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The direct benefit of a second modified live core vaccine for adult shelter dogs and cats: a decision-analytic model

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Abstract

Background. Guidelines suggest revaccinating adult shelter dogs and cats 2 to 3 weeks after a modified live core vaccine at intake, especially when disease risk is high. A second dose on day 14 can prevent disease only in adults that are susceptible, fail their first dose, respond to the second dose and are still present and uninfected when it becomes effective. How many adults qualify, and so the benefit, has not been quantified.

We built a decision-analytic model of direct protection to estimate the number of second doses needed to avert one additional case (number needed to vaccinate, NNV) of feline panleukopenia, canine distemper or canine parvovirus. Cases were infections acquired during shelter care, including those diagnosed after departure. Assuming constant daily infection risk, a low-risk approximation estimated the NNV from shelter records. Infection pressure came from the window case rate, adult cases diagnosed 8–21 days after intake per 1,000 adult-days in care on those days. This window falls after most pre-intake infections appear and before a day-14 second dose takes effect. Lengths of stay came from records at six shelters and from illustrative profiles. Inputs were varied alone and together.

Results. At a base of 0.10 window cases per 1,000 adult-days and 25% of first-dose failures converted, about 6,000–25,000 second doses were needed per case averted at the six shelters ($35,000–$138,000 at $5.50 a dose). The second dose averted only 1%–5% of shelter-acquired adult cases, and 74%–91% arose from infection before the intake dose could protect. A larger or longer slow track lowered the NNV, to 2,500–3,350 when half of adults averaged 90 days. First-dose failure and the share converted, which shelter records cannot measure, each moved the NNV about as much as the window case rate, and further when varied together.

Conclusions. Under our base assumptions, a routine second dose prevents very few shelter-acquired cases of panleukopenia, distemper or parvovirus. The benefit is larger where adults stay longer. Shelters can estimate their own NNV from intake and outcome dates and adult case counts with the accompanying browser tools. These estimates depend on first-dose failure and second-dose conversion, which remain uncertain.

Background

The World Small Animal Veterinary Association (WSAVA) guidelines recommend revaccinating adult dogs and cats in shelters 2 to 3 weeks after an intake dose of modified live core vaccine. For dogs older than five months, the stated reason is precautionary, essentially to protect those that did not respond to the first dose [1]. The Association of Shelter Veterinarians also suggests a second dose for adults still in care, especially when disease risk is high [2]. A single modified live dose appears to protect most susceptible adults [3, 4], within about 7 days [5, 6]. A second dose can therefore help only those whose first dose failed and in whom a second could still succeed. This second adult dose is distinct from the series given to puppies and kittens, which is repeated because maternal antibodies can passively block a vaccine dose until they wane [7, 8]. That series usually ends at 16 to 20 weeks of age, but maternal

antibody can still block a response after it ends. In one field study 37% of kittens vaccinated at 8, 12 and 16 weeks had not seroconverted to panleukopenia virus by 20 weeks [9], and in another 15% lacked protective titers at 17 weeks [8]. The model therefore covers adults at least one year old at intake, and the susceptibility and first-dose failure inputs come from studies of adult animals.

In a shelter, the second dose is given as part of a blanket protocol to every adult animal still in care, so the vaccine cost, staff time and handling stress apply to every adult with a length of stay (LOS) over 14 days. A direct benefit, in contrast, requires an animal whose first dose failed to still be in the shelter when the second dose becomes effective (about 7 days after vaccination, on day 22 in this model) and then to be exposed to infection that the vaccine would have prevented. Earlier shelter modeling studies have addressed outbreak control and transmission [10], but the marginal value of a protocol second dose has not been quantified for any of these antigens.

The objective of this study was to estimate the marginal direct benefit of a second dose given on day 14 to adults in a shelter that vaccinates every adult at intake. Apart from vaccine response estimates, the model needs only counts a shelter can take from its intake and outcome data and an observable measure of infection pressure, adult cases of each disease diagnosed 8 to 21 days after intake per 1,000 adult-days in care on those days. The guidelines the model informs apply to shelters of all types, so results are given both for adult stays observed at six shelters and for illustrative LOS profiles.

Methods

Model overview

This model follows adults, defined as dogs and cats at least one year old at intake, through a single shelter stay under a protocol that gives every adult one modified live core vaccine at intake. It compares this protocol to one that also gives a second dose on day 14 to every adult still present through day 14 (still in the shelter at the end of that day, when the dose is given). The output of this model is the number needed to vaccinate (NNV), or the number of second doses given per additional disease case averted [11, 12]. A case averted is an infection acquired in the shelter that the second dose prevents, whether it would have been diagnosed before or after the animal leaves the shelter. Only direct protection of the vaccinated animal is counted. Effects on other animals, such as reduced transmission, are not. Cost per case averted is the NNV multiplied by the cost of one second dose (see Cost).

A second dose can prevent a case only through a chain of conditions. The adult must be susceptible at intake (probability S), its intake dose must fail (f), the second dose must convert it (r), and it must still be in the shelter and uninfected when the second dose becomes effective. It must then be an animal that would otherwise have been infected in the shelter later in its stay. Per adult admission, the number of second doses given equals D, the share of adults still present through day 14, and cases averted equal $S \times f \times r \times A$, where A is the probability that a converted adult would have been infected in the shelter after the second dose takes effect. The NNV is therefore

NNV = [1 / (*S* × *f* × *r*)] × [*D* / *A*].

The first bracketed term, 1 / (*S* × *f* × *r*), is the vaccine biology, and the second, *D* / *A*, is the LOS and infection pressure. *D* and *A* both depend on how long adults stay, so they are kept together as one factor.

Daily risk and disease counts

Time is measured in whole days after intake. In this model, an animal whose intake dose works can still be infected on days 1 to 7 but is protected from day 8. One whose intake dose fails is at risk for its whole stay unless a second dose, given on day 14, is successful, in which case the animal is protected from day 22 onward. An animal with a stay of *L* days leaves on day *L*, and the second dose goes to animals with stays longer than 14 days. Disease risk was a daily probability *q* of infection while in the shelter, held constant over the stay, so the model links the early cases a shelter observes to later, preventable ones through this assumption. Infection on day *k* appears as a case on day *k* plus a fixed incubation lag. The lag stands for the interval from infection to the event a shelter records, whether clinical onset, clinical diagnosis or a first positive test, which the model does not distinguish. The base lag was set at 5 days for panleukopenia and parvovirus and 10 days for distemper.

When the daily risk is low, adults stop being at risk mainly by leaving the shelter, rather than by being infected. The chance of infection grows almost in proportion to the days at risk, so *A* is close to *q* × *C*, where *C* is the adult-days in care after the second dose can take effect, each adult contributing max(0, *L* − 14 − 7) days. This gives

NNV ≈ [1 / (*S* × *f* × *r* × *q*)] × [*D* / *C*].

At a given daily risk, LOS therefore affects the NNV only through *D* / *C*, the second doses given per adult-day of care after the second dose can take effect. An infection in the shelter on those days counts as averted even if the case would be diagnosed after the animal leaves for adoption or transfer, because the animal was infected while in the shelter. A scenario counting only cases diagnosed before departure was also evaluated.

What a shelter counts. The daily risk cannot be observed directly, so it is taken from the window case rate, an observable indicator of infection pressure that a shelter can calculate from its own data. The window case rate is the number of adult cases diagnosed between 8 and 21 days after intake while still in care, divided by the adult-days in care on days 8 to 21 over the same time span, per 1,000 adult-days. It counts only cases diagnosed in the shelter, unlike the cases averted, which include infections acquired in the shelter but diagnosed after departure. First-week cases are left out because nearly all come from infections acquired before intake or before the intake dose can help, so they say little about the shelter's infection pressure that a second dose could act on, though more about infection in the community. Later cases are left out because a second dose on day 14, which many shelters already give, protects from day 22 and could have prevented some of them. A shelter that gives such a dose can therefore still use its own window count, unless protection begins sooner (Additional file 1, S1). Each adult contributes the

days it was present from day 8 to day 21 after intake, from 0 for those that left within the first week to 14 for those still present on day 21. The denominator is adult-days rather than shelter admissions because, at the same infection pressure, a shelter with longer stays has more adults present on days 8 to 21 and so has the potential to record more cases per admission.

How the model uses it. Under the same approximation, a window case arises either from infection in the first 7 days of an adult whose intake dose worked but had not yet protected it, or from infection of an adult whose intake dose failed. The window count W is therefore close to $S \times q \times (E_w + f \times E_v)$. Here E_w is the adult-days in care on the window days on which first-week infections are diagnosed, days max(8, lag + 1) to min(21, lag + 7), days 8 to 12 for panleukopenia and parvovirus and 11 to 17 for distemper at base. E_v is the adult-days on the later window days, to which only failures contribute. Solving for q and substituting, S cancels in this approximation, and

$$\text{NNV} = D \times (E_w + f \times E_v) / (f \times r \times C \times W).$$

Every quantity except f and r is a count from intake and outcome data and the number of window cases. The counts can all be totals over the same adult admissions or all be averages per admission, and the NNV is the same either way. In this approximation the NNV is inversely proportional to the window case rate and to r. With the window case rate $R = 1{,}000\ W / E$, where E is all adult-days in care on days 8 to 21 whatever the lag, the NNV can be written as

$$\text{NNV} = [D / C] \times [(E_w + f \times E_v) / E] \times 1{,}000 / (f \times r \times R).$$

Once the daily risk is inferred from the window count, LOS is therefore represented twice, through D / C and through the share of window adult-days on which window cases can arise. The shelter-facing rate divides by all adult-days on days 8 to 21 because that is simpler to count than the weighted exposure. Shelters and LOS profiles are compared at the same window case rate, the quantity a shelter observes, rather than at the same daily risk.

Length of stay

LOS profiles were taken from animal-level intake and outcome records at six open-admission shelters, five municipal and one private nonprofit, labeled A to F (Additional file 1, Table S7). Records at A, B, E and F identified adults at least one year old at intake. Records at C and D had no age field, so their curves include all ages and serve as proxies for adult stays. Cats came from all six shelters and dogs from A to D and F, eleven LOS curves in all, with 1,572 to 111,301 stays per curve. Intakes ran from 2012 to 2023 at A, B and D, January 2014 to April 2023 at C, February 2021 to March 2026 at E and September 2020 to September 2026 at F. At A to D and F, stays still open when the records ended, at most 1.1% of any curve, were treated as censored in a Kaplan–Meier estimate. At E, the 31 episodes without an outcome were excluded. Stays of 365 days or more were counted as 365 days rather than excluded, a cap applied in the same way to the illustrative LOS profiles, the browser tools and Additional file 1, S11. At most 0.35% of stays at any shelter reached this cap. Foster placement ended the stay at A, B and C, and foster days

were removed at E, so those stays count only time in the building. At D and F the record stayed open through foster care, so foster days count as days at risk, which favors the second dose. Adult lengths of stay at A and E had means of 9.8 to 10.2 days and medians of 4 to 6 days, at B means of 13.1 days for dogs and 15.9 for cats, and at F 25.5 days for dogs and 25.0 for cats.

Because vaccine guidelines also apply to shelters whose adults have a longer LOS, illustrative LOS profiles were added. Shelters already distinguish fast-track animals, expected to leave quickly, from slow-track animals, expected to need more time or care before an outcome, so each illustrative profile was a mixture of two or three groups of adults, each leaving at a constant daily rate (Additional file 1, S1). Three profiles with the same mean of 21 days show the effect of shape alone, one group, two equal groups averaging 7 and 35 days, and three equal groups averaging 5, 15 and 43 days. A sweep of slow-track profiles then held a fast track at 7 days and put 10%, 25% or 50% of adults on a slow track averaging 35, 60 or 90 days. These are illustrations of how the shape of the LOS distribution moves the NNV, not estimates for particular shelters. LOS profiles were not built from a mean and a median, because a mean and median do not determine the stay quantities that set the NNV (Additional file 1, S7). As an illustration of selective use, the adult dogs of one shelter were also split by size, with the LOS from that shelter's records and an assumed daily risk shared by all sizes (Additional file 1, S12). Selection by neuter status at intake was examined with published antibody prevalence in neutered and intact animals, with the same daily risk, LOS and first-dose failure in both groups, so that the NNV is inversely proportional to the susceptible fraction.

Parameters

Table 1 lists each value, its range and its source. Exact binomial 95% confidence intervals set the ranges for counts. Serum antibody has been validated as a correlate of protection for panleukopenia [13] and canine distemper [14], so first-dose failure and conversion were defined by serology.

Table 1

Model inputs. The window case rate is the number of adult cases diagnosed 8 to 21 days after intake per 1,000 adult-days in care on days 8 to 21, under a protocol of vaccination at intake only.

Parameter	Base	Range	Source
Susceptible at intake, panleukopenia, cats	0.21 (0.45 × 19/40)	0.17 to 0.26	Below 1:40 [33], times the undetectable share among cats below 1:40 [15]. Range is the 95% CI of 50/111, times 19/40. Sets the daily risk, cancels from the NNV
Susceptible at intake, distemper, dogs	0.47	0.35 to 0.60	[16]; 95% CI of 32/68. Sets the daily risk, cancels from the NNV
Susceptible at intake, parvovirus, dogs	0.17	0.13 to 0.22	[34]; 95% CI of 49/285. Sets the daily risk, cancels from the NNV
First-dose failure, panleukopenia, cats	0.11 (2/19)	0.013 to 0.33	[15], undetectable after one dose among cats undetectable before it; exact 95% CI
First-dose failure, distemper, dogs	0.087 (2/23)	0.011 to 0.28	Cohort reanalysis [16], undetectable after one dose; exact 95% CI
First-dose failure, parvovirus, dogs	0.089 (4/45)	0.025 to 0.21	[17], protective cutoff; exact 95% CI
Share of failures converted by a second dose	0.25	0.06 to 0.77	Judgment between a canine cohort [16] and human revaccination data [18, 19]. Low end 0/8 dogs at least 16 weeks old with a Jeffreys prior, high end 92/119 children
Incubation lag, panleukopenia, cats (d)	5	2 to 10	[21, 22]
Incubation lag, distemper, dogs (d)	10	7 to 14	[26, 28]
Incubation lag, parvovirus, dogs (d)	5	3 to 7	[23, 24]
Window case rate, cats (per 1,000 adult-days)	0.10	0.02 to 0.22	Illustrative range shared by all three diseases (Additional file 1, S4). Two shelters with no adult window cases had one-sided 95% upper limits of 0.22 and 0.16

Parameter	Base	Range	Source
Window case rate, dogs (per 1,000 adult-days)	0.10	0.02 to 0.22	Illustrative range shared by all three diseases. High end a scenario value above the adult window case rates of the distemper cohort outbreaks at the observed dog stays (Additional file 1, S4)
Length of stay, observed	Eleven curves at shelters A to F	Reported separately	Animal-level intake and outcome records. Shelters C and D all ages. Stays of a year or more counted as 365 days. Counts computed directly from each curve (Additional file 1, S7)
Length of stay, illustrative profiles	Mixtures of groups each leaving at a constant daily rate. Mean 21 d as one group, two equal groups of 7 and 35 d, or three equal groups of 5, 15 and 43 d. Sweep with a fast track of 7 d and 10%, 25% or 50% of adults on a slow track of 35, 60 or 90 d	Reported separately	Illustrative. Capped at one year, as the observed curves are (Additional file 1, S1)
Onset of protection (d)	7 (intake dose protects from day 8, second dose from day 22)	3 to 14	Challenge protection [20] and seroconversion after one modified live dose [3, 5, 6]. Same for both doses and all antigens
Dose timing	Second dose on day 14 to stays over 14 days	Days 7 to 42	Stays of exactly 14 days also dosed in Additional file 1, S5
Cost per dose	$5.50	Fixed	Assumption. About $2.50 vaccine and consumables plus about seven minutes of technician time. 2026 USD

Susceptible at intake (S). The susceptible fraction sets the daily risk implied by a window count but cancels from the NNV in the counts approximation. For each disease the same antibody threshold defined susceptibility at intake and failure after the first dose, undetectable antibody for cats and distemper and the protective cutoff for parvovirus, so that failures are counted among the same animals counted as susceptible (Table 1 and Additional file 1, S1).

First-dose failure (f). Failure was defined for cats and for distemper as antibody still undetectable after one dose, because a dog or cat with low but detectable antibody after a modified live dose has been primed and is likely protected [1]. The cat value, 2/19, assumes that the cats with undetectable titers 28 days after one dose were among those undetectable before vaccination [15]. For distemper, 2/23 adults given one modified live dose had no detectable antibody 14 or more days later [16]. Only 6/23 had an

intake titer confirming they were susceptible, and 1 of those 6 failed, so a sensitivity analysis set distemper *f* to 1/6. For parvovirus, 4/45 seronegative adult shelter dogs had no protective antibody on day 14 [17]. That test reports only a protective cutoff, so parvovirus failure uses protective antibody titers rather than any antibody response. Derivations are in Additional file 1, S1.

Share of failures converted by a second dose (r). No directly applicable estimate was available. In the distemper source cohort, in which both doses were modified live, a second dose converted 2/11 classifiable first-dose failures of all ages (18%, exact 95% CI 2% to 52%) and none of 8 dogs that were at least 16 weeks old (0%, one-sided 97.5% upper limit 37%) [16]. Human studies of revaccination in seronegative recipients of measles-containing vaccines reported seroconversion of 46% to 77% [18, 19]. Measles virus, like canine distemper virus, is a morbillivirus. The base value of 0.25 is a judgment set between these sources, which differ in species, population, interval and definition (Additional file 1, S1). The range tested was 0.06 to 0.77. Because the NNV is proportional to 1/*r*, the NNV at any other value of *r* is the base NNV multiplied by 0.25/*r*.

Onset of protection. A dose that works was assumed to protect from a fixed number of days after it is given, the same for both doses and all three antigens. The base of 7 days is the first sampling day on which most animals in serologic studies of modified live panleukopenia and parvovirus vaccines were above the positive cutoff [3, 5, 6]. Every whole day from 3, the earliest challenge protection reported in cats [20], to 14 was evaluated (Additional file 1, S1).

Incubation lag. Ranges followed the incubation periods reported in the literature, 2 to 10 days for panleukopenia [21, 22], 3 to 7 days for parvovirus [23–25], and 7 to 14 days for distemper, the lower end of the 1 to 4 weeks or more generally cited [26–28]. Experimental infections of young animals support the base lags. Specific pathogen-free cats inoculated with panleukopenia virus became partly anorexic with mild diarrhea 5 to 6 days later [29], puppies given canine parvovirus orally first showed enteric signs 5 days later [30], and puppies inoculated with a field strain of distemper virus developed fever and lymphopenia 3 to 10 days later and diarrhea, ocular discharge and skin rash after day 9 [31]. Longer lags were not used, because the day 8 to 21 count then increasingly reflects infection before intake, which the model would attribute to the shelter.

Window case rate. The base was 0.10 adult cases diagnosed 8 to 21 days after intake per 1,000 adult-days in care on those days, a round illustrative value. One range was used for all three diseases. The range is illustrative, informed by shelter observations, because adult case rates have not been reported in the literature, and neither end is an empirical bound. The lower end, 0.02, has no data source. Two shelters with no adult panleukopenia between days 8 and 21, in 13,867 and 19,105 adult-days, had exact one-sided 95% upper limits of 0.22 (by coincidence the same value as the upper end of the range) and 0.16, so a rate near zero cannot be excluded. The second, shelter F, also recorded no adult parvovirus or distemper window cases in 9,397 adult-days, an upper limit of 0.32. The upper end, 0.22, is a scenario value informed by two shelter distemper outbreaks in the source cohort, whose adult window case rates correspond to 0.07 to 0.16 per 1,000 adult-days at the observed dog stays, including dogs given

recombinant vaccines [16]. The model uses the same range for panleukopenia and parvovirus, which may have different case rates, because no comparable data were available (Additional file 1, S4). Results were also computed up to 2 per 1,000 adult-days.

Cost

No reported shelter cost data were available, so the cost of one dose was set at $5.50, approximately $2.50 for vaccine and consumables and $3.00 for about seven minutes of technician time. Staff time is largely an opportunity cost, whose value depends on how much of that time is already committed. The value was set low, so a fuller accounting of staff time, cold chain, record-keeping and handling would raise every cost figure in proportion. Because cost only multiplies the NNV, a shelter can rescale any reported cost by using its own cost per dose. Costs are in 2026 United States dollars for a single stay, without discounting.

Outcomes and sensitivity analysis

For each disease and LOS scenario the model reports the share of adults present through day 14, the adult-days in care after the second dose protects, cases averted per 1,000 adult admissions, admissions per case averted, the NNV and the cost per case averted. Each parameter was then moved across its range with the others at base, on a grid of 9 evenly spaced values for *r*, *f* and the window case rate and on every whole day of the lag and onset ranges. The combined extremes evaluated every combination of the range ends of *r*, *f* and the window case rate at every whole-day lag and onset, because the NNV need not move in one direction with the lag. The combinations giving the lowest and highest NNV were taken as the most and least favorable to the second dose within the evaluated ranges, excluding combinations implying a daily risk of 5% or more. First-dose failure and the share converted after a second dose were also varied together at their range ends, and alternative definitions and conventions (for example, excluding rather than capping stays of a year or more) were examined (Additional file 1, S5). No probabilistic analysis was run, because the most influential inputs have no defensible distribution.

To examine timing, the second dose was given on every day from 7 to 42 to every adult still present through that day, recomputing *D* and *C* for that day with the window count unchanged (Additional file 1, S8). To test the assumption of constant risk, the daily risk after day 21 was multiplied by 1.5, 2 or 3, or raised linearly from 1 times at day 21 to 3 times at day 63 and held there, which weights each adult-day in *C* by the multiplier. Because the window count arises from infection no later than day 21, the calibration was unchanged (Additional file 1, S9).

Because the approximation weakens as the daily risk rises, the model was also run in exact form, solving for the daily risk that reproduces the window count and computing *A* from the full chain (Additional file 1, S1 and S10). The exact form was used at the base inputs, at the combined extremes, and as the window case rate was increased until the daily risk reached 5%, to find the lowest NNV that infection pressure alone can give.

Software and checks

The model was written in R 4.4.3 (counts_model.R), with the exact form in the same script. The cohort counts were computed in StataNow 19.5 BE. An independent recomputation from the LOS curves in the code archive, without the model code, reproduced the counts, every NNV in Table 2 for all six shelters and the illustrative LOS profiles, and the exact values at all three rates (Additional file 1, S6). The accompanying browser tools for cats, dogs and the timing of the second dose [32] compute the counts from uploaded intake and outcome dates, from entered totals or from the illustrative stays, and reproduce the model to the dose (Additional file 1, S6). The cat and dog tools pair these calculations with an animated simulation of adults moving through care, in which a shelter can set its adult census, the share neutered on intake, the timing of each dose and who receives the second dose, and see how few adults a second dose can reach. Claude (Anthropic) was used to help write and check the model code and the browser tools and in the independent recomputation (see Declarations). Code, aggregate inputs and the tools are listed under Availability of data and materials.

Table 2

Second doses per additional case averted (NNV) and cost per case averted at the base inputs. Window case rate 0.10 per 1,000 adult-days, share converted 0.25, second dose on day 14 to every adult still present through day 14, $5.50 per dose. Cases are from infections acquired in shelter care, including those diagnosed after departure. Shelter E supplied cats only, and shelters C and D include all ages. Illustrative LOS profiles are not estimates for particular shelters, and the full sweep of slow-track share and length is in Additional file 1, S9. The stay quantities behind each value (D, C, D / C and the window exposures) are in Additional file 1, Table S7b (Table S9a for the slow-track profile), and cases averted per 1,000 adult admissions are in Table S2.

Stay	Panleukopenia NNV	Cost	Distemper NNV	Cost	Parvovirus NNV	Cost
Shelter A	12,588	$69,236	16,254	$89,398	17,705	$97,376
Shelter B	11,208	$61,642	22,065	$121,357	25,018	$137,601
Shelter C	14,396	$79,179	9,136	$50,248	10,189	$56,039
Shelter D	9,054	$49,797	11,048	$60,767	12,164	$66,901
Shelter E	15,340	$84,370				
Shelter F	8,089	$44,488	6,853	$37,690	6,285	$34,570
One group, mean 21 d (illustrative)	11,798	$64,891	15,186	$83,524	13,709	$75,400
Two groups, 7 and 35 d (illustrative)	7,536	$41,449	9,539	$52,463	8,759	$48,174
Three groups, 5, 15 and 43 d (illustrative)	7,126	$39,194	9,034	$49,685	8,282	$45,552
Fast 7 d, 50% slow at 90 d (illustrative)	2,500	$13,749	3,350	$18,423	2,899	$15,945

Results

Base scenario

At the base inputs, the six shelters needed 8,089 to 15,340 second doses per additional case of panleukopenia averted, 6,853 to 22,065 for distemper and 6,285 to 25,018 for parvovirus, or one disease case averted per 15,000 to 135,000 adult admissions (Table 2). The lowest values were at shelter F, where adults stayed longest, about 25.0 days on average for cats, and 50% of adult cats were present through day 14. Across the observed stays at the six shelters, 7% to 37% of admissions were still present on day 22, when a day-14 second dose becomes effective. For adult cats at shelter A, 19% were still present through day 14 to receive a second dose, and each admission contributed 3.2 adult-days of care after the second dose became effective. Per 1,000 adult admissions, the second dose averted 0.015

cases, one per 65,000 admissions. Of the adult panleukopenia cases the model predicted among adult admissions, including adults that left before day 14, about 86% came from infection in the first 7 days, before the intake dose could be effective, while 2% were averted by the second dose (Additional file 1, S2). Across the six shelters and three diseases, the second dose averted 1% to 5% of shelter-acquired adult cases, and 74% to 91% came from infection in the first 7 days.

Length of stay

At the same window case rate, the NNV depended on the shape of the LOS distribution and not only on its mean. With the same mean of 21 days, the panleukopenia NNV was 11,798 for one group of adults, 7,536 for two and 7,126 for three, and the distemper and parvovirus NNVs fell similarly (Table 2, Fig. 1). Across the slow-track profiles, the panleukopenia NNV fell from 17,552 with 10% of adults on a slow track averaging 35 days to 2,500 with 50% averaging 90 days (Fig. 2 and Additional file 1, S9). These differences mostly follow D / C, with a smaller part from the weighting of the window count. Second doses per adult-day of care from day 22 were 0.028 to 0.096 at the six shelters, 0.063 for one group, 0.038 for three, and 0.014 to 0.081 across the slow-track profiles.

Case rate

In the approximation the NNV was inversely proportional to the window case rate, so it fell 11 fold across the range of case rates tested (Fig. 1). At the base rate the implied daily risk at the six shelters was 0.04% to 0.12%, and across all stays evaluated it differed by up to 25% because of the weighting of the window count. With the biological inputs at base, across the window case rates tested and the six shelters, the NNV was 3,677 to 76,700 for panleukopenia, 3,115 to 110,324 for distemper and 2,857 to 125,091 for parvovirus.

At the base rate, the exact form gave NNVs 2% to 10% higher than the initial approximation at the six shelters and up to 13% higher at the illustrative LOS profiles. At higher rates the gap widens. At the upper rate tested, the exact form gave NNVs 1.05 to 1.23 times the approximate value at the six shelters (Additional file 1, S10). In every case evaluated the exact form gave the higher NNV.

Raising the window case rate further in the exact form, with every other input at base, lowered the NNV only to a minimum at a daily risk of about 3%, 1,152 for panleukopenia with one group of adults and 889 with three adult groups.

Sensitivity

Examined one at a time across their ranges, the window case rate, first-dose failure and the share converted each moved the NNV 7 to 24 fold at the six shelters (Fig. 3 shows the illustrative two-group profile). For panleukopenia and distemper, first-dose failure mattered most, and for parvovirus the share converted after a second dose. The onset of protection moved the NNV 3.2 to 7.9 fold and the incubation lag 1.5 to 2.3 fold at the six shelters (Additional file 1, S3). In the approximation, the susceptible fraction had no effect. Varied together at the base window case rate, first-dose failure and

the share converted after a second dose moved the NNV from 743 to 786,470 across diseases and the six shelters (Additional file 1, S3).

Alternative definitions and conventions were also examined. Giving the second dose also to animals whose outcome falls on day 14 raised the NNV by 5% to 12%. Counting infections as averted only if diagnosed before departure raised it by 10% to 63%. Excluding stays of a year or more, rather than capping them at 365 days, raised the NNV by 0% to 21% at the six shelters. Placing cat failure at the protective cutoff lowered the cat NNV by 14%. Setting distemper first-dose failure to 1/6 cut the distemper NNV to 54% of its base value (Additional file 1, S5).

If the daily risk after day 21 rose 1.5, 2 or 3 times, the NNV fell to 67%, 50% or 33% of its constant-risk value at every stay. A linear rise to 3 times the base risk by day 63 gave 39% to 53% of the constant-risk NNV, the larger reductions at longer stays (Additional file 1, S9).

Combined extremes

With every input set to favor the second dose, the exact form gave NNVs of 252 to 416 for panleukopenia, 161 to 366 for distemper and 228 to 551 for parvovirus across the six shelters, or $886 to $3,030 per case averted (Additional file 1, Table S3d). These combinations had the high end of the window case rate, first-dose failure and share converted after a second dose, and an onset of protection of 3 days. At the illustrative three-group LOS profile, the corresponding values were 226, 199 and 258. With every input set least favorable to it, the NNV exceeded 1 million for each disease at every shelter (Additional file 1, Table S3d).

Timing of the second dose

Moving the second dose later reduced both the number of second doses given and the cases averted (Fig. 4). Compared with day 14, a second dose on day 21 lowered the NNV at every LOS profile except the single-group profile, where it did not change. Revaccination at day 21, the end of the WSAVA interval of 2 to 3 weeks, averted 70% to 92% of the cases that a day-14 dose would have prevented, and used only 54% to 85% of the doses, across diseases and LOS profiles. Revaccination at day 7 averted 109% to 152% of the day-14 cases but used 1.28 to 2.24 times the number of doses (Additional file 1, S8).

Selective second doses

In the analysis by dog size, shelter records supplied the LOS profiles and the infection pressure was assumed. Under an illustrative daily risk shared by all dog sizes, set by 0.10 window cases per 1,000 adult-days for all adults, large adult dogs stayed 31.4 days on average against 7.2 for medium and 7.8 for small adults. Large dogs needed 3,944 second doses to avert one case of parvovirus, medium 18,583 and small 21,464. Medium and small adults received 31% of all second doses and accounted for 8% of all cases averted (Additional file 1, S12).

In the source studies, which included animals of all ages, antibody at intake was more common in animals that arrived neutered, 70% versus 34% for panleukopenia in cats [33], 79% versus 33% for distemper [16] and 86% versus 64% for parvovirus in dogs [34]. As an illustration, with the same daily risk, LOS and first-dose failure, adults that arrived neutered would have about 2.2, 3.2 and 2.5 times the NNV of intact adults for panleukopenia, distemper and parvovirus.

Discussion

At the base inputs, about 6,000 to 25,000 routine second doses for every adult still present through day 14 were needed to avert a single case at the six shelters, and about 2,900 to 130,000 second doses across the range of window case rates evaluated. The benefit of this second dose is small because each link in the chain removes most of the remaining animals. At the six shelters 11% to 50% of adults were still present through day 14, few of those were both susceptible and failed by the first dose, a second dose was assumed to convert one in four of those animals, and the converted animals then had to be infected after day 21 while still in the shelter. Calibrating to the window count ties the model to data shelters can access. At the base inputs the model predicts about 0.84 adult panleukopenia cases per 1,000 adult admissions over the stay at shelter A, most of them in animals no second dose could help.

Why length of stay matters

At a given daily risk, LOS enters only through D / C, so a shelter where many adults are present through day 14 but few stay long after day 21 gives many doses for little time protected. A shelter where adults present through day 14 go on to stay for many more weeks gains more protection for each dose. A LOS profile in which all adults leave at a constant rate puts many adults in care through day 14 but few very far beyond it, while including a slow track adds more protected days for each dose. At the same window case rate and the same 21-day mean, a profile with three tracks gave NNVs 1.7 times lower than the constant-rate profile. Because a mean and median alone do not fix D / C, the browser tools use a shelter’s own dates as input.

Effect of higher infection pressure

A shelter with a much higher adult disease incidence might be expected to benefit most from a second dose, and a higher daily risk does lower the NNV. However, most of the additional cases the model predicts are those a second dose cannot prevent. These additional cases occur first in animals infected before the intake dose took effect, second in first-dose failures infected before the second dose could protect, and third in first-dose failures the second dose does not convert. Disease risk alone also cannot push the NNV down indefinitely. As daily risk rises, more first-dose failures are infected before the second dose protects on day 22, and in the exact form the NNV stops falling at a daily risk of about 3% and begins to rise beyond it. At that point the NNV to prevent a case of panleukopenia was still 889 to 1,152 at the three illustrative LOS profiles with a 21-day mean.

Timing of the second dose

Within recommended vaccination intervals, later dosing results in fewer second doses given, because fewer adults are still present to receive it, but prevents fewer cases, so the preferred timing of second vaccination depends on how a shelter weighs additional prevention against the doses required. At most LOS profiles later dosing means fewer doses per case averted, except for the constant-rate profile, in which the NNV does not depend on the day of the dose. For cats at shelter A, moving the second dose from day 14 to day 21 would give about 70,000 fewer doses (about $400,000) and avert 4 fewer cases per million adult admissions. Giving the dose earlier than day 14 averts more cases at a higher NNV but falls outside the recommended interval. Within that interval, the second dose averts very few cases on any chosen day.

What matters most

Besides LOS, the window case rate, first-dose failure and the share converted dominate the NNV, followed by the onset of protection (Results, Sensitivity). Of these, only the window case rate can be determined from a shelter's own records. The others depend on the vaccine product and the animal's immune response, which shelter records cannot resolve.

The two vaccine-response inputs are the least certain. The first-dose failure estimates come from small samples of 19 to 45 animals, and from the low to the high end their 95% intervals span 9 to 26 fold. These intervals reflect sampling error only, not uncertainty about whether the animals were susceptible at intake, which for distemper could be confirmed in only 6/23 dogs. The share converted is a judgment. If human revaccination data represent adult shelter animals better than data from the canine cohort do, r could be near 0.77 and every NNV about one third of its base value. If the study cohort is closer to reality for dogs, r could be well below 0.25. A study with enough power to settle r would need to enroll a very large number of adult animals, because only a small percentage fail their first dose. The early end of the vaccine onset range is not well understood, because serologic studies often start sampling at 7 days, only one small challenge study covers earlier days, and minimum protective antibody titers are not well established.

The window case rate itself has limits. The count includes cases infected before intake, which the model attributes to the shelter. That inflates the implied daily risk and favors the second dose, most for distemper. At its base lag of 10 days, a distemper case diagnosed on days 8 to 10 must have been infected before intake. In the source cohort 1/7 adult window cases fell in those days, and leaving out such cases would have raised the distemper NNV by about 17%. If risk before intake had equaled that in the shelter, those days would hold 35% to 42% of window cases at the observed dog stays and the NNV would be 1.5 to 1.7 times higher (Additional file 1, S3). Cases found by contact tracing or surveillance rather than clinical signs raise the count compared with a shelter that tests only sick animals, and the dog cohort that informs the upper end counts first positive PCR tests rather than clinical onset.

Implications for shelter protocols

In a shelter where most adults leave within a few weeks and adult window cases are rare, a routine second dose buys little direct protection, on the order of $35,000 to $138,000 per case averted at the six shelters studied here. The value of the second dose rises in scenarios where a substantial share of adults stay for months, where infection pressure is high, up to the limit described above, or where first-dose failure is common. Because the benefit is concentrated in the long-stay tail, a second dose given only to adults expected to stay long would provide more protected days for each dose than one given to every adult still present through day 14. Size is known when the second dose is due. In the size example, withholding the second dose from medium and small adult dogs would have eliminated about a third of the second doses given while losing less than 10% of the cases averted. Shorter stays for smaller dogs are not particular to that shelter. Across 17 municipally funded shelters in five states, small and medium dogs were adopted faster than large dogs early in the stay after adjustment for age group [35], and national median stays to adoption were longer for large dogs than for small dogs, by 2 days in 2019 and 6 days in 2024 [36]. Both sources describe adoption only.

Neuter status at intake is another basis for selection, because adults that arrive neutered are more often already immune, and all 23 dogs with a positive PCR test in the distemper cohort were intact [16]. In an illustrative comparison, adults that arrived neutered would have about two to three times the NNV of intact adults (Results), so a second dose given only to adults that arrived intact would retain most of the benefit of a routine second dose while saving about a fifth to a half of second doses, the share of adults that arrived neutered in these populations.

Applying the model to a shelter

A shelter can determine its own inputs from a spreadsheet of adult intake and outcome dates over the years its current intake protocol has been in place, ideally around five. From those dates the shelter can count the adults still in care through day 14, and the adult-days in care on days 8 to 21 and after day 21. Next, the adult cases of the disease of interest diagnosed 8 to 21 days after intake, while still in care, can be counted, defining a “case” as a recorded diagnosis, confirmed by testing where possible. For example, 4,000 adult cats with stays like those at shelter A would contribute about 12,100 adult-days between days 8 and 21. A single panleukopenia diagnosis among them gives 0.083 per 1,000 adult-days. If none were recorded, 3,000 divided by the adult-days on days 8 to 21 gives an approximate 95% upper limit, here 0.25 per 1,000 adult-days. The LOS counts can also be taken from the Kaplan–Meier output of the open-source mLOS software [37], which also handles adults still in care at the start or end of the period (Additional file 1, S11). The browser tools take the dates directly and keep them in the browser. A shelter at or below the base window case rate of 0.10 per 1,000 adult-days with LOS profiles like those at the six shelters sits at or above the base NNVs in Table 2.

The span of the combined extremes, from 161 to millions of doses per case averted, comes from setting every input at the same end at once. Two of those inputs, the window case rate and the LOS profile, a shelter can measure from its own records. First-dose failure and the share converted it cannot, so a

shelter that uses its own records comes closer to an accurate NNV for its population but still faces a wide range.

Limitations

Much of the input data comes from small studies, single cohorts or single outbreaks, which may not represent all shelters. For example, the panleukopenia first-dose failure count assumes a titer pairing that was never published, but is likely to hold because a cat with detectable antibody is unlikely to fall below detection after a modified live dose. The protective-cutoff alternative gives a lower NNV because it counts primed low responders as failures. The distemper first-dose failure estimate includes 17 dogs whose susceptibility at intake was not confirmed. If some were already immune at intake, *f* is too low and the distemper NNV too high. Parvovirus failure uses a protective-titer cutoff, which on the same reasoning probably overstates *f* and understates the parvovirus NNV. The upper end of the window case rate is a scenario value informed by one shelter's distemper outbreaks, with care-days estimated from occupancy, and those outbreaks include cases in recombinant vaccine recipients, so it likely overstates infection pressure for a modified live protocol. Panleukopenia and parvovirus borrow it, although they may have different case rates. Curves at two shelters include juveniles, whose stays may differ from those of adults.

The model counts only direct protection from infection in the shelter. Infection pressure does not end when an animal leaves, and a second dose may protect an animal after adoption or transfer, while fewer cases in the shelter may reduce exposure for others. Neither is counted, and both would lower the NNV. For these reasons, a shelter that already gives a second dose may record a lower window count than it would under a protocol of vaccination at intake only.

Daily risk was held constant over the stay, and this assumption is what connects the window cases a shelter observes to the later, preventable ones. Matching the early window count does not show that risk stays constant. If risk falls after intake, the constant-risk assumption overstates the benefit of the second dose. If it rises, for example as susceptible animals accumulate, infected animals are admitted or animals are moved between wards, the model understates the benefit, which comes entirely from infection after day 21 (Additional file 1, S9). The approximation that drives the main results favors the second dose slightly at the base rate and increasingly at higher rates, where the exact form is reported.

The analysis does not address outbreak response or the herpesvirus and calicivirus components of feline combination vaccines, whose lower potency is the reason given for two adult doses in cats outside shelters [1]. Animals younger than one year were not modeled, and because a single dose fails more often in them, a second dose after the series ends may be worth more in them than these adult results suggest. Core antigens are given in combination products, but each pathogen behaves differently, so each component would need to be assessed on its own, and these results cannot by themselves settle the overall value of repeating a combination vaccine.

Conclusions

Under the base assumptions, this model predicts little additional direct protection against panleukopenia, distemper or parvovirus from routine second vaccination of adults. The benefit is larger where adults present through day 14 go on to stay much longer, because more of their stay falls after the second dose takes effect. Greater benefit is possible if first-dose failure is more common or when a second dose protects a larger share of those animals sooner. Shelters can use their own intake and outcome dates and adult case counts, entered in the accompanying browser tools, to investigate the expected benefit, although uncertainty about vaccine response rates remains.

Abbreviations

CI, confidence interval. LOS, length of stay. NNV, number needed to vaccinate. PCR, polymerase chain reaction. USD, United States dollars. WSAVA, World Small Animal Veterinary Association.

Declarations

Ethics approval and consent to participate. Not applicable. No animals were used or handled for this study. Shelter intake and outcome records were obtained through public records requests, except at shelters E and F, whose records were used with the shelters' permission. All other inputs are aggregate counts from published studies.

Consent for publication. Not applicable.

Availability of data and materials. The R model, the Stata files for the cohort counts and the aggregate inputs, including the day-by-day stay curves for shelters A to F, are archived in Zenodo [38]. Record-level data for shelters A, B, D, E and F are not shared because they were provided for this analysis by the shelters or under public records requests. Requests should be made to the shelters. The Orange County records and the mLOS files used in Additional file 1, S12 are deposited in Zenodo [39–42]. The browser tools for cats, dogs and the timing of the second dose, including the animated simulation in the cat and dog tools, are available online [32].

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Authors' contributions. Rachael Kreisler: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Software, Visualization, Project administration, Writing – original draft, Writing – review and editing. Lena DeTar: Resources, Writing – review and editing. Michael L. Mavrovouniotis: Methodology, Software, Validation, Formal analysis, Data curation, Writing – original draft, Writing – review and editing. All authors read and approved the final manuscript.

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Figures

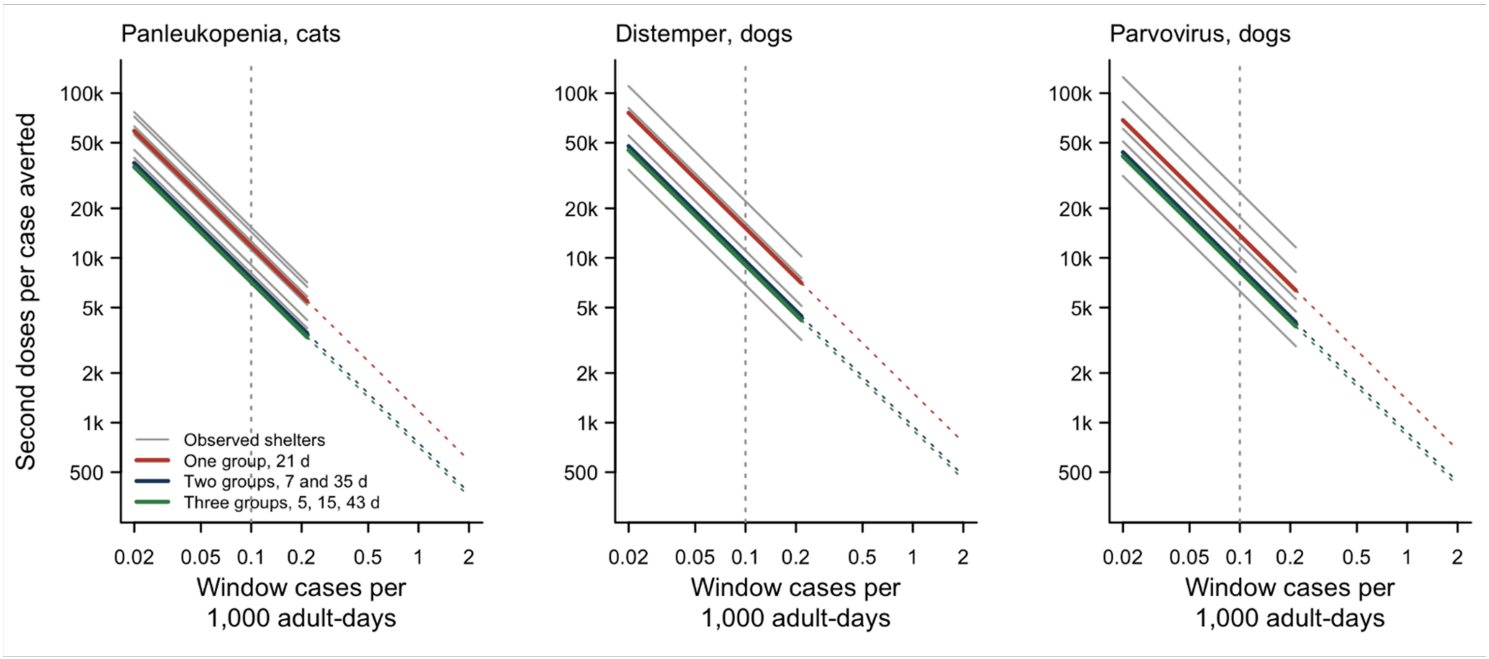


Figure 1

Second doses per case averted by window case rate. Second doses per additional case averted, by the window case rate (adult cases diagnosed 8 to 21 days after intake per 1,000 adult-days in care on days 8 to 21, under a protocol of vaccination at intake only), from the counts approximation. Other inputs at base. Grey lines are the eleven observed stay curves at shelters A to F, and colored lines are three illustrative LOS profiles with the same 21-day mean, split into one, two or three groups of adults by LOS.

Heavy lines span the evaluated range, 0.02 to 0.22, and thin dotted lines extend the illustrative profiles to 2 per 1,000 adult-days. The vertical dotted line is the base window case rate. The approximation understates the NNV slightly at the base rate and more at higher rates. At the upper end of the range the exact form is 1.05 to 1.23 times the approximation at the six shelters (Additional file 1, S10). Log scales. At $5.50 a dose, 1,000 doses cost $5,500.

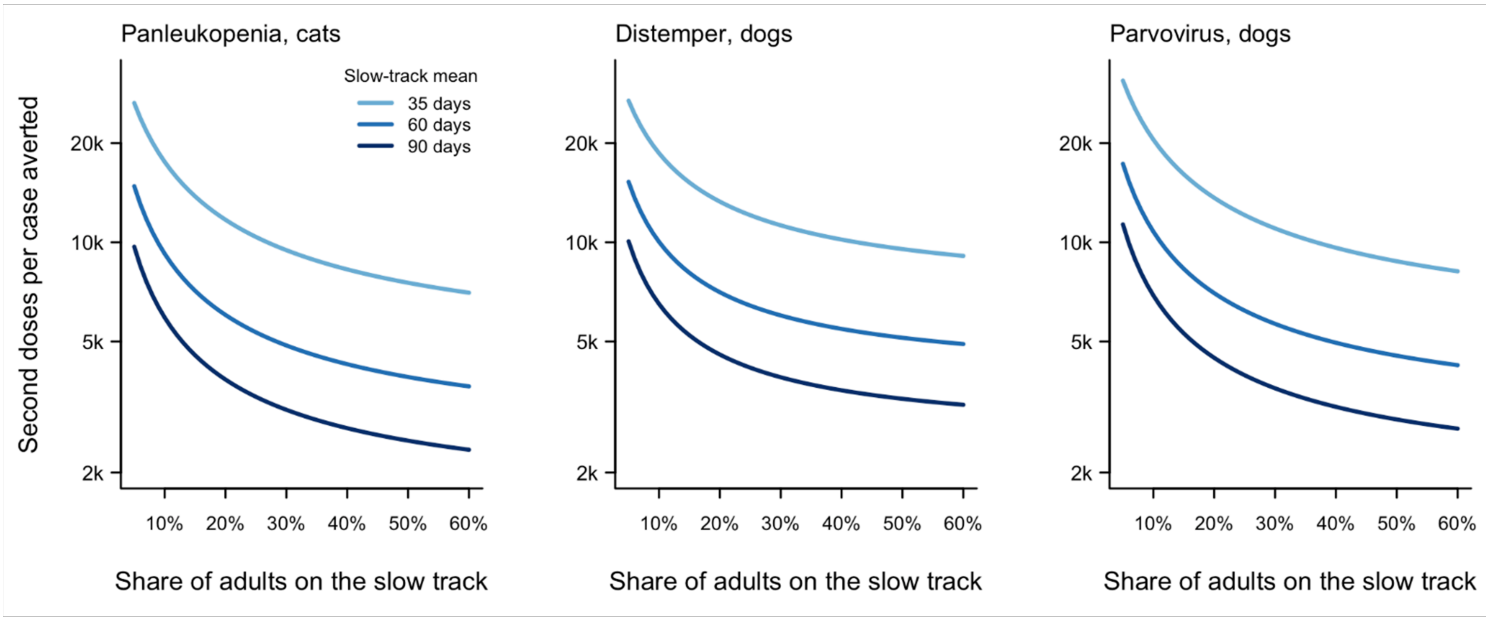


Figure 2

Second doses per case averted by the share of adults on a slow track. Second doses per additional case averted by the share of adults on a slow track, for illustrative LOS profiles with a fast track averaging 7 days and a slow track averaging 35, 60 or 90 days. Window case rate 0.10 per 1,000 adult-days, other inputs at base. Most of the benefit of a second dose is for the adults who stay long after day 21. Log scale. Values at 10%, 25% and 50% are in Additional file 1, Table S9a, and every share from 5% to 60% is in slow_track_sweep.csv.

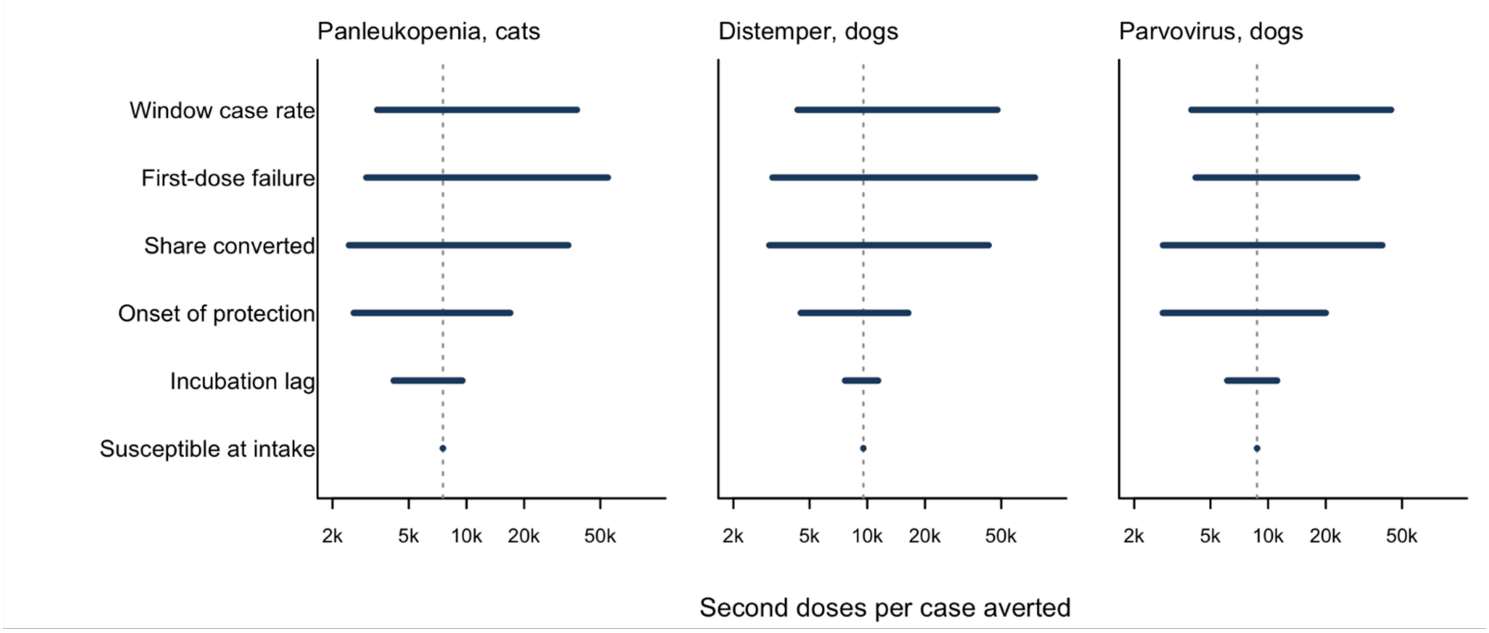


Figure 3

One-way sensitivity of second doses per case averted. One-way sensitivity at the illustrative two-group LOS profile (equal groups averaging 7 and 35 days). Each line spans the NNV across one parameter's range with the others at base. The window case rate is per 1,000 adult-days. The susceptible fraction cancels from the NNV in the counts approximation. Values for every LOS profile are in Additional file 1, S3.

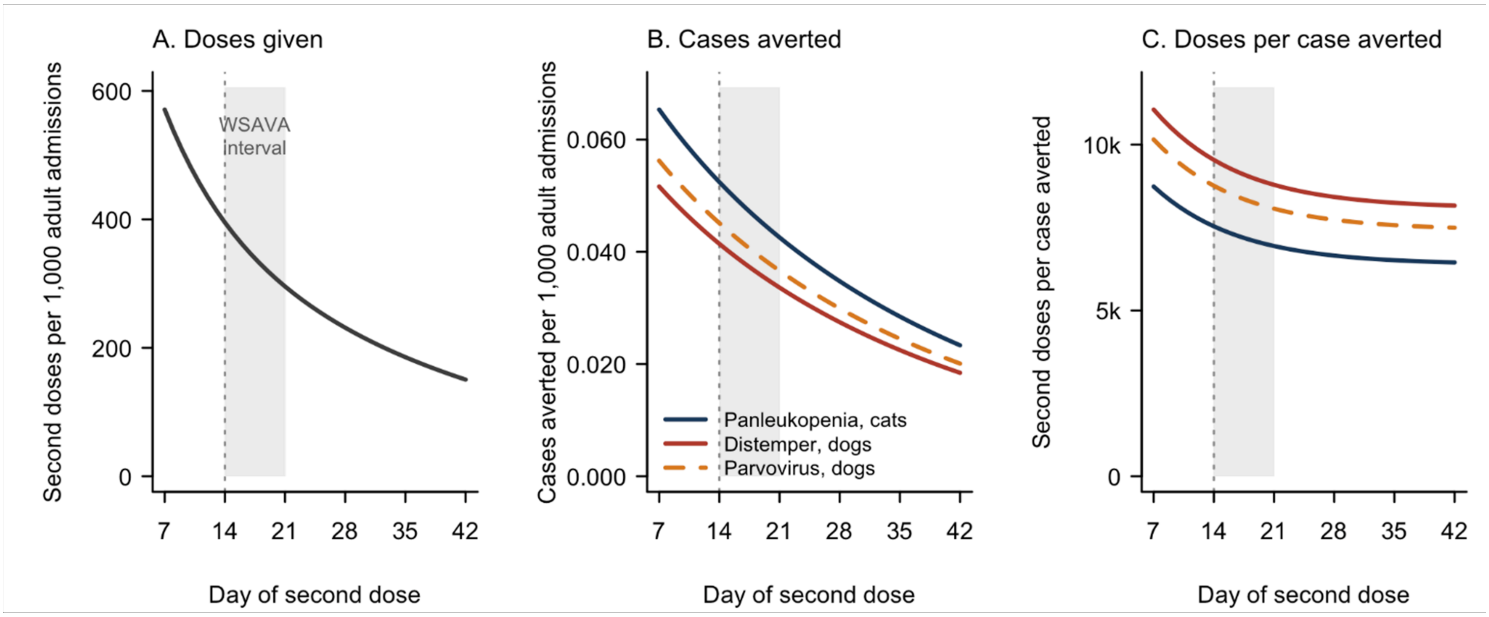


Figure 4

Doses given, cases averted and doses per case averted by day of second dose. Timing of the second dose at the illustrative two-group LOS profile (equal groups averaging 7 and 35 days), other inputs at base. A, second doses given per 1,000 adult admissions, the same for every disease because the stay is

the same. B, cases averted per 1,000 adult admissions. C, number of second doses per case averted. The shaded band is the interval of 2 to 3 weeks after the first dose recommended by WSAVA. The dotted line is day 14. A later dose uses fewer doses per case averted, but averts fewer cases overall. Observed stays are in Additional file 1, S8.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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