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Tool Summary

Johne's disease requires renewed attention from cow-calf producers and is particularly crucial for anyone considering herd expansion or for seed-stock suppliers. However, Johne's disease can be an important cause of economic loss and an animal welfare concern for any affected herd. The biosecurity principles examined as part of a Johne's control program also apply to a number of other diseases that pose a risk to expanding herds, for many of which there are no vaccines or the vaccines have limited evidence of effectiveness.

The dynamic risk assessment tool constructed as part of this project is unique in that it is built on production, disease and testing data from Canadian beef herds. It also allows us to explore the impact of uncertainty in many factors that impact our decisions rather than simply guessing about what might happen by taking into account the element of chance in disease spread, the variation in time for disease progression among different animals, and finally the uncertainty regarding limitations in test performance. This program provides a tool to help us organize information and navigate a very complex problem over a ten-year time horizon. However, this tool is NOT a crystal ball. It is not intended to predict what will happen in an individual herd nor to provide specific recommendations on what an individual producer should do to manage this disease.

It is intended to help veterinarians and producers compare the relative costs and benefits of different disease management options under a range of different herd management scenarios and to be a learning tool for disease management.

Single Customizable Experiment vs. Comparing Multiple Testing Options

There are two types of experiments you can choose from to evaluate testing options.

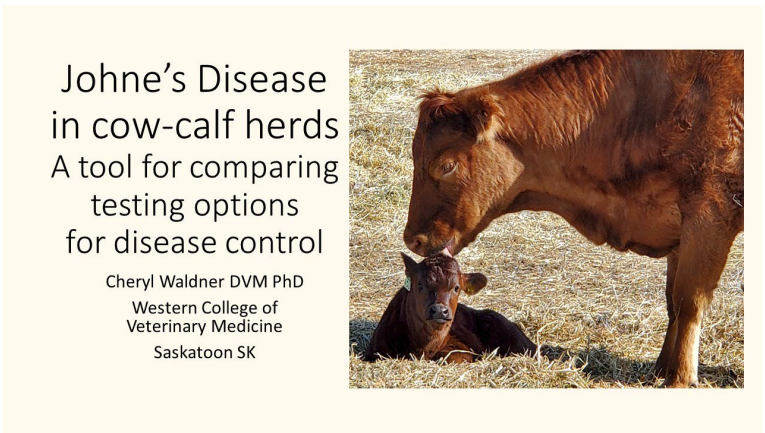
1. *Single customizable experiment* runs the model with the selected inputs and single strategy (or no testing) over one 10 year span. Therefore, it will only return one set of outputs.
2. *Comparing multiple testing options* AKA Monte Carlo experiments run the model multiple times showing multiple outputs to allow for variation from uncertainty and variability in the data while comparing different testing strategies with the same inputs.

Both are effective, however a single customizable experiment would be good to get an idea of how the tool works and to get a general idea of how testing options could impact your operation. Conversely, the Monte Carlo experiments represents variations of what could be possible and allows you to directly compare different testing strategies on the same graph.

Links to Instructional Videos

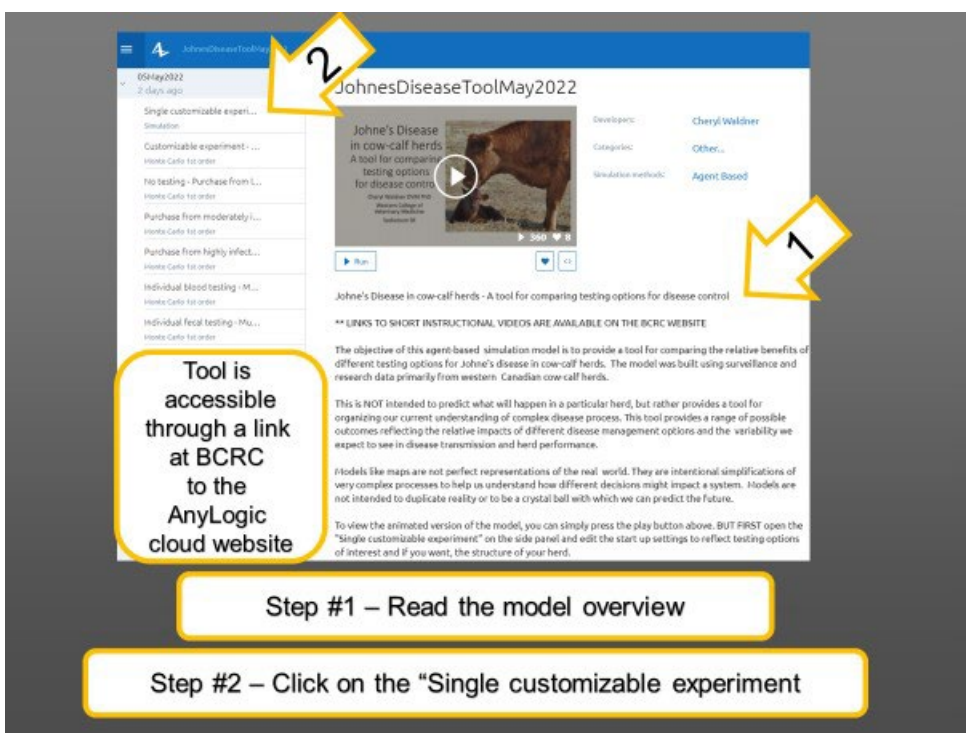
1. *Introduction and Overview*
2. *Customizing the Model Inputs to Answer Your Questions*
3. *Understanding the Model Results*
4. *Exploring Variation and Uncertainty with Multiple Experiments*

Single Customizable Experiment



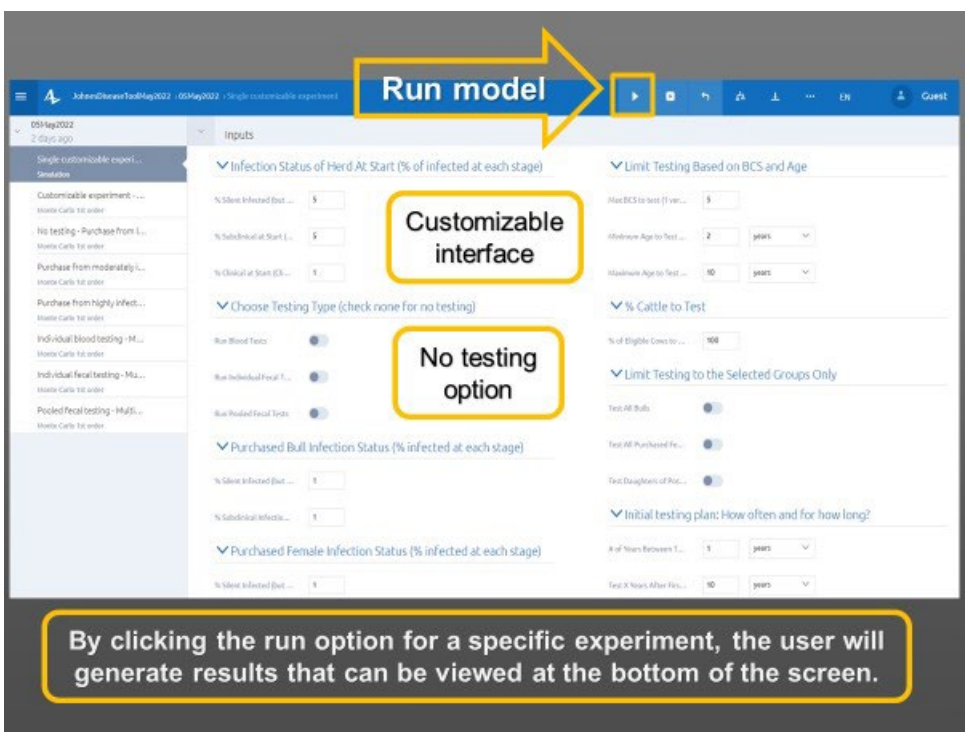
Overview of the Model

When the link on the BCRC website is accessed, the following view is presented.

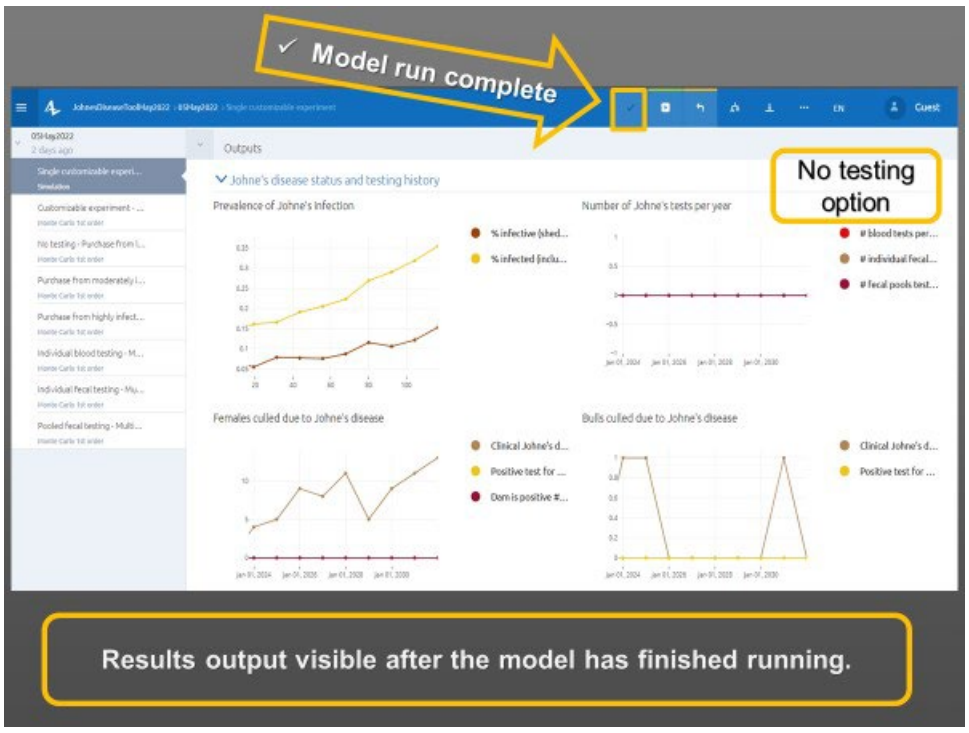


Read the model overview before you start.

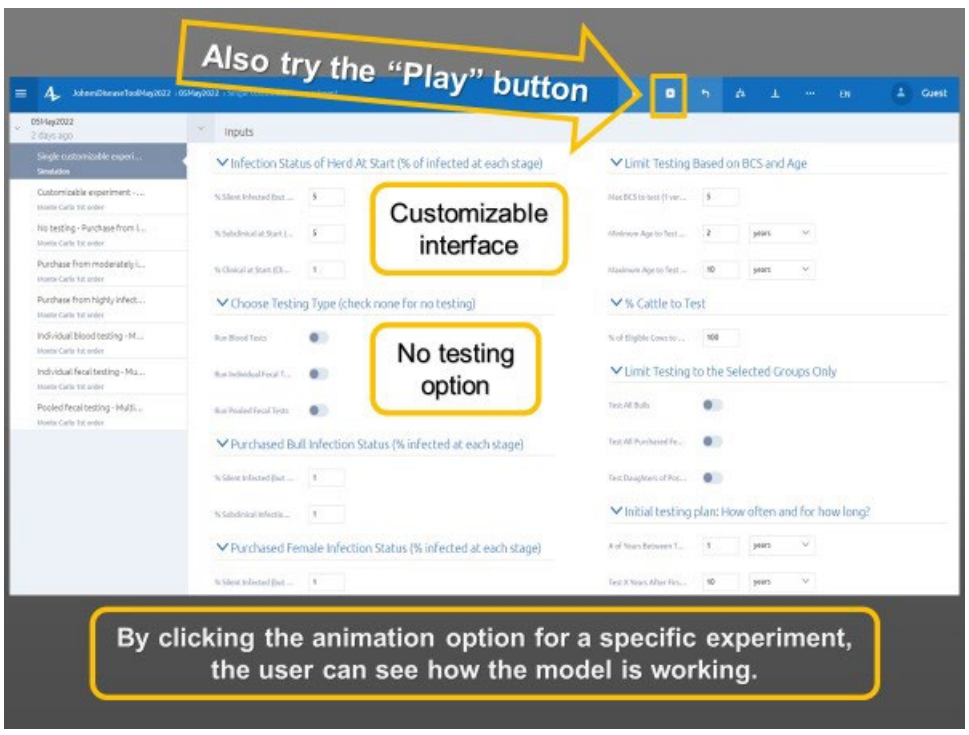
Then select the "Single customizable experiment". There is an input section that allows you to customize the model. Below is an example of a "Single customizable experiment" modeling the impact on a herd if no testing is done.



Followed at the bottom of the screen by model outputs.

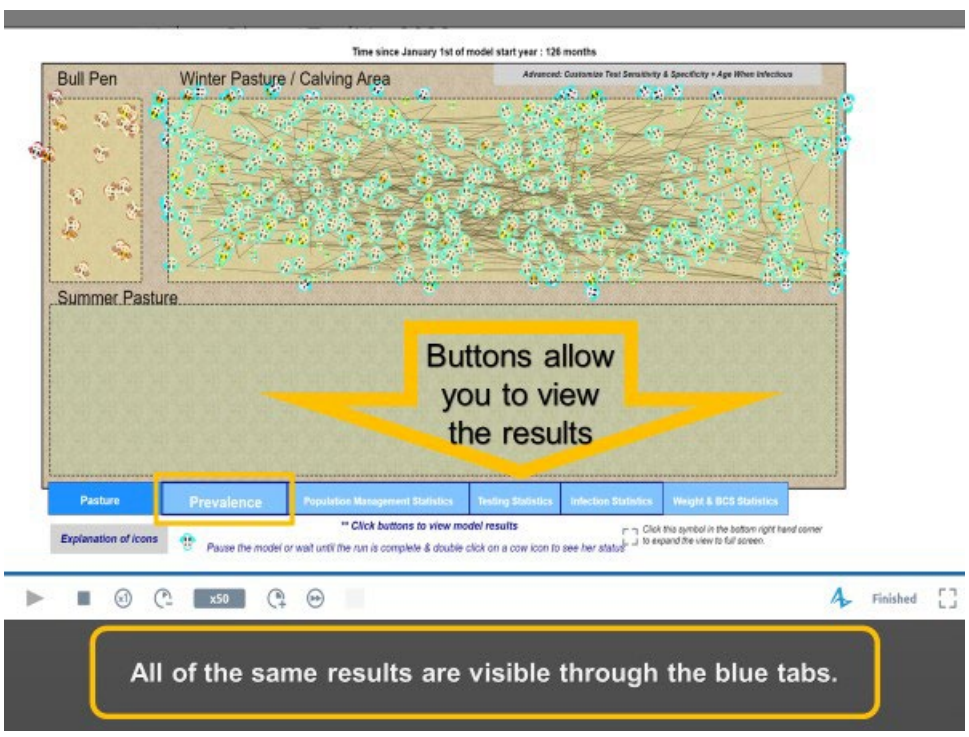


The run interface can be used to generate the graphics on the main interface OR you can try the “Play” button after you have updated the inputs to get a glimpse of how the model creates and manages a herd of cows, bulls, replacements and calves.

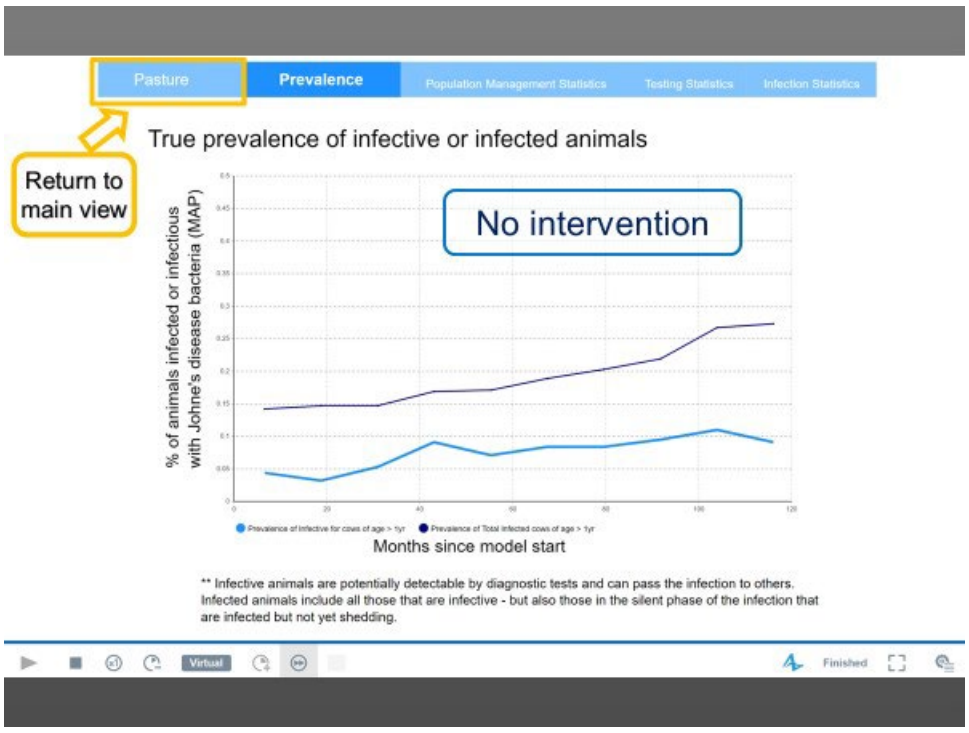


The animated “Pasture” interface shows you the herd as it cycles through the 10 year model time frame.

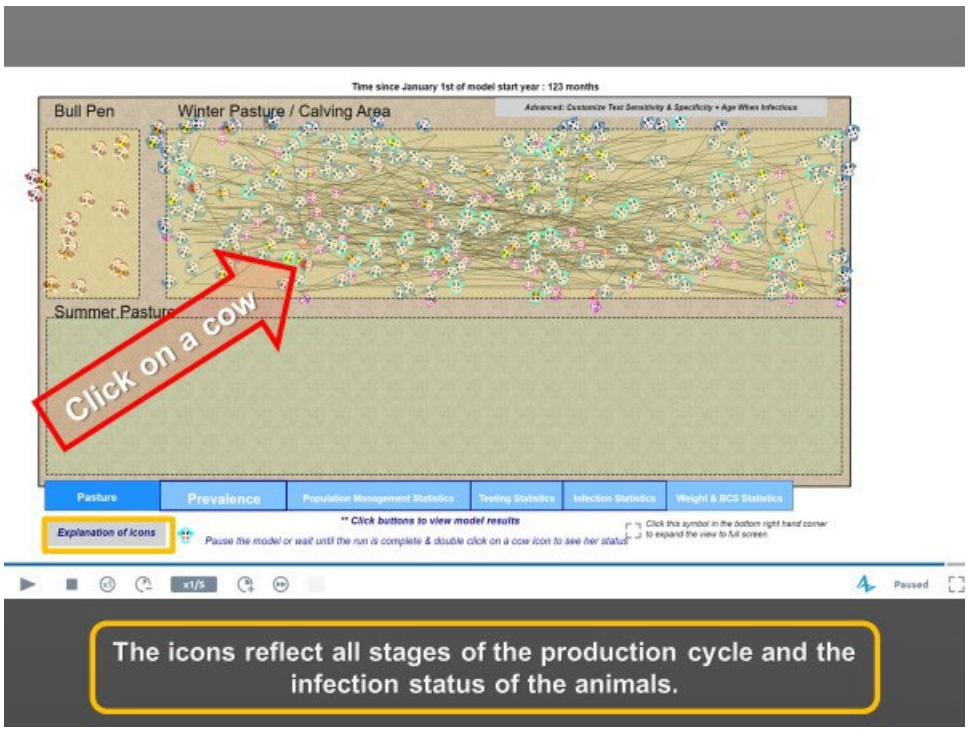
The model starts April 1, 2022 and runs for 10 years.



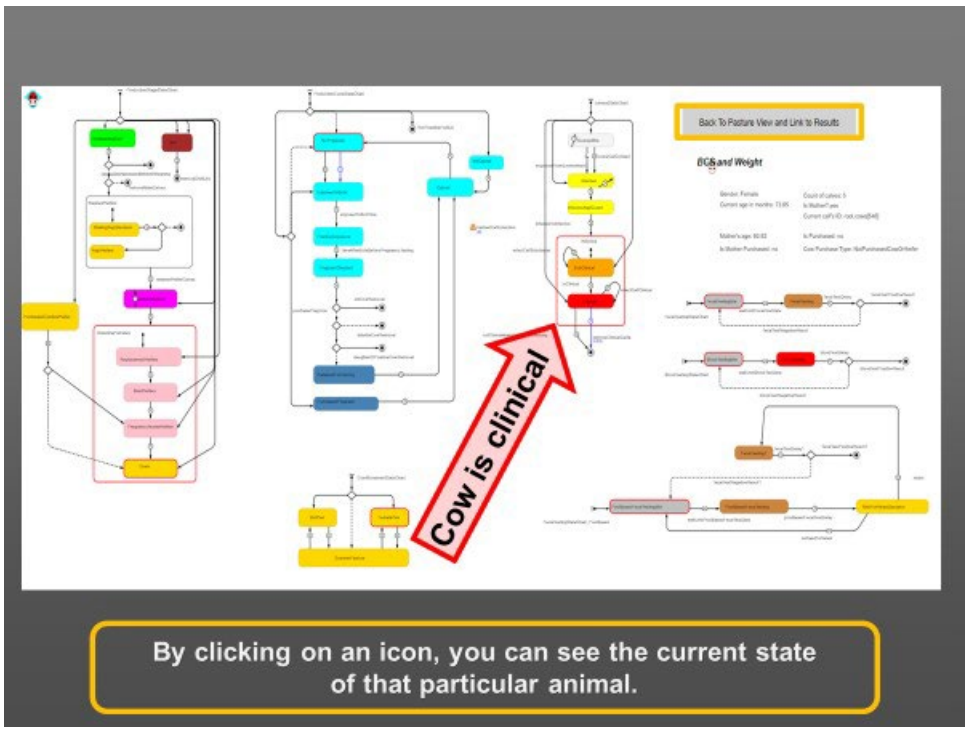
The same results visible on the main view under “Run” are also available under “Play” by clicking on the blue tabs.



You can click on the various tabs to check out the results – note the results will reflect the current “Input” settings for the single experiment on the main screen as they were when you pressed the “Play” button.

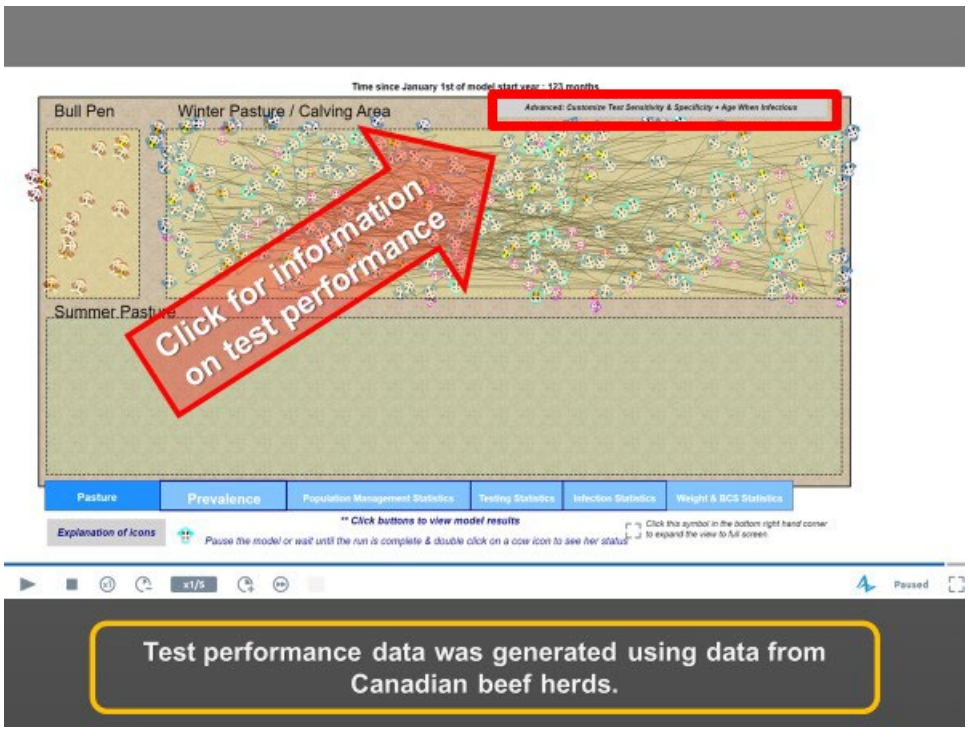


Click on a cow to see the detailed status for each animal.



The various charts describe the animal you are viewing, its stage in the production cycle , its infection status, a bit about its history, its current testing status, and its current location.

When you are done hit the button to return to the “Pasture” view.

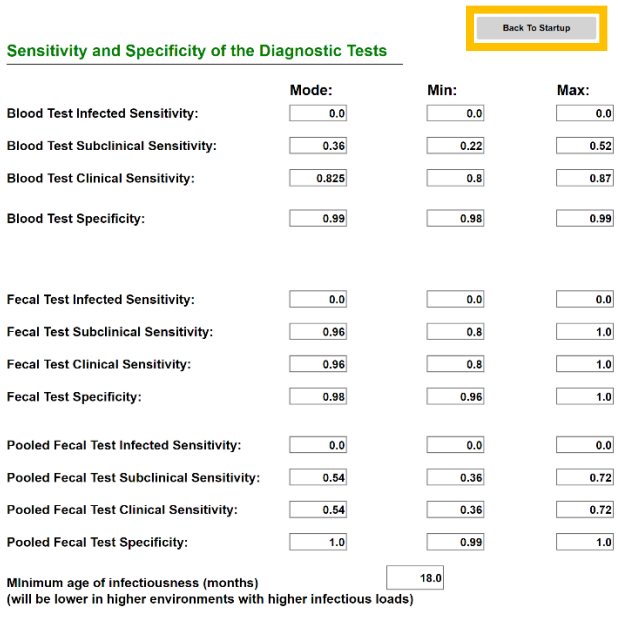


Sensitivity and Specificity

It is possible to view **the sensitivity and specificity** of the various tests through a button located on the bottom of this page as well as changing the minimum age that an animal can become infectious. The default minimum is 18 mo. However, there are many factors that can result in most animals not being infectious until they are at least 2 yrs.

The values for sensitivity and specificity were estimated from Bayesian Latent Class Analysis of data collected as part of the Canadian Cow-Calf Surveillance Network in 2019.
The only exception was for the values for blood test clinical sensitivity. The references for that set of values are as follows:

- Sweeney, R.W., Whitlock, R.H., Buckley, C.L., and Spencer, P.A. 1995. Evaluation of a commercial enzyme-linked immunosorbent assay for the diagnosis of paratuberculosis in dairy cattle. J. Vet. Diagn. Invest. 7: 488-493. https://journals-sagepub-com.cyber.usask.ca/doi/abs/10.1177/104063879500700411
- Bech-Nielsen, S., Jorgensen, J.B., Ahrens, P., and Feld, N.C. 1992. Diagnostic Accuracy of a Mycobacterium phlei-Absorbed Serum Enzyme-Linked Immunosorbent Assay for Diagnosis of Bovine Paratuberculosis in Dairy Cows. Journal of Clinical Microbiology. 30(3): 613-618. https://jcm.asm.org/content/jcm/30/3/613.full.pdf
- Billman-Jacobe, H., Carrigan, M., Cockram, F., Corner, L.A., Gill, I.J., Hill, J.F., Jessep, T., Milner, A.R., and Wood, P.R. 1992. Aus Vet J. 69(2): 25-28. https://onlinelibrary-wiley-com.cyber.usask.ca/doi/abs/10.1111/j.1751-0813.1992.tb07426.x



	Mode:	Min:	Max:
Blood Test Infected Sensitivity:	0.0	0.0	0.0
Blood Test Subclinical Sensitivity:	0.36	0.22	0.52
Blood Test Clinical Sensitivity:	0.825	0.8	0.87
Blood Test Specificity:	0.99	0.98	0.99
Fecal Test Infected Sensitivity:	0.0	0.0	0.0
Fecal Test Subclinical Sensitivity:	0.96	0.8	1.0
Fecal Test Clinical Sensitivity:	0.96	0.8	1.0
Fecal Test Specificity:	0.98	0.96	1.0
Pooled Fecal Test Infected Sensitivity:	0.0	0.0	0.0
Pooled Fecal Test Subclinical Sensitivity:	0.54	0.36	0.72
Pooled Fecal Test Clinical Sensitivity:	0.54	0.36	0.72
Pooled Fecal Test Specificity:	1.0	0.99	1.0

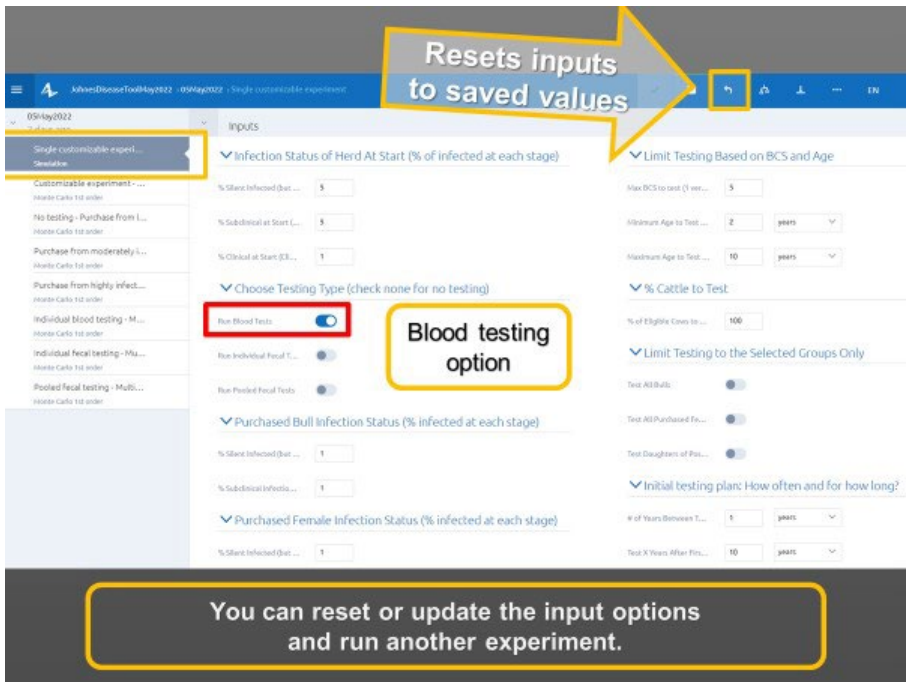
MInimum age of infectiousness (months) 18.0
(will be lower in higher environments with higher infectious loads)

For each run, values for the various sensitivities and specificities are selected by the model at random. The average will be selected the most often and values approaching the extreme minimums and maximums increasingly less frequently.

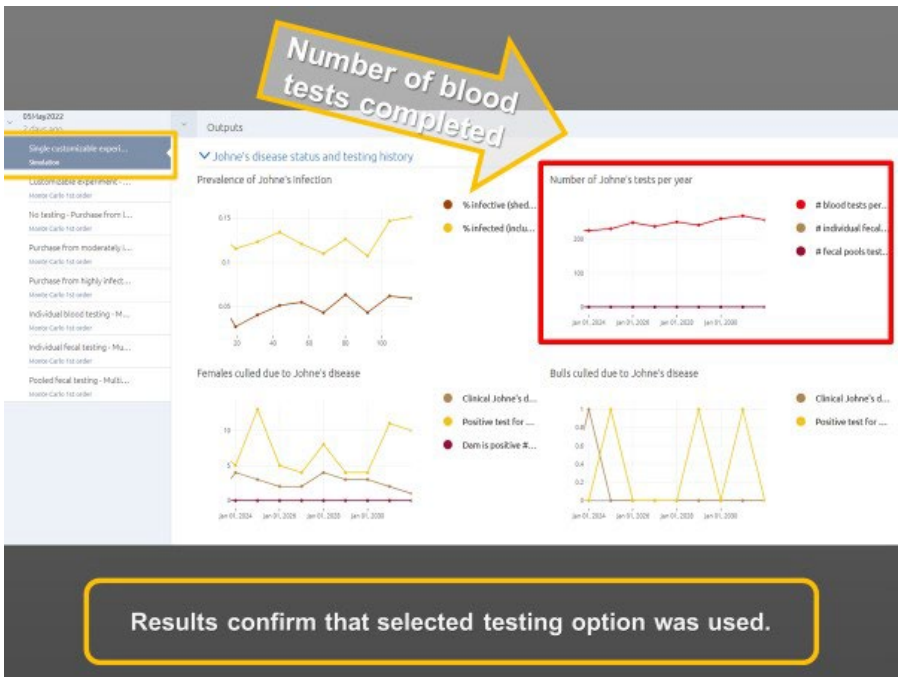
**Note - the sensitivity of the tests for animals that are infected but not yet infectious is set to zero for the model as it is very unlikely the blood test will be able to detect them before they start shedding and by definition if they are not shedding, the fecal test can’t detect them.

The animation will stay open for a maximum of 5 min. After that you can either restart it or return to the main input screen and continue to explore the model options.

Selecting Testing Options



To select a specific type of test, just toggle the switch to the on position (see above).



You can view the impact of testing in the graphs at the bottom of the screen. You will see the % of animals greater than 2 years of age that are infectious or shedding the Johne's organism as well as the total % of animals greater than 2 years of age that are infected – some of which will be in the silent stage of infection.

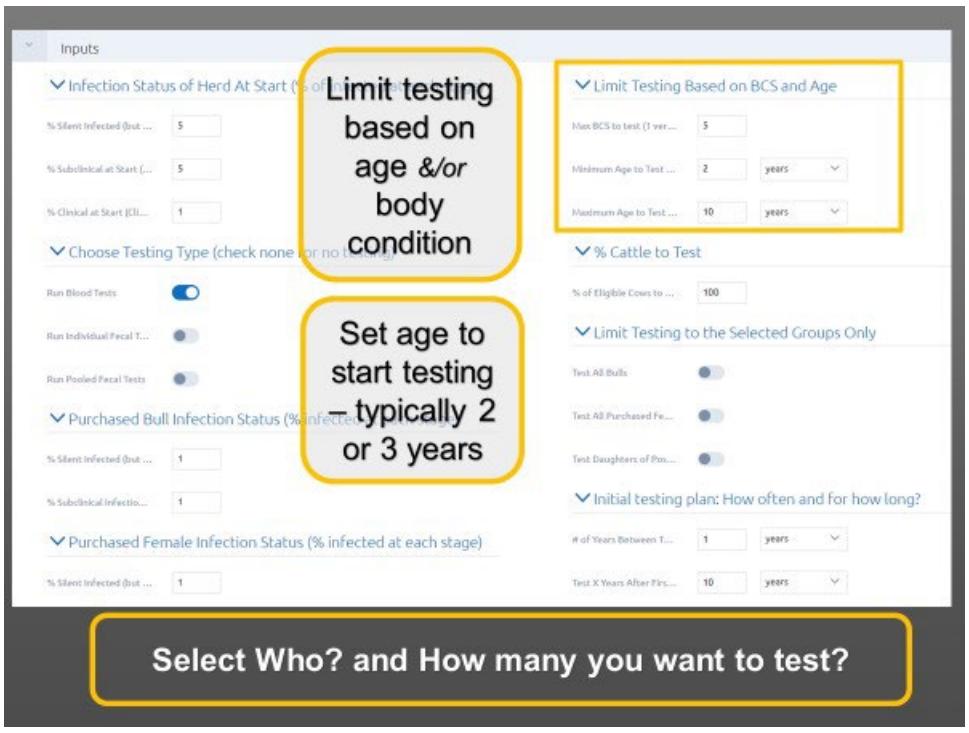
You will also be able to view the number of tests completed given the directions for testing set out above in the input screen.

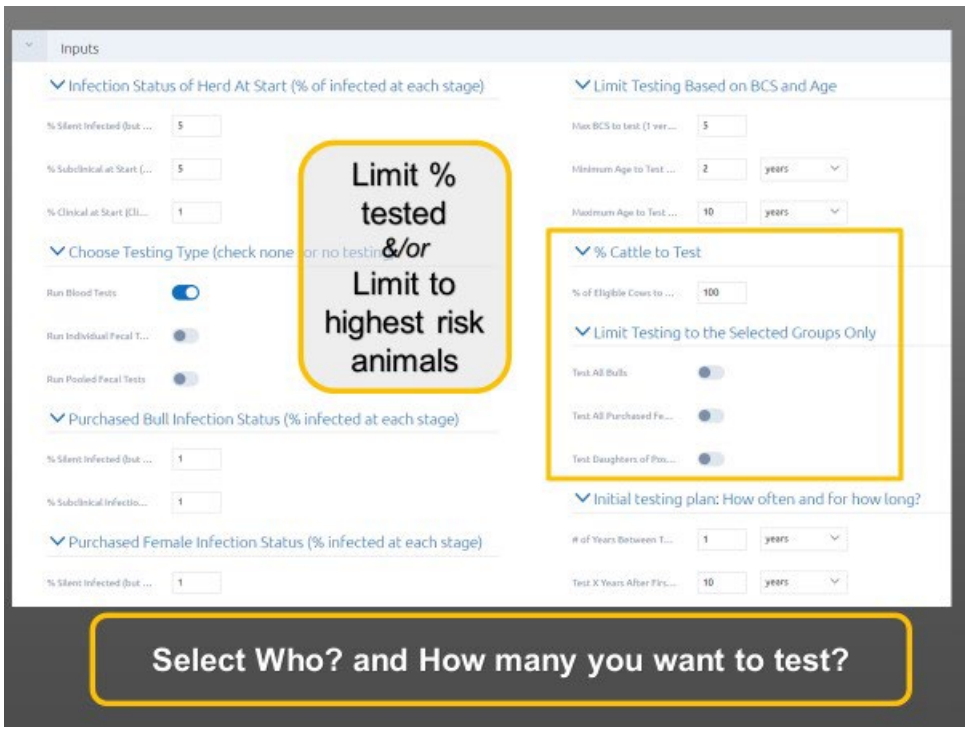
This is a critical piece to check to ensure that you have your inputs set up as you intended.

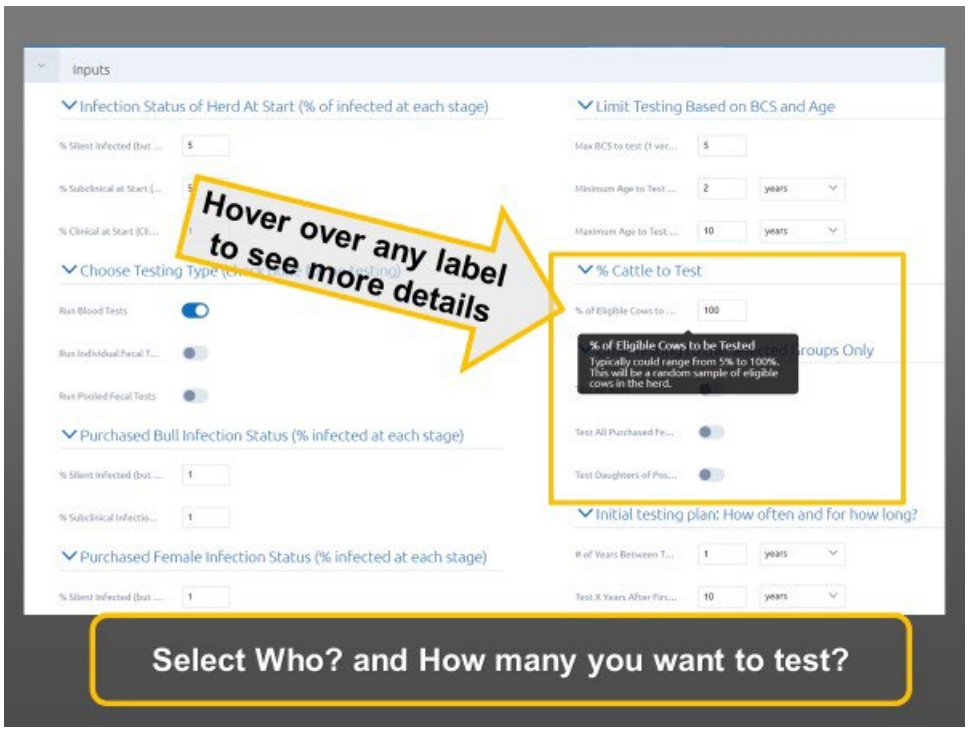
Selecting Who to Test and How

There are several options for limiting the number of animals to be tested that include:

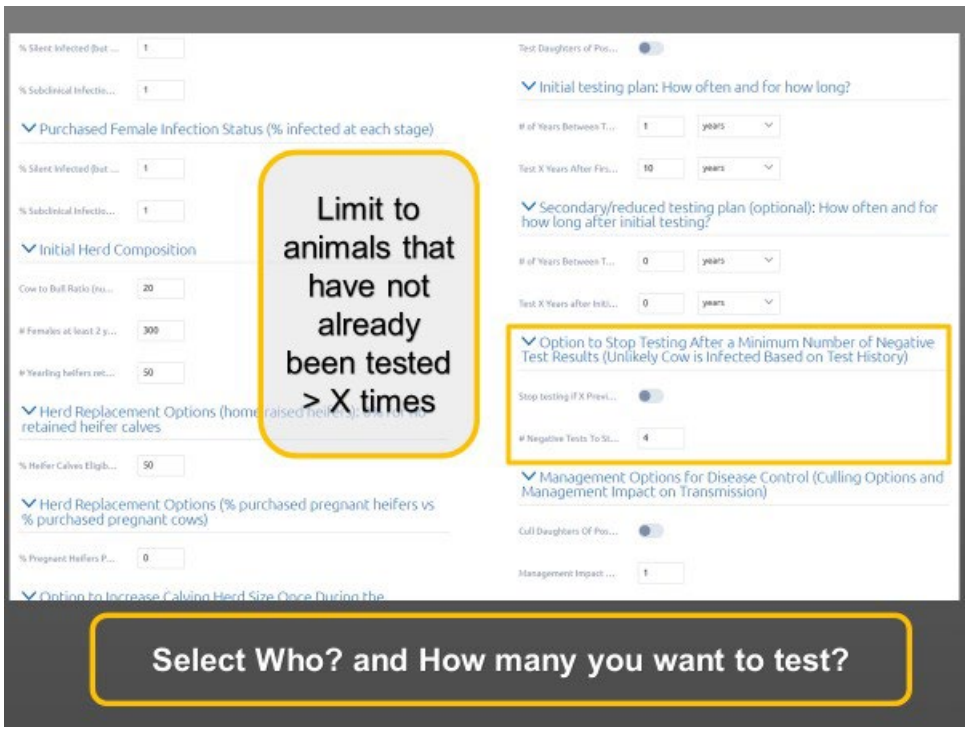
- Testing animals older than a certain age – typically this would be 2 or 3 years.
- Testing animals less than a specific age. Finding potential shedders in animals greater than 10 years of age is unlikely but not impossible.
- Testing animals that are thinner than a specific body condition score. Note body condition is set up in the model based on a 5 point scale where 1 is very thin and 5 is fat.
- Testing only specific groups within the herd:
    - Bulls
    - Purchased cows or heifers
    - Test daughters of dams that have either developed clinical disease or tested positive
- Testing a random sample of the eligible animals.







Finally, you can limit testing to only those animals that have not already tested negative more than a specified number of times. The basis for this is that if an animal has already tested negative more than X times, it is unlikely that it will later become positive.

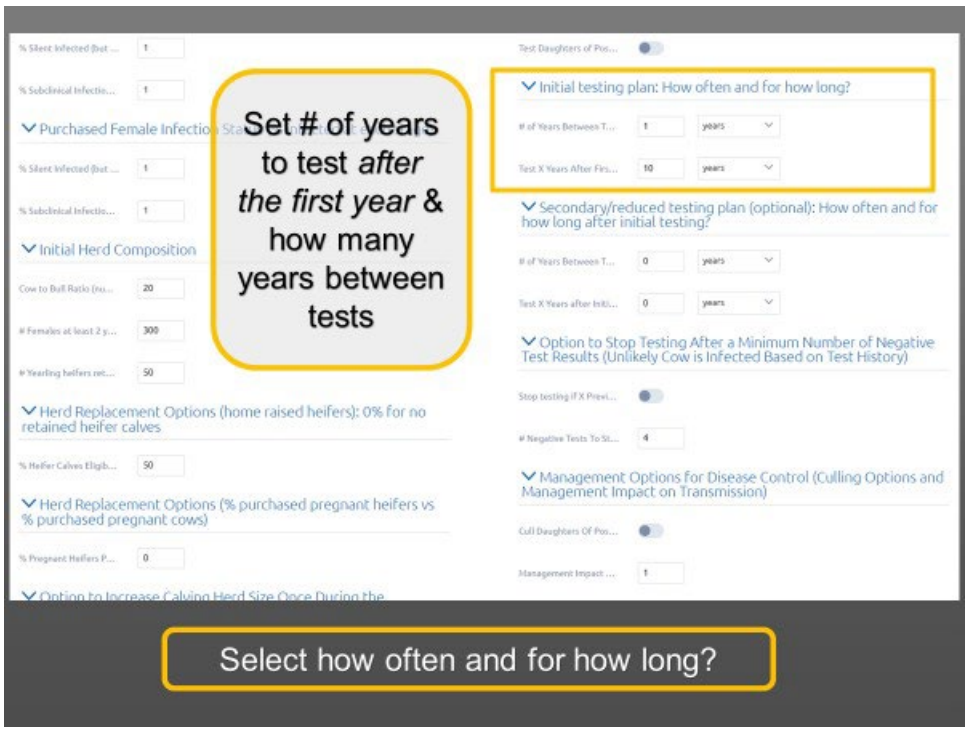


Once you have selected who you want to test, the next task is to select how often you want to test and for how long (how many years).

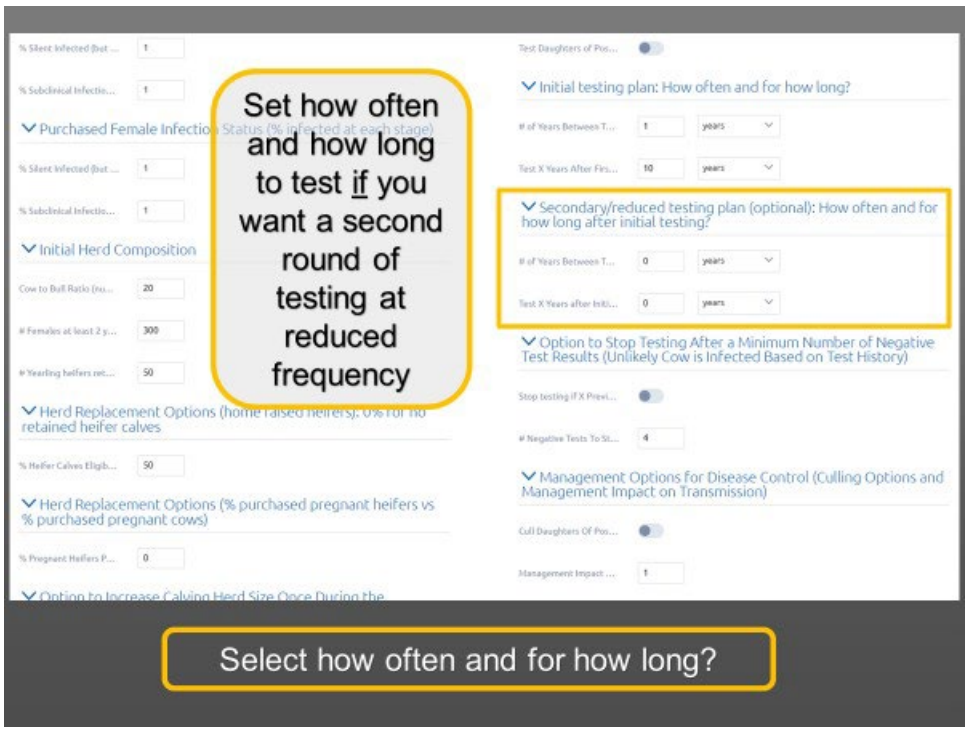
First, enter the number of years between tests.

- To test once a year, enter 1.
- To test 2 times per year, enter 0.5.
- To test every 2 years, enter 2.

Second, enter how many years after initial test(s) that you want to test at this frequency.



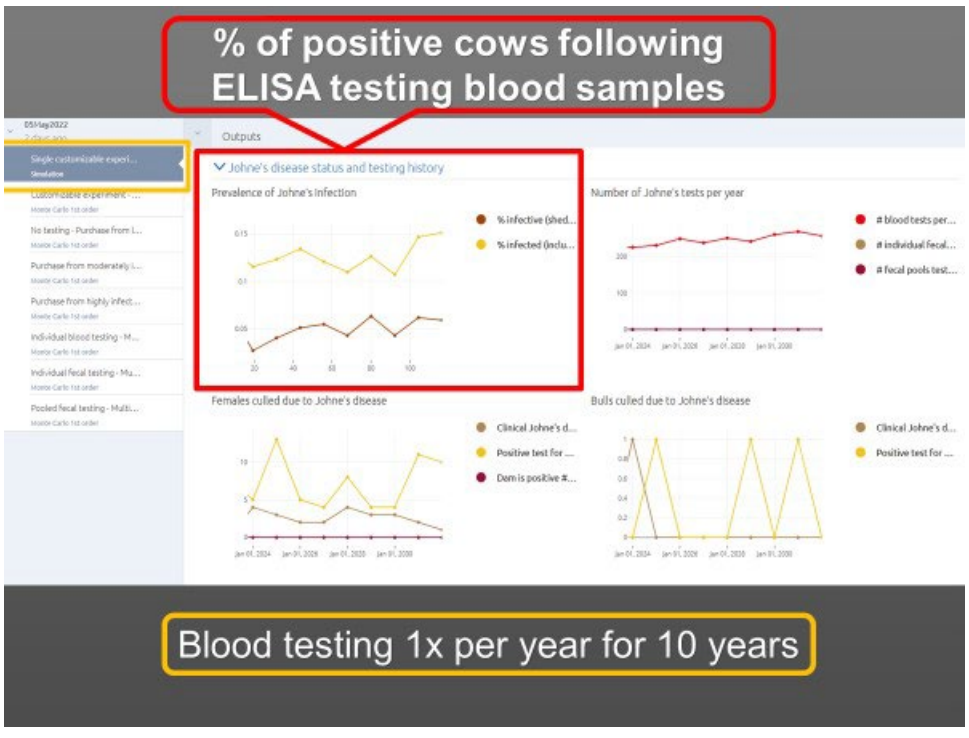
You also have the option below to test for a number of years at a higher rate, followed by a few years at a reduced rate. This is a way to save resources while maintaining disease control.



Once you have decided on your testing options and run the model, go back and check on your results.

Once you have checked to make sure everything worked as intended, take a look at the prevalence of infection in your herd.

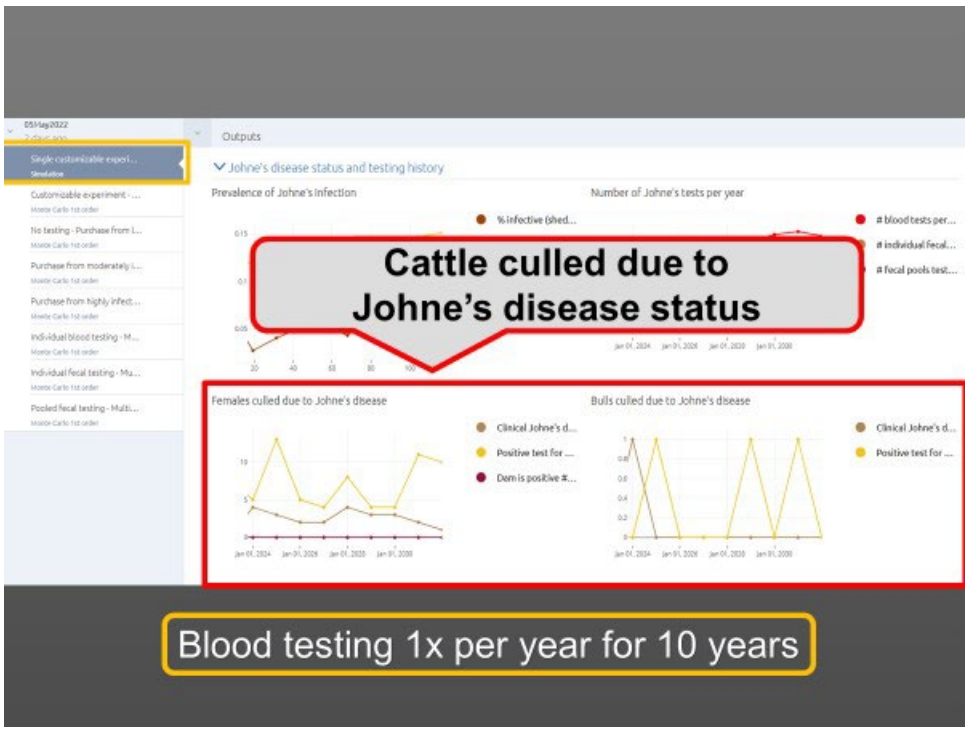
Analyzing Results



** NOTE – this is NOT the test positivity rate. This is the actual percentage of animals greater than 2 years of age in the model that are in various stages of infection. Those that are infectious can potentially be detected by the tests. Those that are in the silent phase cannot reliably be detected.

The results section also shows the number of cows and bulls culled due to Johne's disease. This includes the number culled as clinical cases and the number culled because they tested positive.

** Note - there is display panel within the animation that shows the number that were false positives and negatives.



The model also summarizes the impacts of Johne's on the calf crop.

First, as the culling rate increases, the number of heifers will increase. This will impact calf survival and weaning weights as calf weaning weight is impacted by cow age for all cows less than 5 and greater than 10. This adjustment is based on data from the BCRC website.

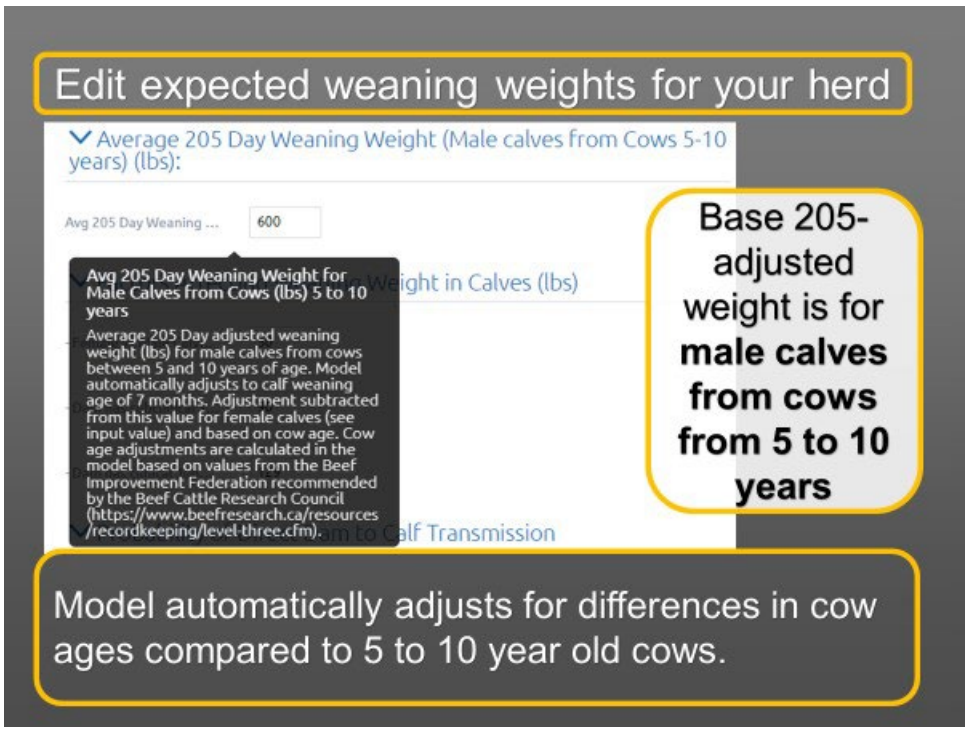
The Beef Improvement Federation (BIF), an international organization dedicated to standardizing animal performance records across breeds and countries, recommends that weaning weights be standardized to 205 days-of-age and a mature age-of-dam basis. The chart below provides adjustment factors to use when calculating 205-day weights.

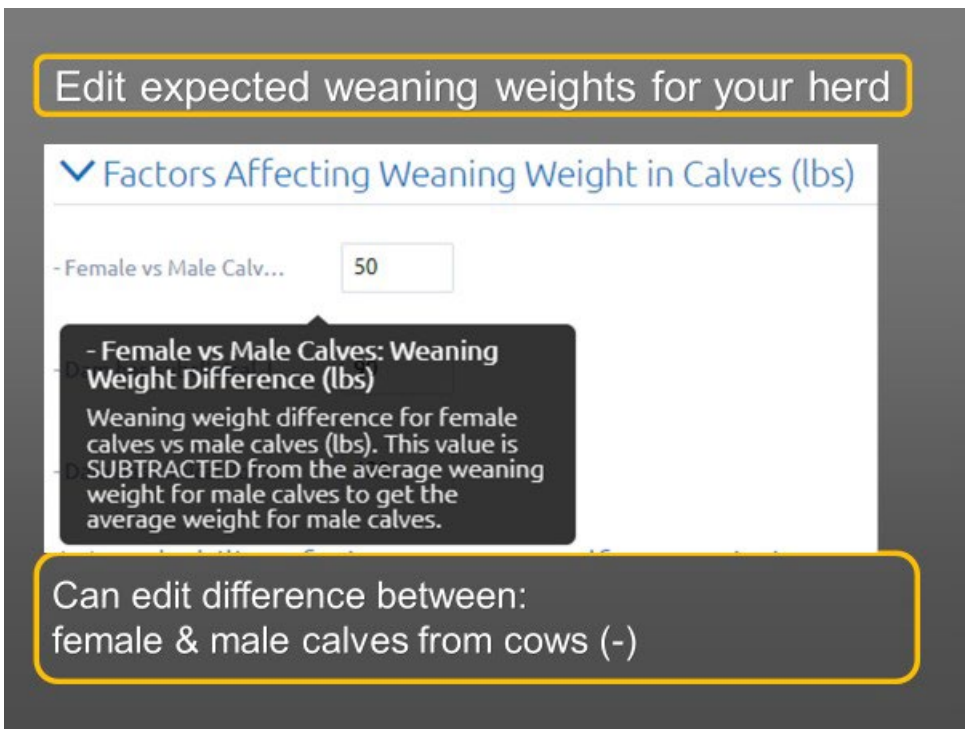
Table 1: BIF Standard Adjustment Factors for Weaning Weight

Age of Dam at Birth of Calf	Male	Female
2	+60	+54
3	+40	+36
4	+20	+18
5-10	0	0
11 and older	+20	+18

Calves from cows that are in the silent stage of Johne's are assumed to have expected weaning weights while calves of cows in the subclinical or clinical stages have substantially decreased weaning weights.

The target weaning weight for the herd for male calves from mature cows can be set in the model input section as well as the weaning weight difference between female and male calves.





The last panel on the results section summarizes the herd inventory. This includes total breeding females broken down by cows > 2 years old, yearling heifers until calving and replacement heifers up to 1 year of age.

Bulls are summarized as yearlings and bulls between 2 and 6 years of age.

Other displays describe females and bulls culled for reasons other than Johne's. For bulls this is limited to age for simplicity. Females can be culled due to age (> 12 years), because they are not pregnant, and/or to adjust inventory by selling pregnant heifers if too many replacement heifers are kept in any year.

All bulls are assumed to be purchased.

Females can be home raised heifers or purchased cows or pregnant heifers.

The number of replacements required will be less predictable and will vary more widely where Johne's is active in the herd (as seen by annual fluctuations in the numbers of replacement heifers retained).

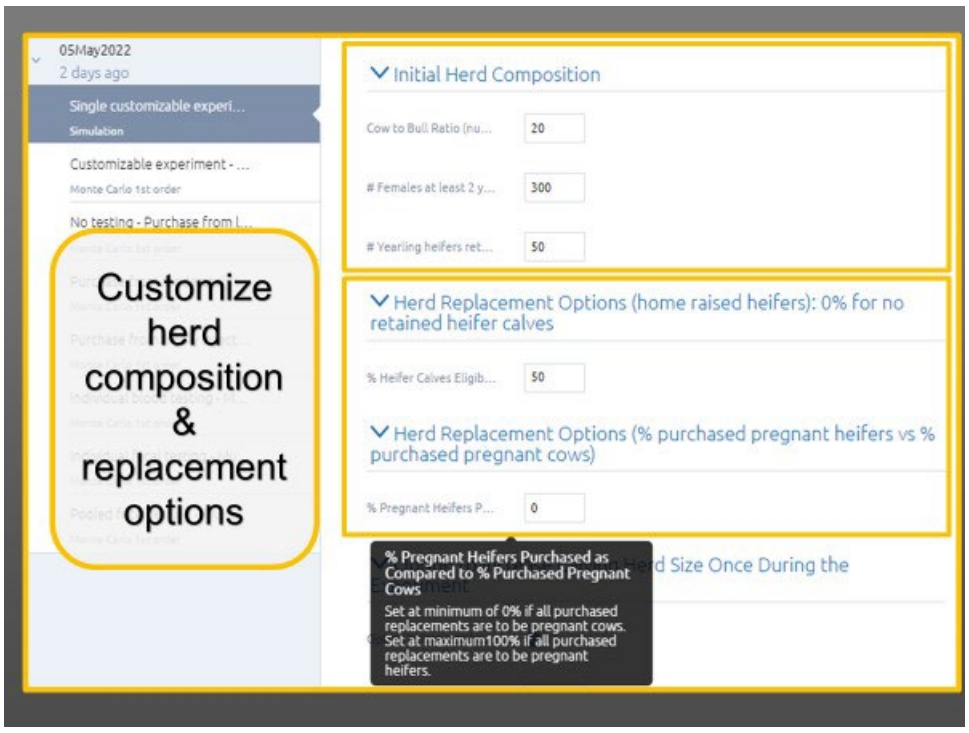
You can choose the replacement strategy on the input section. The model will attempt to keep the number of calving cows at the original number (inputted as cows greater than 2 years of age) unless told to increase herd size.

The model first assesses based on inputs if you want to keep any replacement heifers. This is set by determining the % of Heifers eligible to be replacements. If you don't want to keep any heifers, set this to zero.

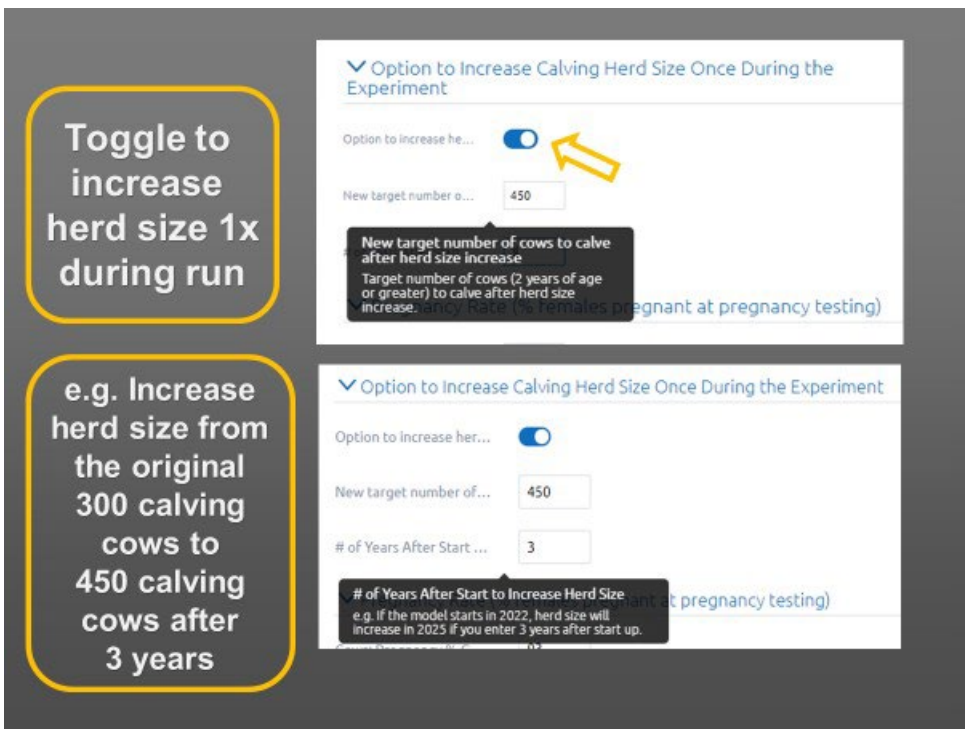
If you expect a certain percentage of your home raised heifers will be eligible as replacements, set that value. Typically this might be 30 to 50% of all female calves weaned. The model will only keep the number necessary to maintain herd size.

If the number of heifers kept one year is not sufficient to ensure the calving herd stays the same size, pregnant females will be purchased in the model. The percentage of pregnant heifers purchased as compared to pregnant cows can be set in the inputs.

Customizing Herd Composition and Replacement Options



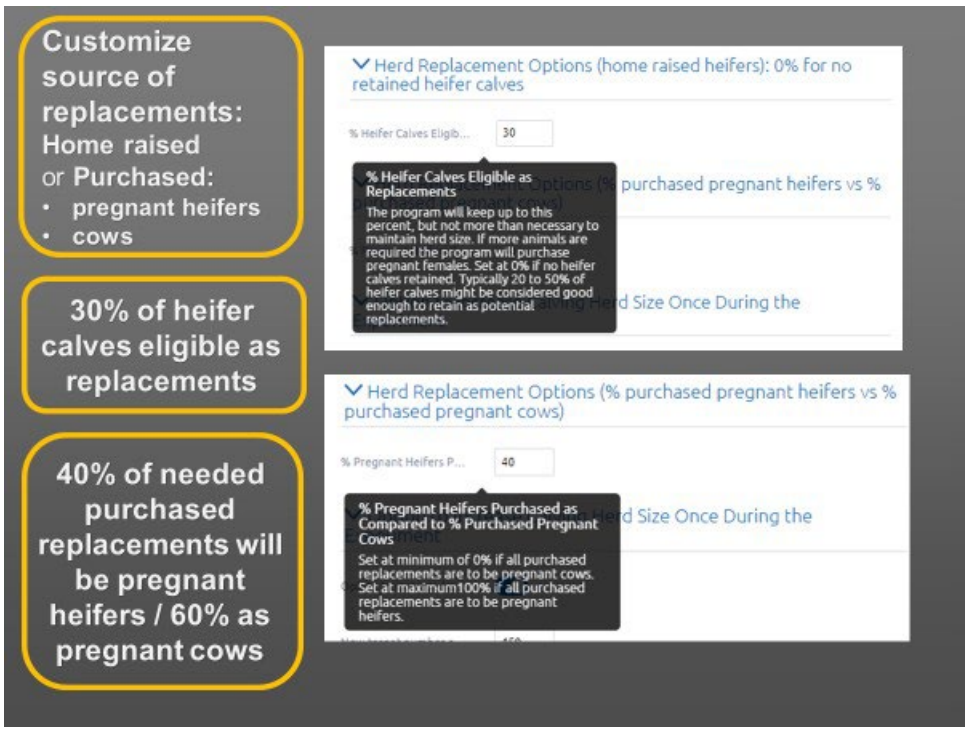
In the settings above, the model will keep up to 50% of home raised heifers in any year. If the number of heifers was not enough due to unexpected Johne's culls, the model will purchase pregnant cows to maintain calving herd size. No pregnant heifers will be purchased as the percentage of pregnant heifers is set to zero.



You can choose to increase herd size once during the model run. Toggle the option to increase herd size to on, set the year that you want herd size to increase and then set the new number of cows that you want to calve. (The model is currently not set to decrease herd size.)

With the settings above, you will increase calving herd size from 300 to 450 after the third year. So in this example, we start in 2022 and will increase herd size in 2025.

The increase will be composed of keeping up to 30% of home raised heifers (see settings on the next page) and then purchasing pregnant females. Forty percent of the pregnant females will be heifers based on the inputs selected below.



"Herd Replacement Options" allows the user to:

- Increase herd size by a defined percentage at one point during the 10 yr model run.
  (Currently it is not possible to decrease herd size although that option could be explored if there was sufficient need.)
- Customize the source of replacement females. *All bulls are purchased by default in the model as yearlings and exposed to breeding at 15 mo of age.
  - The user is first asked to define the percentage of total heifer calves that are available as potential replacements. If this value is set to 0, no heifer calves will be retained. This value would typically be somewhere between 20 and 50 %. The default is set to 50%.

    When culls are replaced after pregnancy testing, the model will first look to home raised replacement heifers to see if there is an adequate number to keep the number of calving females at the target value defined at start up.

  - The user is then asked to describe what type of animal should be purchased if it is necessary to purchase replacement females. The first number to set is the percentage of purchases that will be pregnant heifers. If this value is set to 0, only cows will be purchased when necessary. If this value is set to 100, only pregnant heifers will be purchased as necessary for replacements.

- Finally, the user is asked to define when the cows will be purchased. The default is purchasing pregnant cows in the fall after pregnancy testing, when needed to maintain herd size.

The changes can and should be verified after the model is run by checking the "Herd Inventory Summary".

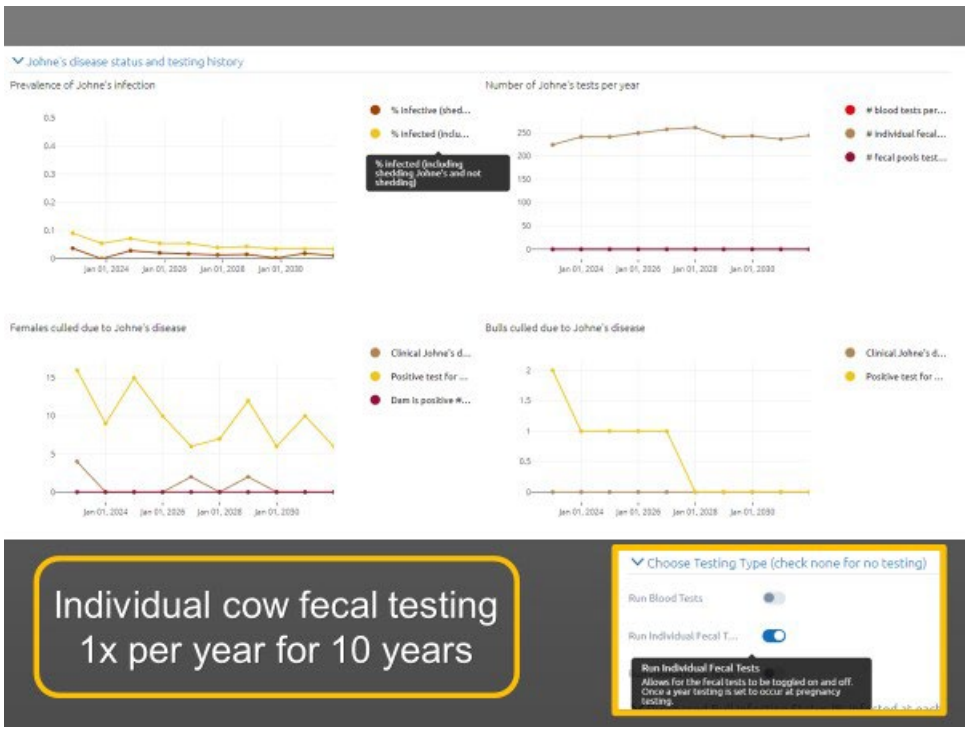
Note in the photo below, the increase in the number of cows and calves born after year 3 in the first graph as well as corresponding increase in the number of bulls to maintain the defined bull to cow ratio.

The increase is made up of a mix of home raised heifers, purchased heifers and purchased cows as defined in the screen above.

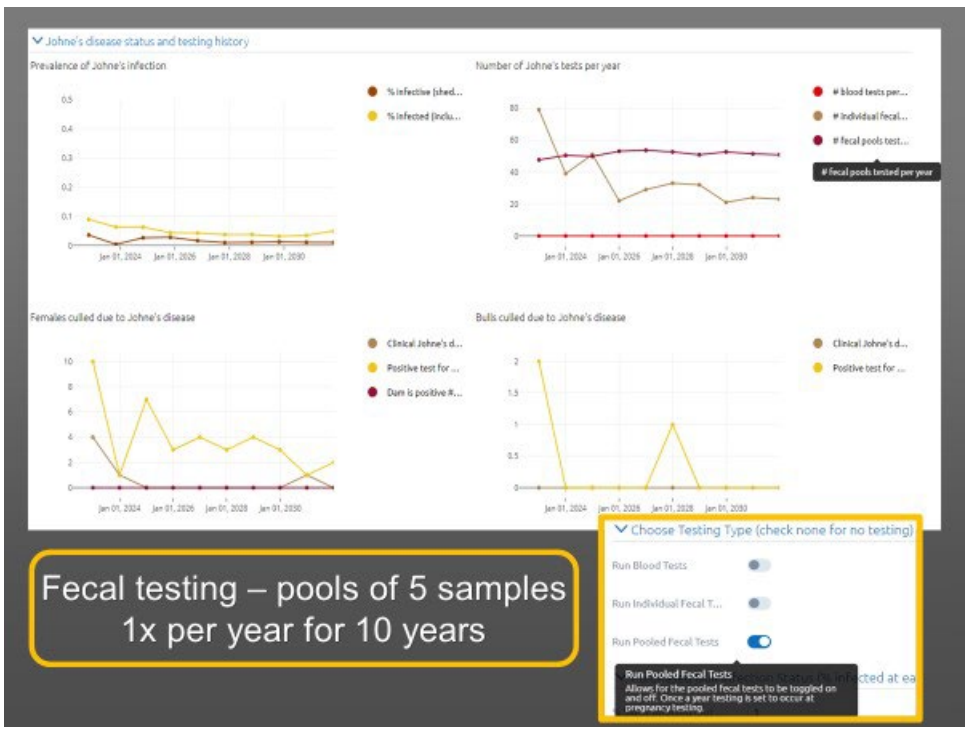
**Note - the number of bulls automatically adjusts to match the number of breeding females.

Individual vs. Pooled Testing

For fecal PCR testing you can choose to test cows either individually (one sample tested per cow) or as part of a pooled testing protocol (multiple samples in one test). With pooled testing, each cow is sampled individually but the lab combines the samples into groups of 5 to save on testing costs. If one of these pools tests positive for Johne's, then all of the cows included in that pool need to be individually retested to figure out which cow(s) tested positive.



** Note - for individual testing only individual tests are reported in the test count. For pooled tests, there is a count of pools tested plus a count of the number of individual tests necessary to check the positive pools.



The number of individual tests will vary depending on the percentage of positive pools. By testing pools of animals first, rather than each individual animal, ideally less tests will be required resulting in lower testing costs. However, if most or all the polls test positive, pooled testing will result in a higher testing cost.

Customizing Transmission Rate

In addition to changing testing and herd replacement strategies, you can also investigate the potential impact of other Johne's management strategies.

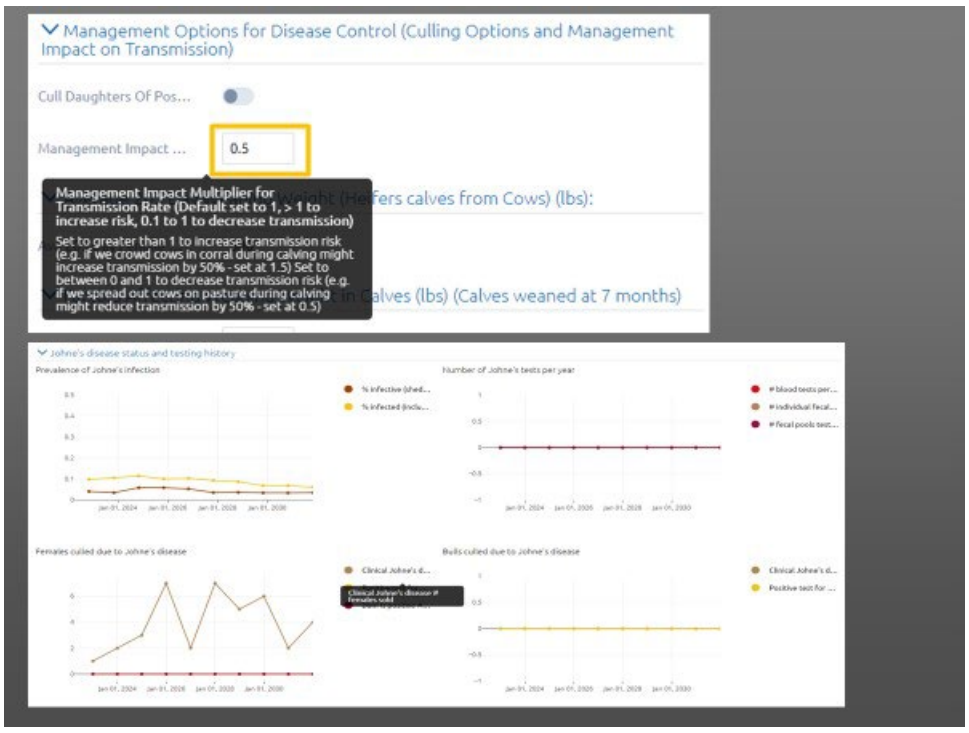
One common recommendation is "Cull daughters of cows culled for Johne's at pregnancy testing – not based on testing of daughters, just family history". You can check the appropriate box which will be combined with your preferred testing strategies.

Johne's transmission in cow-calf herds can be decreased by improving calving season management. This can be done by using the same strategies to reduce neonatal calf diarrhea (scours).

Examples of disease mitigating strategies include: calving on dry pasture with low calving density, bedding frequently to keep udders clean and dry (especially when confined calving is necessary), providing shelters for calves separate from cows, and moving cow-calf pairs to a clean nursery area soon after calving or routinely moving cows that have not calved yet to a clean pasture. The exact impact of these strategies on transmission is unknown. If you already have biosecurity measures in place, you can reduce the likelihood of transmission in the "**Management Impact Multiplier for Transmission Rate**"

- The default rate is 1, entering a lower value reducing transmission rate. E.g., entering 0.75 would simulate 25% reduction in transmission rate.

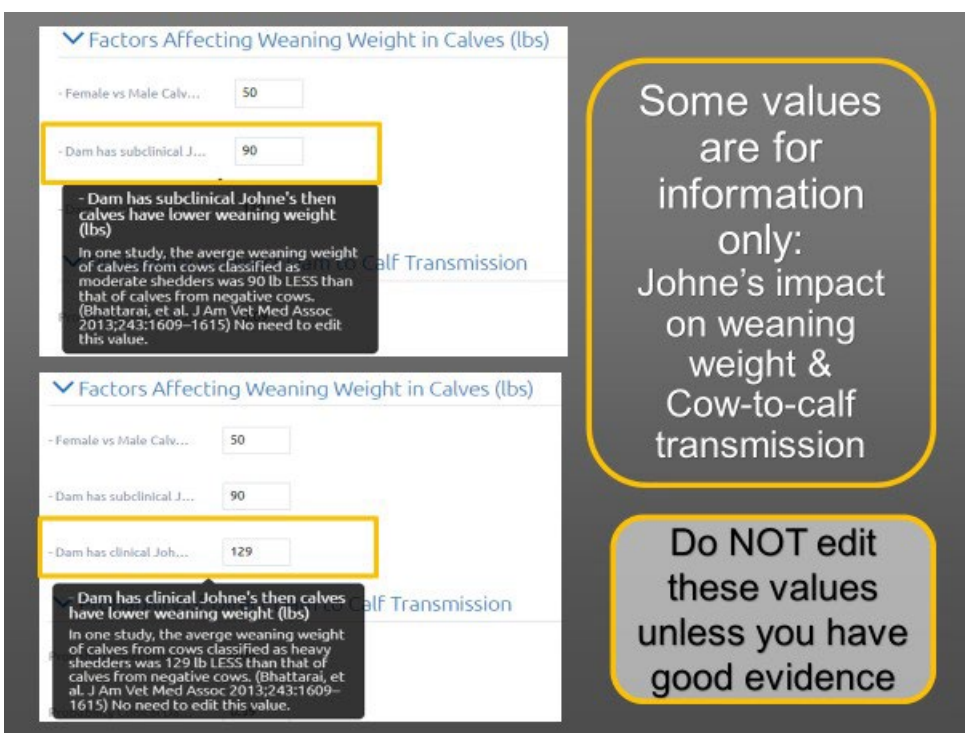
- You can also account for increased risks of transmission e.g., during bad weather or in very crowded or wet conditions by setting the value at > 1. E.g., Entering 1.25 would simulate a 25% increase in transmission rate.

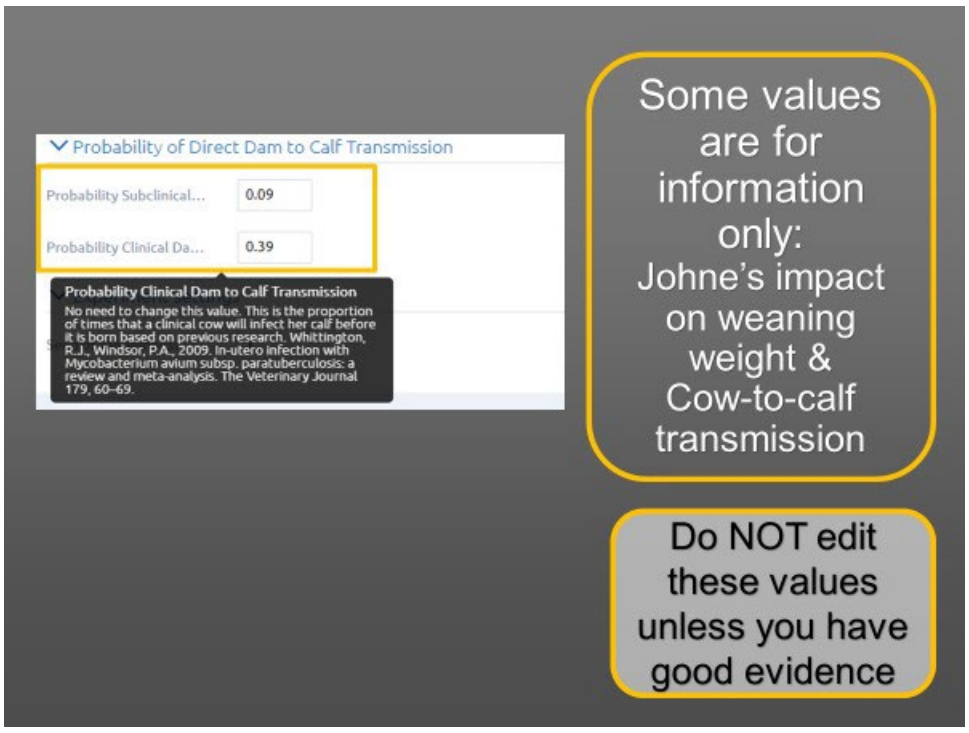


Values to NOT Change

- Weight differences in calves from dams with subclinical and clinical Johne's disease
- Probability of calves directly infected (in utero) by their dams

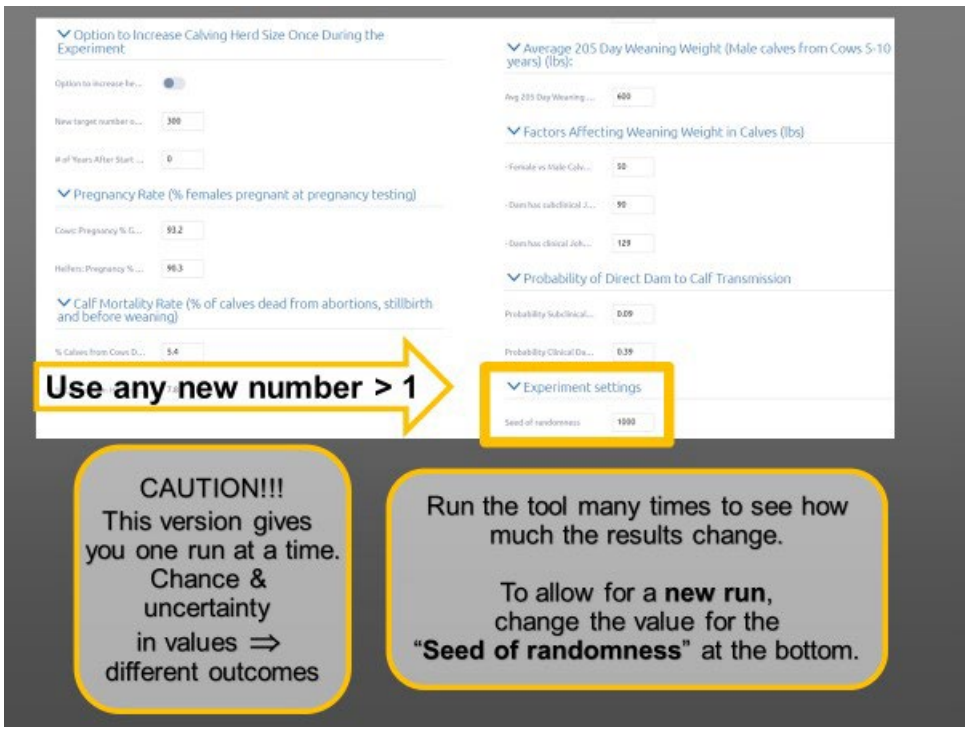
These values are for <u>information purposes ONLY</u>. **DO NOT EDIT**.





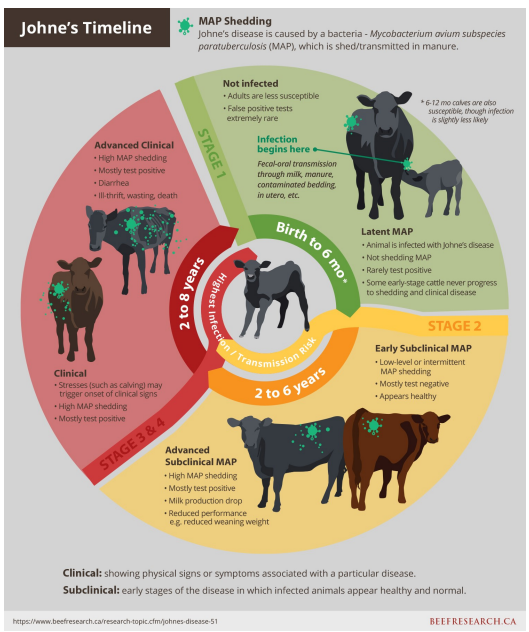
** Note - While relatively easy to navigate, the *single customizable experiment* version of the model only provides one set of outputs at a time. The numbers will (and should) vary from one run to the next due to the impact of chance on how the infection spreads through the herd, the expected variation in the duration of infection in individual animals, and uncertainties about how well the diagnostic tests perform.

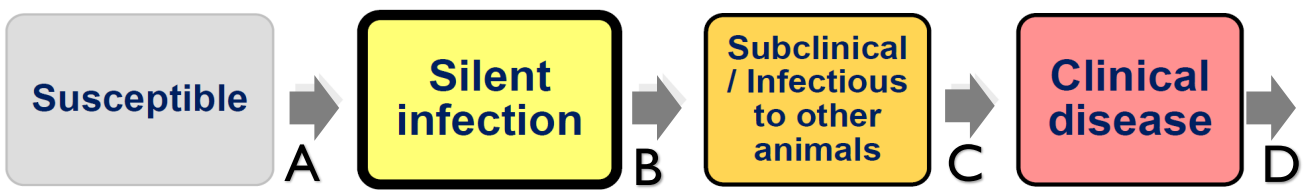
Run the tool multiple times to see how much the results will change.



Factors Impacting Variation

One of the factors impacting the variation in results from one model run to the next is the uncertainty in how long it takes the disease to progress in individual animals (see graphics below).





While few of these exact values are reported in the literature, estimates are inferred to generate a pattern of onset of shedding and clinical disease consistent with what has been observed in previous reports.

A – latent period – 0 to 7 mo (age of weaning in this model).

B – duration of silent infection is the time from exposure to starting to shed the MAP bacteria that cause Johne's disease: mean/mode 29 mo (17 to 53 mo)*. The infection is considered latent until the calves are weaned at 7 mo. The resulting effective range to starting to shed is typically 3 years with a range of 2 to 5 years. But can be as early as 18 mo for calves infected at birth.

** Elliott, G. N., et al. 2014. Environmental risk factors in the incidence of Johne's disease. Critical Reviews in Microbiology. 41(4): 488-507.*

C – subclinical duration is the time during which the animal sheds MAP bacteria in its feces but does not have clinical signs: mean/mode 24 mo (6 to 60 mo).

**Tiwari A, et al. Johne's disease in Canada Part I: clinical symptoms, pathophysiology, diagnosis, and prevalence in dairy herds. Can Vet J. 2006;47(9):874-882.*

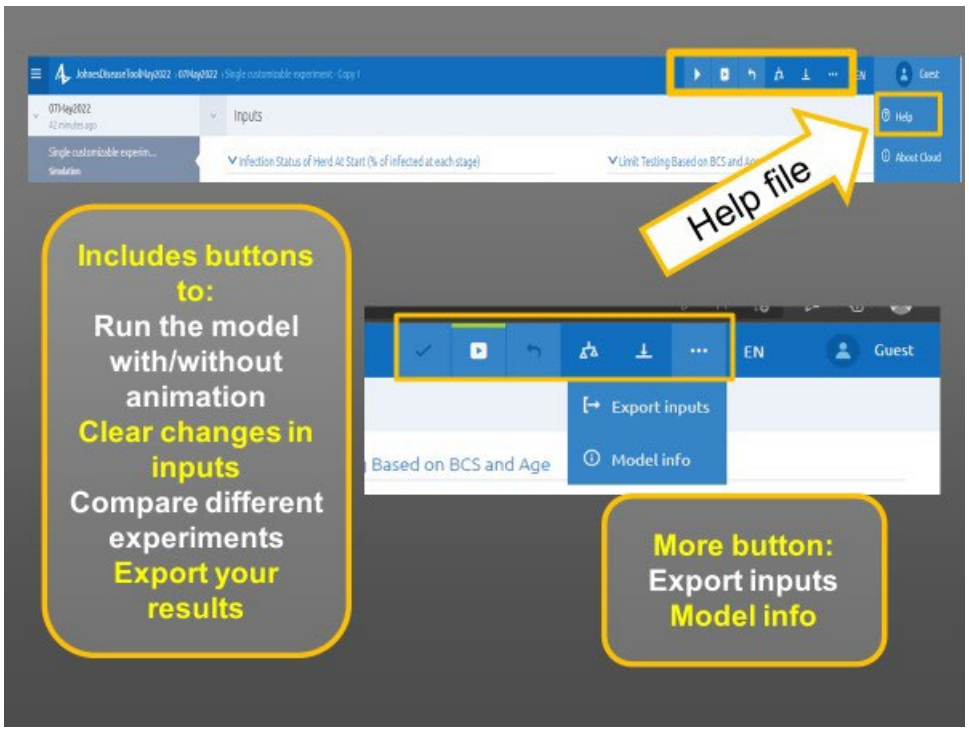
D – time from first clinical signs to removal from the herd: mean/mode 2 mo (1 to 4 mo)*.

**Expert opinion & Clinical stage of disease may last between 3-6 months: (Tiwari et al., 2006)*

The result is a distribution of time from infection to clinical signs of 2 years to 10 years.

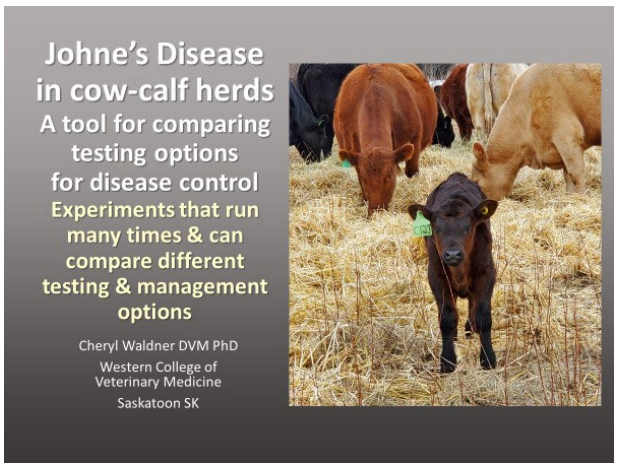
**Tiwari A, et al. Johne's disease in Canada Part I: clinical symptoms, pathophysiology, diagnosis, and prevalence in dairy herds. Can Vet J. 2006;47(9):874-882.*

Don't hesitate to click on buttons and try different options. The model inputs can be reset to saved values and you can try again if you don't get the intended result. There is a simple help file to assist with navigation.

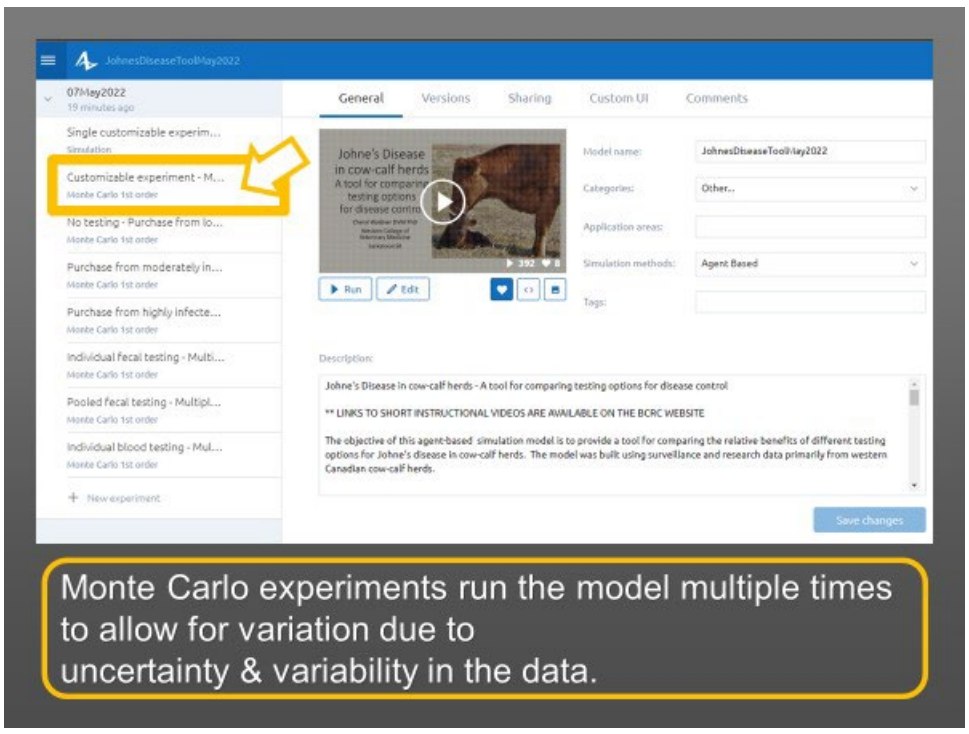


Up to this point, we have been using the single experiment version of the model to learn how to navigate and get familiar with the options. However, to better understand how Johne's disease might respond to specific testing and management choices, we recommend you use the experiments that run multiple times and display the variability in the results that is expected due to the nature of the disease itself as explained earlier and due to the uncertainty in how well the various tests will perform.

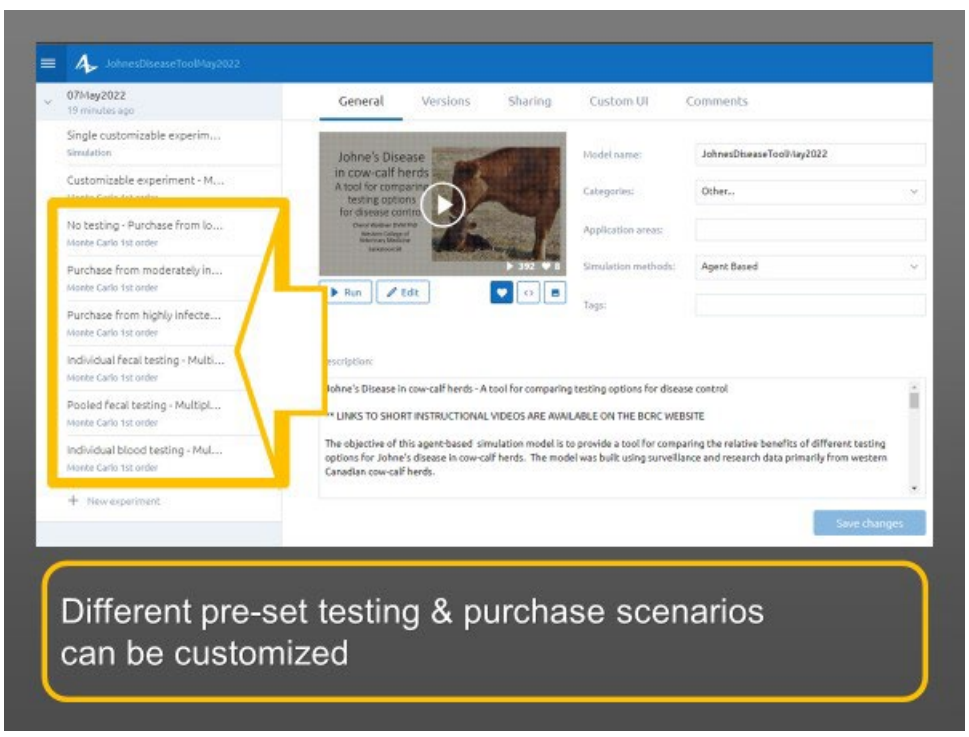
Comparing Multiple Testing and Management Options



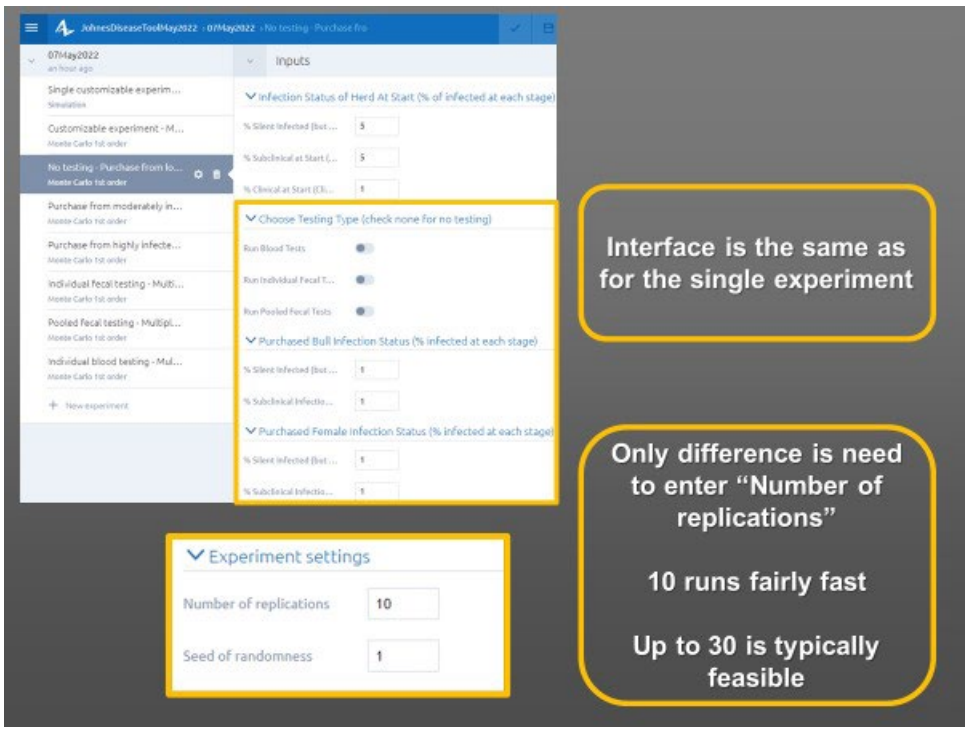
Overview



There are a number of options with preset scenarios that can be customized to answer more specific questions.

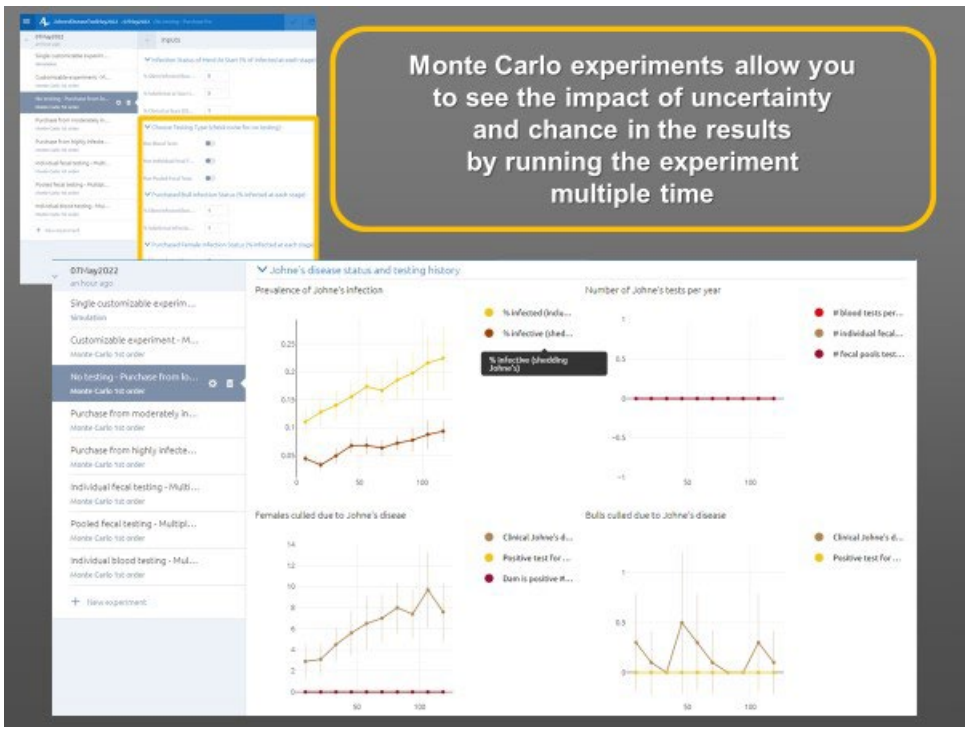


** Note - the interface is exactly the same as for the preset experiments with one exception - You must enter the number of times you would like the model to run. These models have a preset of 10 which runs relatively quickly, but you can run up to 30 times in a reasonable period of time.

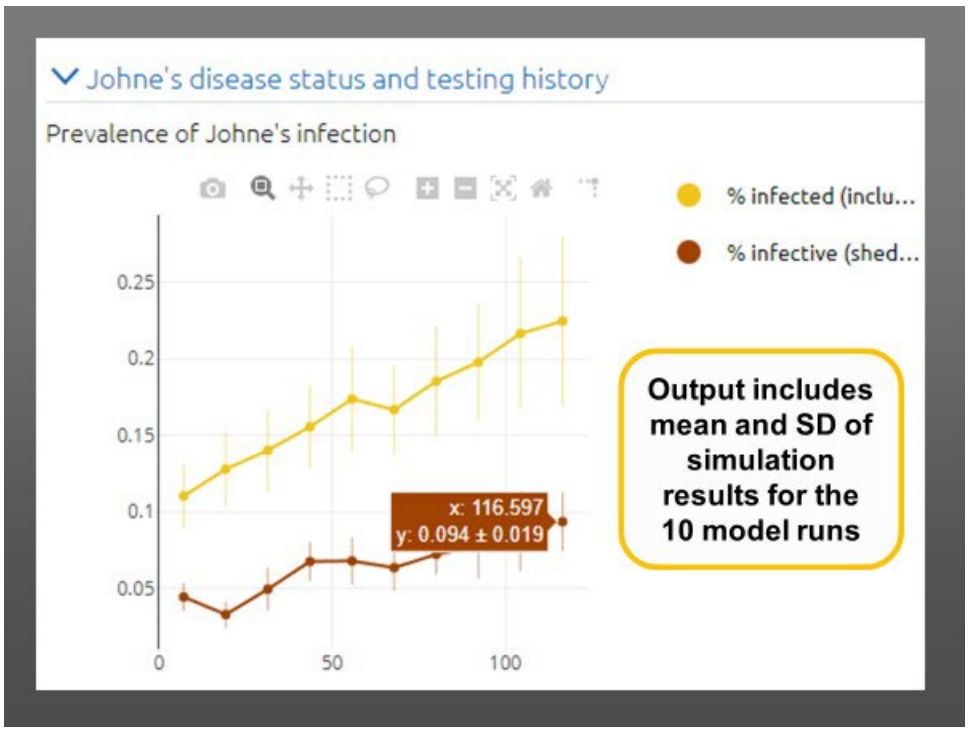


After inputting personalized herd data, run the model by selecting the "Play" button on the top right of the screen.

After the run is complete, you can view the graphs at the bottom of the screen.

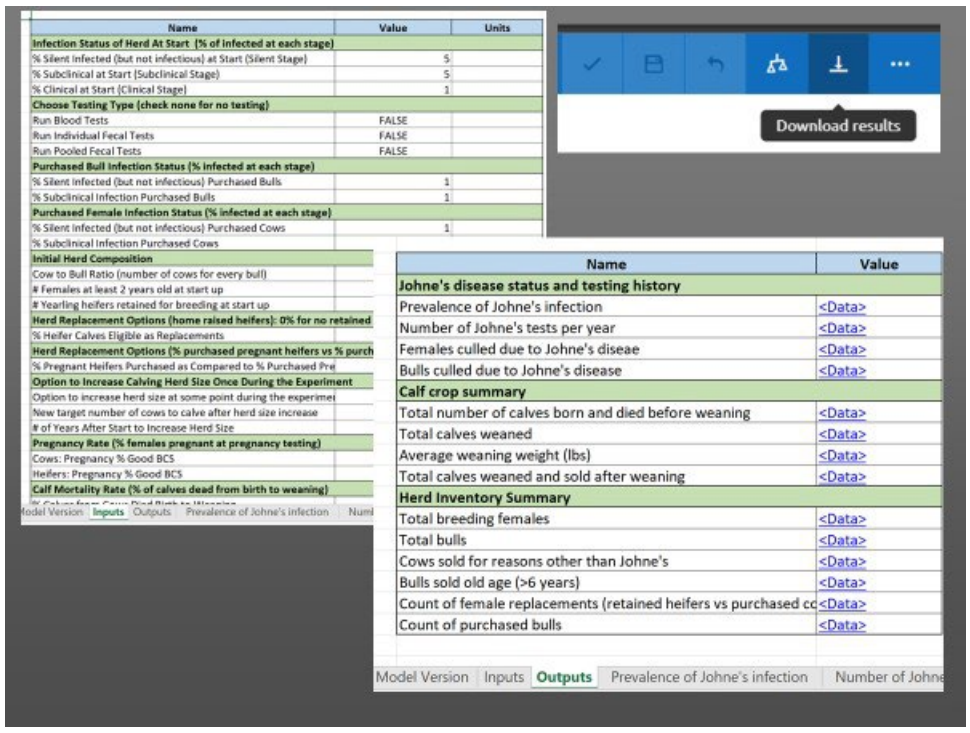


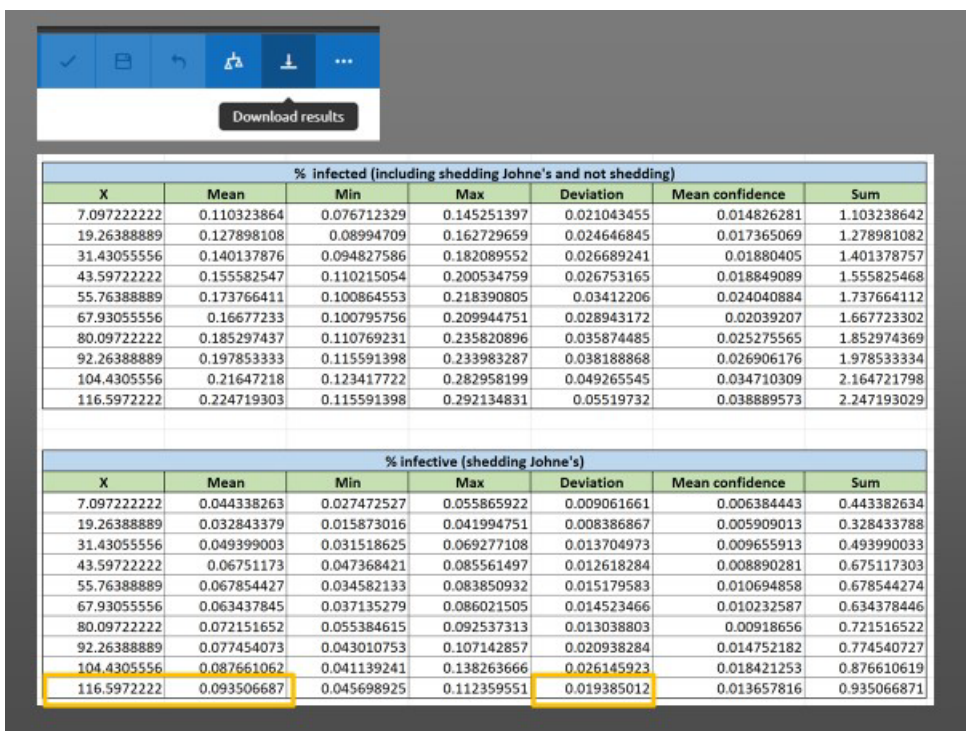
The graphs show the average of the multiple runs and the vertical bars on the graphs show the deviation around the average resulting from run to run variation.



Downloading Results

Detailed results can be downloaded to excel for further analysis using the download function at the top of the screen.





% infected (including shedding Johne's and not shedding)						
X	Mean	Min	Max	Deviation	Mean confidence	Sum
7.097222222	0.110323864	0.076712329	0.145251397	0.021043455	0.014826281	1.103238642
19.26388889	0.127898108	0.08994709	0.162729659	0.024646845	0.017365069	1.278981082
31.43055556	0.140137876	0.094827586	0.182089552	0.026689241	0.01880405	1.401378757
43.59722222	0.155582547	0.110215054	0.200534759	0.026753165	0.018849089	1.555825468
55.76388889	0.173766411	0.100864553	0.218390805	0.03412206	0.024040884	1.737664112
67.93055556	0.16677233	0.100795756	0.209944751	0.028943172	0.02039207	1.667723302
80.09722222	0.185297437	0.110769231	0.235820896	0.035874485	0.025275565	1.852974369
92.26388889	0.197853333	0.115591398	0.233983287	0.038188868	0.026906176	1.978533334
104.4305556	0.21647218	0.123417722	0.282958199	0.049265545	0.034710309	2.164721798
116.5972222	0.224719303	0.115591398	0.292134831	0.05519732	0.038889573	2.247193029

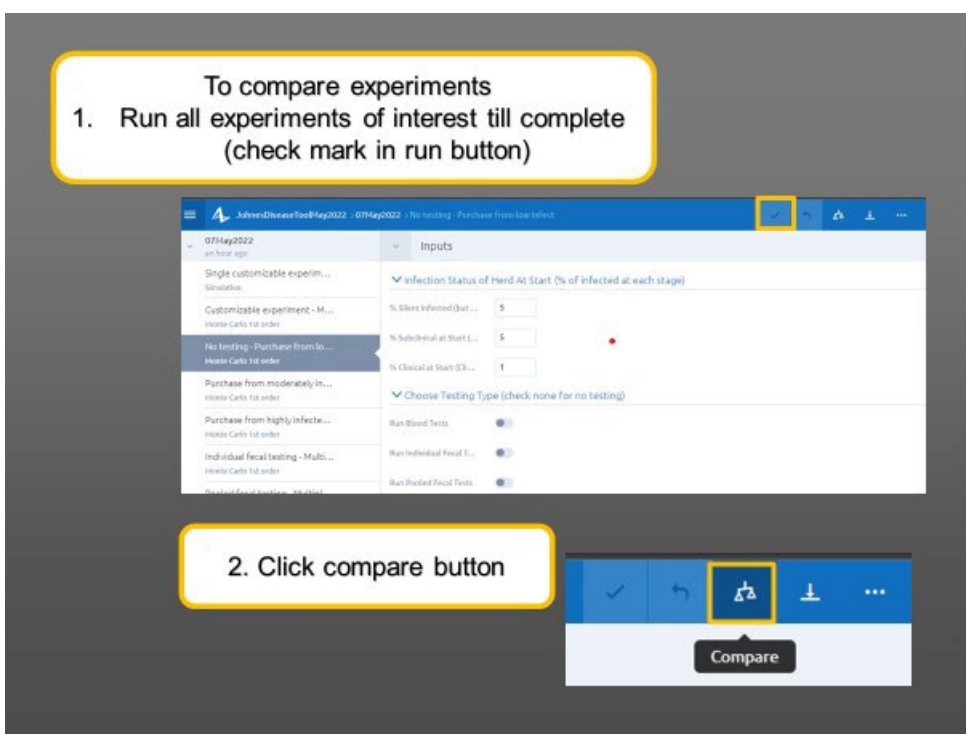
% infective (shedding Johne's)						
X	Mean	Min	Max	Deviation	Mean confidence	Sum
7.097222222	0.044338263	0.027472527	0.055865922	0.009061661	0.006384443	0.443382634
19.26388889	0.032843379	0.015873016	0.041994751	0.008386867	0.005909013	0.328433788
31.43055556	0.049399003	0.031518625	0.069277108	0.013704973	0.009655913	0.493990033
43.59722222	0.06751173	0.047368421	0.085561497	0.012618284	0.008890281	0.675117303
55.76388889	0.067854427	0.034582133	0.083850932	0.015179583	0.010694858	0.678544274
67.93055556	0.063437845	0.037135279	0.086021505	0.014523466	0.010232587	0.634378446
80.09722222	0.072151652	0.055384615	0.092537313	0.013038803	0.00918656	0.721516522
92.26388889	0.077454073	0.043010753	0.107142857	0.020938284	0.014752182	0.774540727
104.4305556	0.087661062	0.041139241	0.138263666	0.026145923	0.018421253	0.876610619
116.5972222	0.093506687	0.045698925	0.112359551	0.019385012	0.013657816	0.935066871

Comparing the Results of Multiple Experiments

There is also an option to directly compare the results of experiments using the compare function at the top of the screen.

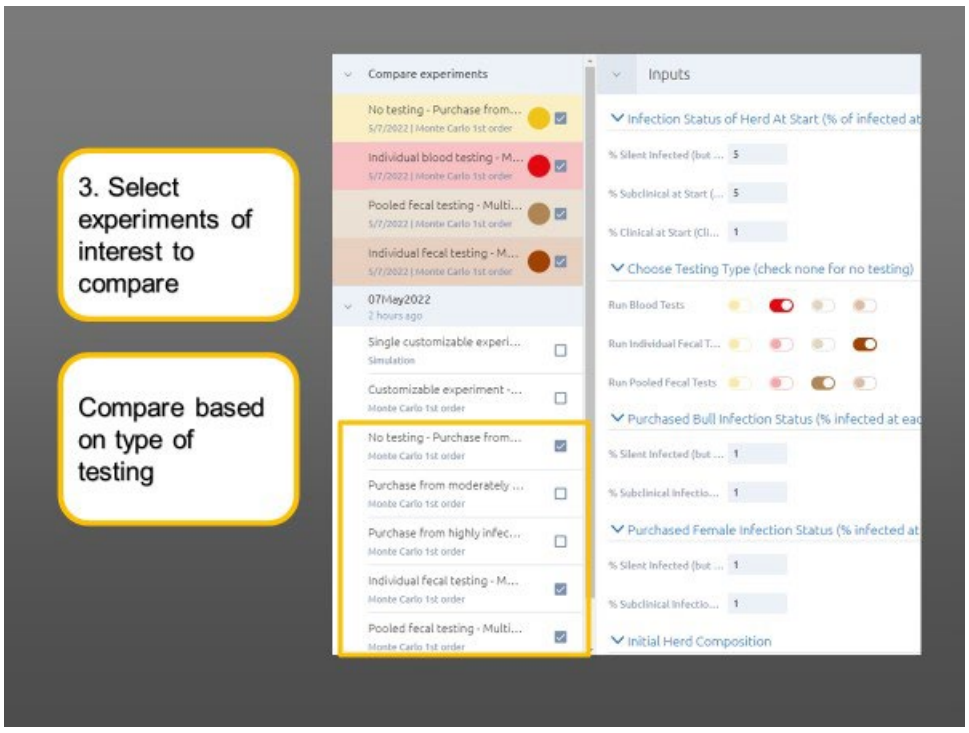
First run all of the experiments that you want to compare.

Then click on the compare button.



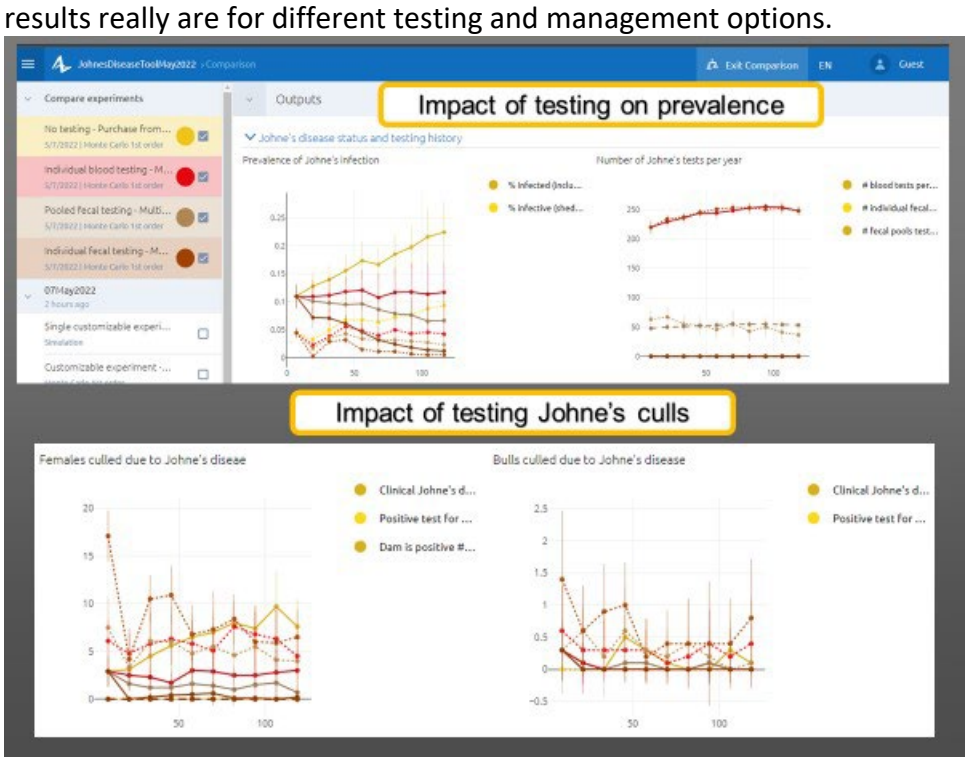
Next select the experiments you want to compare by clicking on the boxes.

** Note - these are big files so there can be a bit of a lag as you select the boxes.



By selecting the desired boxes, results of all the experiments you asked to compare will now be visible on a single graph at the bottom of the screen.

The display can end up a bit cluttered if you select too many options, but provides a very good indication of how different the results really are for different testing and management options.



Buying Cattle from Infected Herds

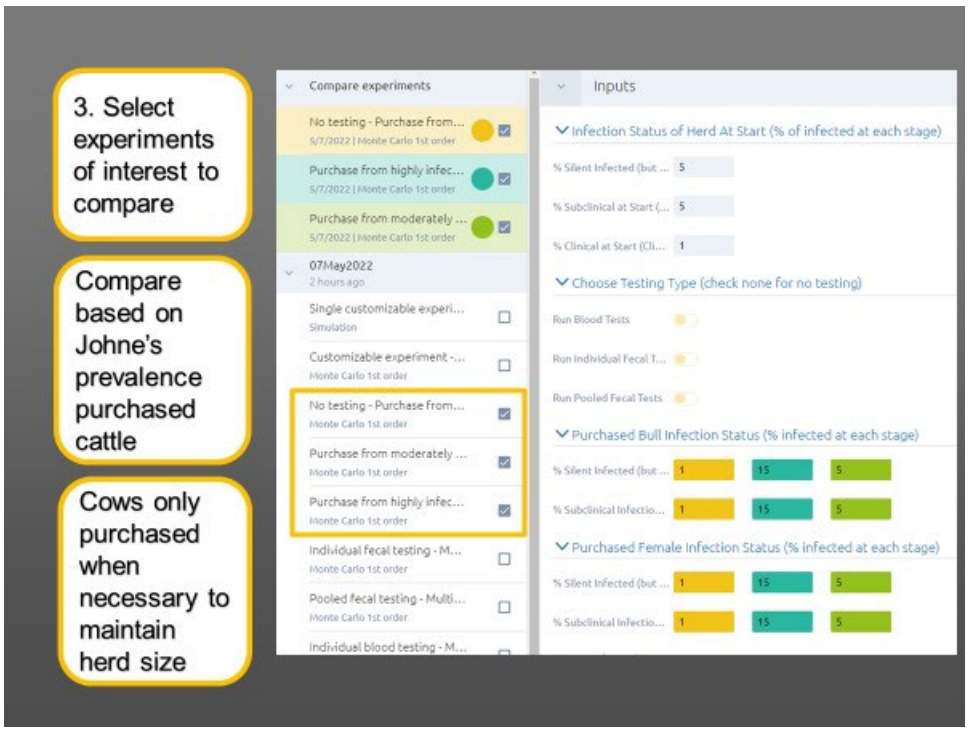
The second set of experiments below the "Monte Carlo" experiments compares the risks for buying in cattle from other herds.
The default option is set to the expected rate for a random cow.

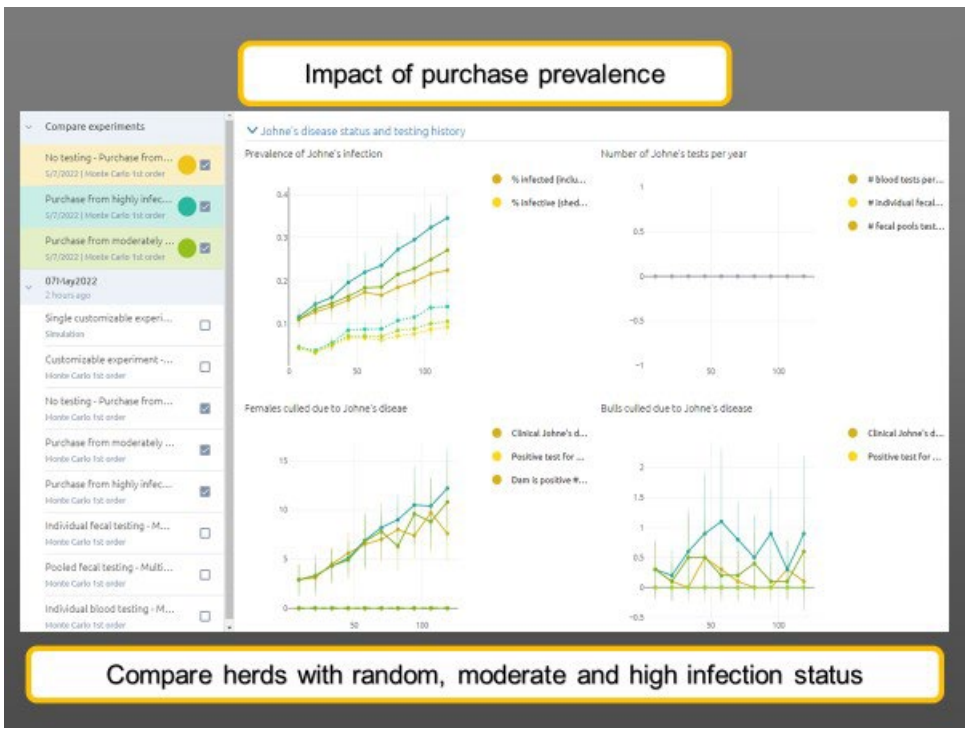
However, there is a very real risk when we buy cattle that we are buying from an infected herd. There are two scenarios based on data from across Canada testing projects in beef herds:

1. Purchasing from a moderately infected herd and;

2. Purchasing from a highly infected herd.

In both cases, the model preset is only buying cows to maintain herd inventory. To observe the potential effects of buying from infected herds, try changing the settings to increase herd size. Typically, you will see in increase in percentage of cows with Johne's disease, higher replacement costs and lowered weaning weights.





Take home message

This tool is built on data from beef herds in western Canada

- ✓ And it does account for a lot of sources of uncertainty

BUT – it is NOT a crystal ball

- ✓ And is not intended to tell you what to do in your herd
- ✓ Rather it will help you compare the relative costs and benefits of different options

Acknowledgments

Thank you to Yang Qin. Her modeling and programming skills were critical to the development of this model.
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