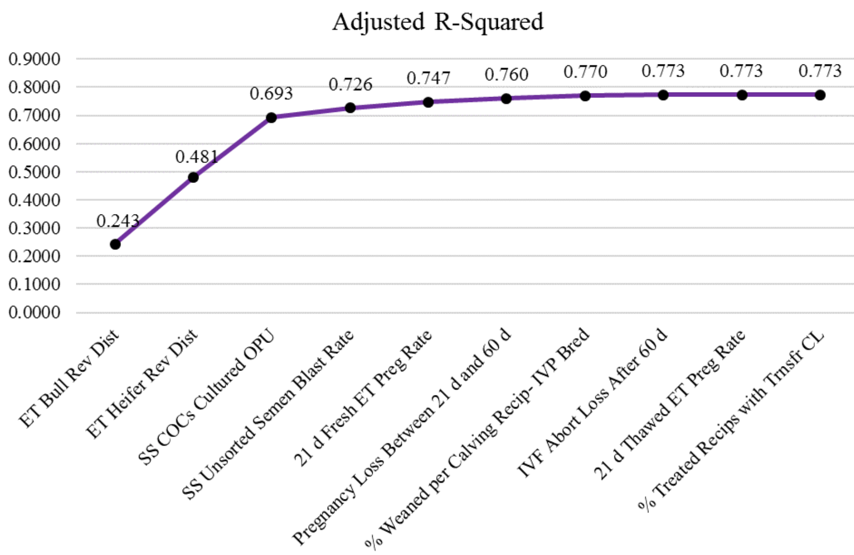

Figure 9. Cumulative distribution of the R-squared value associated with the stochastic variables influencing the scenario of IVP SS- unsorted semen- owned donors- owned recipients- market developed bulls and heifers.
Preg Rate (pregnancy rate 21 d post-ovulation). Blast Rate (blastocyst rate). SS COCs Cultured OPU (number of cultured oocytes per OPU).

ROI (%)	MOET	IVP NS	IVP SS
Mode	-37.4	13.5	-16.3
5%	-39.0	-5.5	-34.3
25%	-22.0	13.9	-10.2
Median	16.9	37.1	20.5
75%	71.3	74.1	66.0
95%	194.5	166.9	169.8
Mean ± 90% C.I.	38.6± 0.437	53.7 ± 0.326	38.4± 0.374
SD	84.0	62.6	71.8
Probability of Negative Return	40.0	9.6	34.0

Table 1. Mode, 5th percentile, 25th percentile, median, 75th percentile, 95th percentile, mean, and standard deviation of the ROI resulting from the scenario of unsorted semen- owned donors- owned recipients- market developed bulls and heifers.

4. Discussion

A strength of the proposed simulation approach is that is makes it possible to examine the range of potential outcomes for a given production strategy with a combination of expediency, negligible resource use, and number of trials that could not be replicated in the field. Mean values of economic and production measures are important, but the distributions of biological uncertainties embedded within the model cause many output distributions to vary greatly in shape, often straying far from a normal distribution. Thus, it is possible for distribution means and most likely outcomes to diverge from one another substantially. Therefore, equal, if not greater, attention should be paid to the percentiles and probabilities associated with each output distribution. Furthermore, a deeper investigation into the varying production outputs that cause differences between the economic outputs of the scenarios in question is feasible, although not described in the scope of this paper.

The mean ROI for MOET, 38.6%, and IVP SS, 38.4%, were not significantly different at 90% confidence (Table 1). Mean ROI for IVP NS, 53.7%, was significantly greater than the mean ROI for both MOET and IVP SS at 90% confidence (Table 1). Besides the differences in output means, there is also a noticeable difference in the standard deviations of means (Table 1).

Along with noting the standard deviation of output means, an effective method of risk appraisal is an analysis of the probability distribution associated with each economic and production output. When considering ROI, the most likely outcomes for MOET, IVP NS, and IVP SS are -37.4%, 13.5%, and -16.3%, respectively (Table 1). The medians for each respective ROI distribution are 16.9%, 37.1%, and 20.5% (Table 1). Perhaps the greatest measurement of financial risk is the probability of negative return. Regarding this measurement, MOET, IVP NS, and IVP SS had probabilities of 40.0%, 9.6%, and 34.0% (Table 1), respectively. It seems rational that IVP NS has the lowest probability of negative return, because IVP NS is less influenced by the success or failure of expensive human intervention (no exogenous hormone protocols for synchronization or stimulation of donors) than either MOET or IVP SS.

Although each individual firm may consider risk differently, using the most likely outcome and probability of negative return, one can argue that for the given scenario both the MOET and IVP SS programs are in contention for the economically riskiest methods of ET. Alternatively, if one defines risk as an uncertainty of outcome, MOET also has the greatest standard deviation of ROI, at 84.0% (Table 1). Not surprisingly, considering many risk-reward trade-offs, MOET also has the greatest ROI at the 95^{th} percentile (Table 1). Depending on a firm's risk aversion, IVP NS could be an attractive method under the given scenario, as it boasts the, the lowest probability of negative return, the greatest most likely return, and the smallest standard deviation around the mean. Simultaneously, the 95^{th} percentile ROI of IVP NS, 166.9%, rivals that of IVP SS, 169.8% (Table 1).

The statistical results are shown in Figure 2 and 3, Figure 5 and 6, and Figure 8 and 9. For Scenario 1, the three largest regression values are the number of transferable embryos per collection, the revenue distribution for heifers, and the revenue distribution for bulls. For Scenario 2 and Scenario 3, the three largest regression coefficient values are the revenue distribution for heifers, the revenue distribution for bulls, and the number of oocytes incubated per OPU. According to the R-squared values, the regression model for each of the scenarios does not completely explain the outcome of the scenario. This is, in part, because of the incorporation of binomial distributions, which are not included in the regression analysis, as a method of implementing the stochastic variables that represent a mean probability, such as pregnancy rate. It is likely that the results of the binomial distributions account for a large proportion of the variation that the model utilizing only stochastic variables cannot explain.

5. Conclusions

Inherent to the identity of the beef industry is the variation of environment, cattle type, and management practices between operations. Thus, a critical aspect of the stochastic model described and applied in the preceding pages is the ability to incorporate user-defined variable values, specific to an individual operation, as parameters for the program in question. The stochastic elements of the model create a more realistic outlook than the use of means in deterministic models, as distributions defining the biological uncertainty for a multitude of reproductive outcomes are incorporated into the model. The core function of this model should be as a consultative tool using the generated distributions of NPV, ANPV, and ROI as an aid in the assessment of the economic risk linked to a user-defined MOET or IVP program.

This model does not account for the increased magnitude and rate of genetic gain that is possible through ET and the potential long-term impact those genetic improvements may have on a breeding program. Accounting for the long-term economic impact of accumulated improvements or changes in production efficiency is a potential next step in analyzing the economics of ET. This model could serve as a foundational template for that opportunity.

The pace of change in the IVP industry is rapid enough that many advances are not reported in the scientific literature before being implemented in industry. Furthermore, it is likely that IVP companies may regard technological advancements as trade secrets that yield a competitive advantage in the marketplace. Thus, a challenge in the application of this model is creating and maintaining an accurate representation of expected production outcomes from the most current ET practices.

The numerical and logical analysis afforded through the stochastic simulation of alternative scenarios through this model allows for in-depth assessment of ET programs not previously available. The caveat is that any model, no matter how robust, will never be completely accurate, as all are a simplified version of a complicated reality. That said, there is ample opportunity for the commercial application of this stochastic model to complement the deterministic, instinctive, and experience based elements of the decision-making process pertaining to the prediction of the economic outcome of an ET program, through methodology that the ET industry has not fully exploited.

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