Economic Risk Analysis of Embryo Transfer Programs through Stochastic Simulation

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Outline

I. Current application of financial risk/investment analysis
II. Opportunity for financial risk/investment analysis in ET programs
III. Different ET program methods
IV. Use of systems approach and stochastic modeling to analyze economic risk of ET programs

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Investment Analysis

- Breakeven Points
- Life of Investment
- Investment Decision Tools
  - Net Present Value (NPV)
  - Annuity Equivalent NPV
  - Return on Investment (ROI)
  - Several other options and methods
- Risk Analysis
  - Range of potential return
  - Probability of each level of return

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Cattle Feeding Investment Analysis

- Before buying a pen of cattle
  - Calculate breakeven
    - Cost of gain
    - Interest
    - Buy Price
    - Sell Price
  - Determine marketing/risk management strategy
    - Unprotected
    - Hedging
    - Contracting
    - Grid vs. Carcass Weight vs. Live Weight
- Breakeven- large data samples predict….
  - Performance
    - Days On Feed (DOF)
    - Average Daily Gain (ADG)
    - Feed:Gain (F:G)
    - Etc.

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ET Program Investment Analysis

- Who really does this properly?
  - Assume very few
  - Based on past averages
  - Intuition and Optimism
- Large investment
  - Financial
  - Time
  - Labor
- Goals for genetic gain outweigh cash flow concerns?

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ET Program Investment Analysis Challenges

- Prediction Challenges
  - Dynamic Environments
  - Small Sample Size
  - Record Keeping
    - Accurate conception, ovulation, embryo production
- Variability of Outcomes
- Multiple Methods of ET

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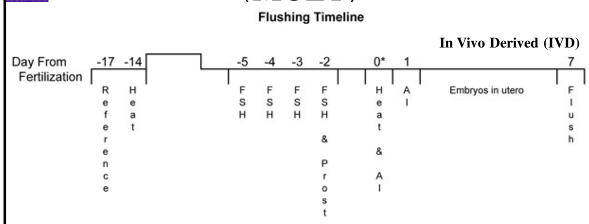
Multiple Ovulation Embryo Transfer (MOET)



- Freeze/Transfer to recipient on roughly Day 7 of cycle
- Possible every 30-60 days

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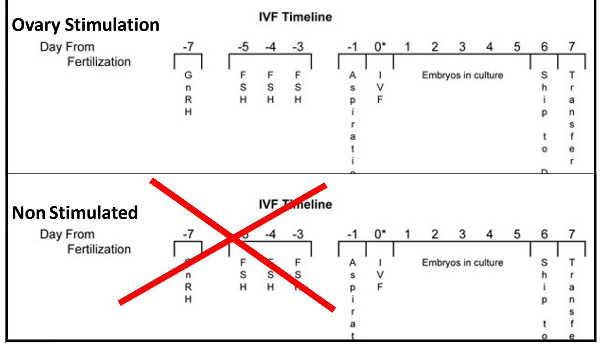
In Vitro Fertilization (IVF)/ In Vitro Production (IVP)



The Question

- What type of ET, if any, makes economical sense for a given operation?

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Objectives

- Use prediction model to generate economic value and analyze risk in bovine ET projects
- User defined
- Account for variation in production of embryo transfer program in beef cattle
- Convert financial output into comparable economic terms
- Explore sensitivity analysis and optimization

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Why Model?

- Simplified version of reality
- Less expensive
- More timely than the real world
- Explain situations that can't be easily replicated
- Gain understanding before application

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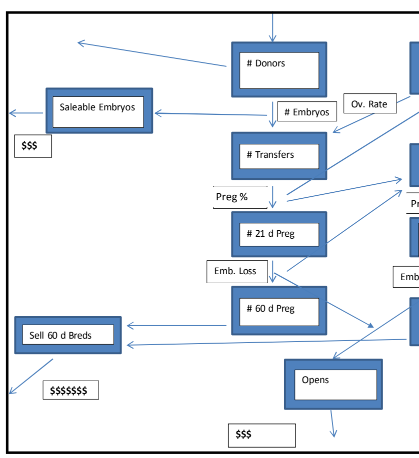
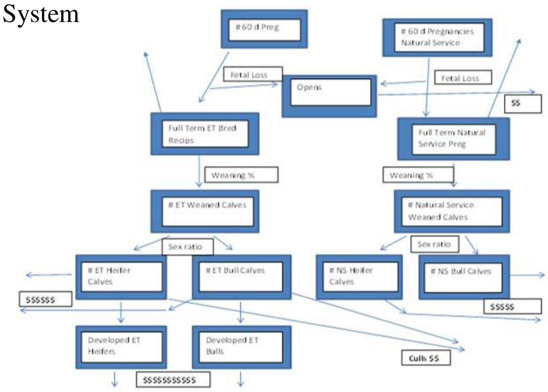
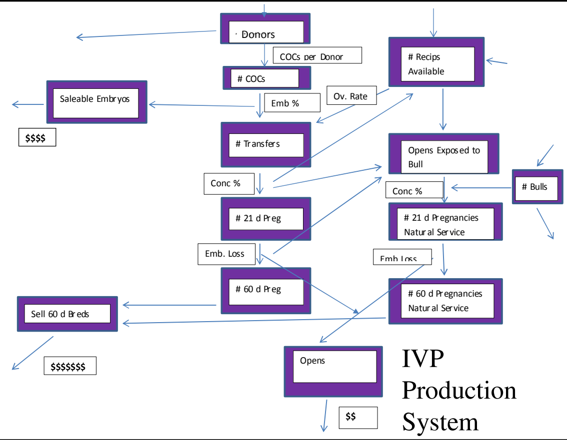


MOET Production System

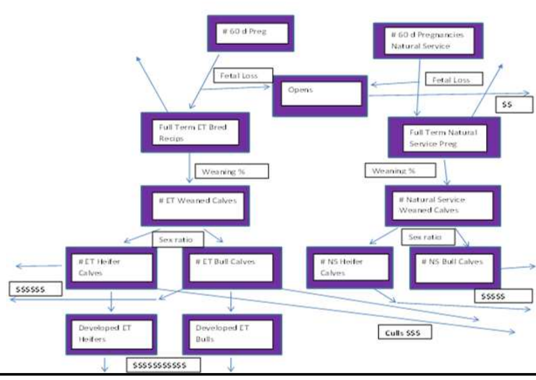
MOET Production System





IVP Production System

IVP Production System



Risk Analysis Prediction Model

- Current 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 Ovum Pick-Up (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

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Accounting for Production Variation

- Stochastic Model
  - Selects a random value from a defined range for each different iteration/replication
  - Unlike deterministic, which uses a set value
- Monte Carlo Simulation
  - Latin Hypercube
- Estimate Population Distributions
- @Risk© Software

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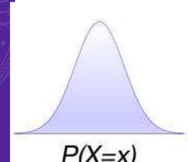
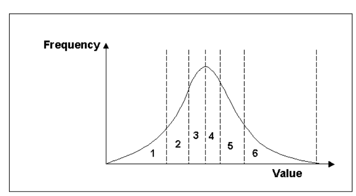
Random Number Generation





Monte Carlo Simulation Sampling **Latin Hypercube Simulation Sampling**

Image: http://www.xmswiki.com

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Estimating Population Distributions

- Needed for Latin Hypercube Simulation
- Use results found in literature and industry
  - Used all data from beef cows and heifers and dairy heifers
  - Omitted recipient data from lactating dairy cows
  - Omitted embryo production data and recipient data from bos indicus females

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Estimating Population Distributions Values >1

- When determining distribution of production levels greater than 1 (ex: mean number of oocytes/OPU)…
  - Apply Akaike Information Criterion to sample data to determine shape
  - Use @Risk© AICc distribution fitting tool
  - Values are meaningless until compared, lower is preferred
  - Akaike Information Criterion
    - $AICc = AIC + 2k(k+1)/(n-k-1)$
    - $AIC = -2(\text{log-likelihood}) + 2k$
    - n= sample size
    - k= number of estimated parameters
  - Calculate weighted mean and weighted SD from sample data to generate final parameters of distribution
  - Apply logic and industry knowledge to adjust if needed
    - Ex) truncate at 0

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Estimating Population Distributions for Mean Probabilities ($0 \le p \le 1$)

- When determining distribution of mean probabilities ($0 \le p \le 1$) (ex: probability of pregnancy)…
  - Distribution of sample means will be normal (central limit theorem)
  - Use sample means to generate standard error of the mean (SEM)
  - Create normal distribution using weighted mean from sample data
  - Substitute SEM for SD

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Estimating Population Distributions for Mean Probabilities ($0 \le p \le 1$)

- Distribution of mean probability is used as input in binomial distribution
- Binomial distribution parameters
  - p= true probability (input is probability distribution of true mean)
  - n= number of independent trials subject to p probability
  - Two outcomes from distribution: success or failure
- Binomial distribution is the distribution actually used to determine output in the model
- Output within model is the number of successes

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Estimating Population Distributions for Mean Probabilities ($0 \le p \le 1$)

- Example) Number of recipients pregnant at 21 d of gestation (14 d after transfer) following transfer of fresh IVD embryos
  - Binomial Distribution
  - Probability of pregnancy (p)= normal distribution with mean= 0.77 and SEM= 0.09
  - n= number of recipients that received embryo
  - Output to be used in next step of model= number of recipients pregnant at 21 d

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Economically Relevant Distributions

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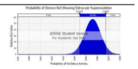
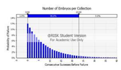
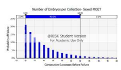
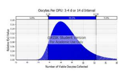
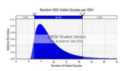
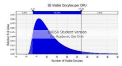
Stochastic Variable	Distribution Type	Distribution Parameters	Distribution
Percentage of Donors Showing No Signs of Estrus Following Superovulation	Normal	Mean=0.056 SEM=0.007 Trunc. Min=0 Trunc. Max=INF	
Number of Embryos Collected per Flush Following Superovulation and Insemination Using Unsorted Semen	Negative Binomial	p=0.12 r=1	
Number of Embryos Collected per Flush Following Superovulation and Insemination Using Sex-Sorted Semen	Negative Binomial	p=0.21 r=1	
Number of Viable Oocytes Collected per Non-Synchronized, Non-Stimulated (NS) OPU with 3-4 d or 14 d Interval	Lognormal	Mean=7.24 SD=2.71	
Number of Viable Oocytes Collected per NS OPU with Random Interval	Lognormal	Mean=8.8 SD=6.73	
Number of Viable Oocytes Collected per Follicular Wave Synchronized, Ovarian Stimulated (SS) OPU	Lognormal	Mean=11.5 SD=8.3	

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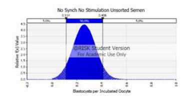
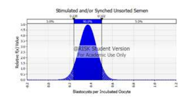
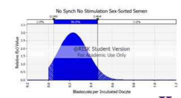
Stochastic Variable	Distribution Type	Distribution Parameters	Distribution
Percentage of Incubated Oocytes Developed into Blastocysts Following Fertilization Using Semen Unsorted for Sex, Following No Synchronization or Stimulation of OPU Donors	Normal	Mean=0.26 SEM=0.09 Trunc. Min=0 Trunc. Max=1	
Percentage of Incubated Oocytes Developed into Blastocysts Following Fertilization Using Unsorted Semen, Following Ovarian Stimulation Accompanied by Synchronization or Only Follicular Synchronization of OPU Donors	Normal	Mean=0.37 SEM=0.08 Trunc. Min=0 Trunc. Max=1	
Percentage of Incubated Oocytes Developed into Blastocysts Following Fertilization Using Sex-Sorted Semen, Following No Synchronization or Stimulation of OPU Donors	Normal	Mean=0.23 SEM=0.14 Trunc. Min=0 Trunc. Max=1	

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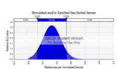
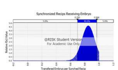
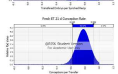
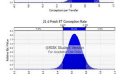
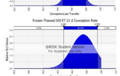
Stochastic Variable	Distribution Type	Distribution Parameters	Distribution
Percentage of Incubated Oocytes Developed into Blastocysts Following Fertilization Using Sex-Sorted Semen following Ovarian Stimulation and Synchronization or Only Follicular Synchronization of OPU Donors	Normal	Mean=0.33 SEM=0.13 Trunc. Min=0 Trunc. Max=1	
Percentage of Synchronized Recipients Receiving Embryo	Normal	Mean=0.85 SEM=0.09 Trunc. Min=0 Trunc. Max=1	
21 d Pregnancy Rate Following Transfer of Fresh IVD Embryos	Normal	Mean=0.78 SEM=0.09 Trunc. Min=0 Trunc. Max=1	
21 d Pregnancy Rate Following Transfer of Fresh IVP Embryos	Normal	Mean=0.64 SEM=0.10 Trunc. Min=0 Trunc. Max=1	
21 d Pregnancy Rate Following Transfer of Frozen-Thawed IVD Embryos	Normal	Mean=0.75 SEM=0.16 Trunc. Min=0 Trunc. Max=1	

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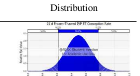
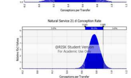
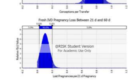
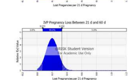
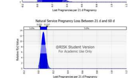
Stochastic Variable	Distribution Type	Distribution Parameters	Distribution
21 d Pregnancy Rate Following Transfer of Frozen-Thawed IVP Embryos	Normal	Mean=0.50 SEM=0.17 Trunc. Min=0 Trunc. Max=1	
21 d Pregnancy Rate Following Service by Natural Sire	Normal	Mean=0.77 SEM=0.074 Trunc. Min=0 Trunc. Max=1	
Pregnancy Loss Between d 21 and d 60 of Gestation Following Transfer of Fresh IVD Embryos	Normal	Mean=0.11 SEM=0.06 Trunc. Min=0 Trunc. Max=1	
Pregnancy Loss Between d 21 and d 60 of Gestation Following Transfer of Frozen-Thawed IVD Embryos	Normal	Mean=0.23 SEM=0.08 Trunc. Min=0 Trunc. Max=1	
Pregnancy Loss Between d 21 and d 60 of Gestation Following Transfer of IVP Embryos	Normal	Mean=0.20 SEM=0.08 Trunc. Min=0 Trunc. Max=1	
Pregnancy Loss Between d 21 and d 60 of Gestation Following Service by Natural Sire	Normal	Mean=0.07 SEM=0.03 Trunc. Min=0 Trunc. Max=1	

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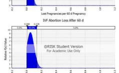
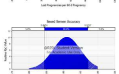
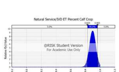
Stochastic Variable	Distribution Type	Distribution Parameters	Distribution
Fetal Loss After d 60 of Gestation Following Transfer of IVD Embryos	Normal	Mean=0.05 SEM=0.03 Trunc. Min=0 Trunc. Max=1	
Fetal Loss After d 60 of Gestation Following Transfer of IVP Embryos	Normal	Mean=0.05 SEM=0.05 Trunc. Min=0 Trunc. Max=1	
Fetal Loss After d 60 of Gestation Following Service by Natural Sire	Normal	Mean=0.02 SEM=0.01 Trunc. Min=0 Trunc. Max=1	
Percentage of Desired Sex Resulting From Use of Sex- Sorted Semen	Normal	Mean=0.91 SEM=0.04 Trunc. Min=0.8 Trunc. Max=1	
Percentage of Calves Weaned per Calving Cow for Pregnancies Derived from IVD Embryo or Natural Service	Normal	Mean=0.90 SEM=0.04 Trunc. Min=0 Trunc. Max=1	

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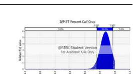
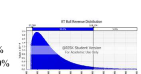
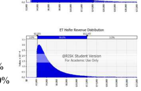
Stochastic Variable	Distribution Type	Distribution Parameters	Distribution
Percentage of Calves Weaned per Calving Cow for Pregnancies Derived from IVP Embryos	Normal	Mean=0.88 SEM=0.07 Trunc. Min=0 Trunc. Max=1	
Revenue Distribution of Developed Bulls	Lognormal	Mean=5000 SD=4000 Trunc. Min=5% Trunc. Max=100% Shift=1500	
Revenue Distribution of Developed Heifers	Lognormal	Mean=3500 SD=4000 Trunc. Min=5% Trunc. Max=100% Shift=1500	

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General Model Assumptions

- No correlation between traits/measurements
- All recipients enter the system as purchased opens
- All calves weaned same day
- If calf lives to weaning, it lives through development

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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

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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 recipient 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.

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Embryo Production Model Assumptions

- 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.

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Revenue Model Assumptions

- Bred recips sold as 60 d breds
  - No calf at side
- Calf development revenue occurs in same fiscal year that calves are born
  - Potentially not the case in real world

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Expense Model Assumptions

- **Return= Revenue- Variable Costs**
- **Does not include overhead or whole ranch costs**
  - Facilities
  - Random vet costs (pulling calves, emergencies, etc)
  - Labor when not applied to ET program
  - Equipment
  - Taxes

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Economic Output

- Net Present Value
  - $NPV = \sum_{n=1}^{N} \frac{ANCF_n}{(1+i)^n} + \frac{RESID_N}{(1+i)^N} - INV$
  - N=life of investment
  - i= discount/interest rate
  - $ANCF$= annual net cash flows
  - $RESID$= residual value
  - INV= original investment cost

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Economic Output

- Annuity Equivalent NPV
  - $A = NPV\left[\frac{i}{1-(1+i)^{-N}}\right]$
  - A= Annuity Equivalent NPV
  - NPV=Net Present Value
  - i= discount/interest rate
  - N= investment life in years

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Return on Investment

- *ROI* = (Net Profit / Total Investment) x 100
- Not adjusted for time

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Program Scenario Options

- Own Donors (or not)
- Own Recipients (or not)
- Embryo Production Method (MOET, IVP NS, IVP SS)
- Sex-Sorted or Unsorted Semen
- Biopsied or Non-Biopsied Embryos (MOET)
- Marketing Options
  - Sell 60 d bred recipients
    - Sexed pregnancy
    - Unsexed pregancy
  - Sell Weaned Calves
  - Sell Developed Bulls/Heifers
  - Sell leftover embryos

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Example) 3 Scenarios

- **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.

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Example) All Scenarios: Unsorted Semen- No Biopsy- Owned Donors- Owned Recipients- Market Developed Bulls and Heifers

- 100 recipients
- 5 MOET Donors (2 Flushes)
- 5 IVP Donors (5 aspirations)
- Own donors and recipients
- Unsorted Semen
- 6 calf crops
- Market Developed Bulls and Heifers according to price distribution
- Market Natural Service and Cull calves via feeder calf slide
- 5% discount rate
- **100,000 iterations**

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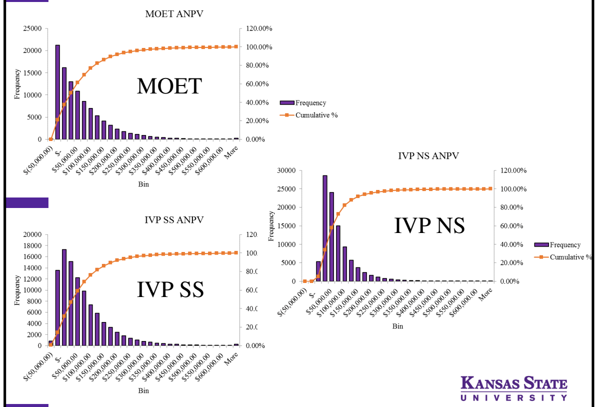
Scenario Results: ANPV



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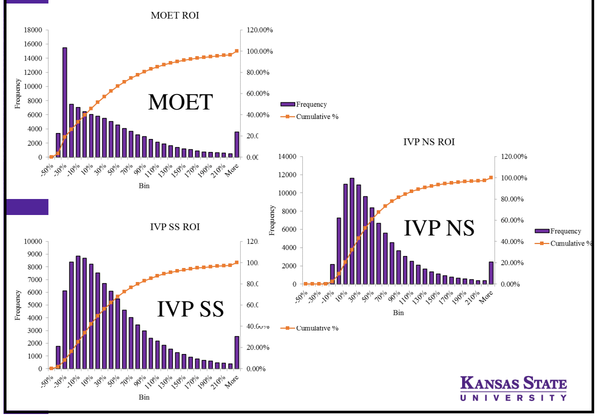
Scenario Results: ROI



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Scenario Results: ANPV

ANPV ($)	MOET	IVP NS	IVP SS
Mode	(36,136.47)	11,330.08	(13,349.03)
5%	(37,698.63)	(485.41)	(39,515.81)
25%	(19,847.21)	17,457.02	(9,775.75)
Median	23,972.81	40,630.35	30,865.14
75%	92,872.19	80,046.64	94,768.29
95%	253,972.08	185,595.71	245,330.27
Mean ± 90% C.I.	54,719.12±552.23	60,343.31±360.44	58,171.93±527.59
SD	106,166.50	69,295.08	101,430.06

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Scenario Results: ROI

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

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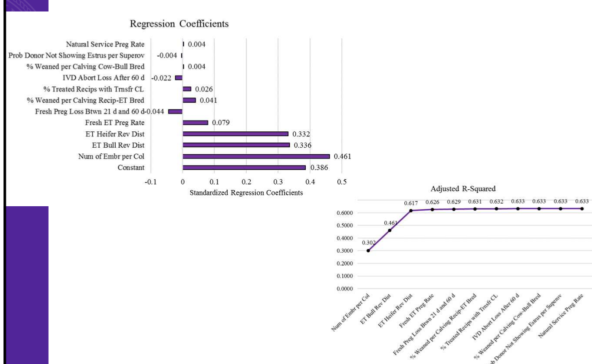
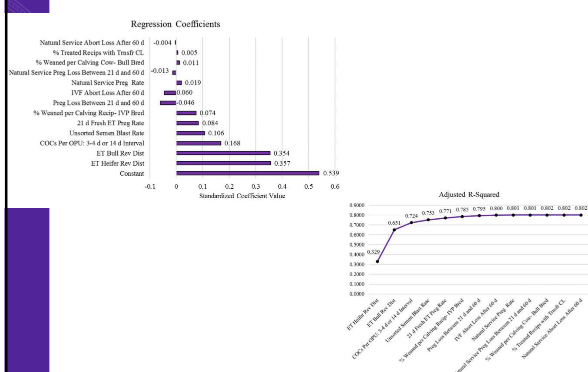
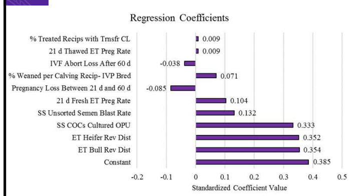
Scenario 1-MOET: Stepwise Regression on ROI

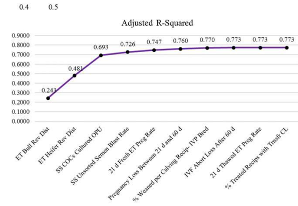


Scenario 2- IVP NS: Stepwise Regression on ROI



Scenario 3- IVP SS: Stepwise Regression on ROI





Next Steps

- More in-depth sensitivity analysis
- Explore optimization techniques
- Account for genetic change over time
- Requires continuous updates with an ever-changing ET industry
  - Especially regarding IVP and biopsy technology
- Model application

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Conclusion

- Stochastic simulation of alternative scenarios allows for in-depth assessment of economic risk
- Ability to incorporate user-defined variable values, specific to an individual operation
- Changing parameters and variable distributions is fairly simple (model structure is the hard part)
- Any model, no matter how robust, will never be completely accurate, as all are a simplified version of a complicated reality

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Questions?

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