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| Rating |  | Rate Lower | | | | | Rate Higher | | |  |
| Category | Study Design | Limitations | Inconsistency | Indirectness | Imprecision | Publication Bias | Large Effect | Dose Response | All plausible Confounding | Total Quality |
| Notation | Randomized Trails -> High  Observational Study -> Low  Expert Opinion -> -1 | No serious limitations  Serious limitations() | No serious inconsistency  Serious Inconsistency() | No serious indirectness  Serious Indirectness() | No serious imprecision  Serious Imprecision() | Undetected |  |  |  | High, Moderate, Low, Very Low |
| Explanation | For this meta analysis almost all the data is from observational studies. So we will be starting with low quality of evidence. Also by the guidelines many of the tests are biased since they were looking for a specific pathogen in an animal group. | For observational studies a lot of the comparison are for effect studies such as inclusion of control population, flawed measurement of exposure and outcome, control confounding, no follow up.  Risk of bias based on study design falls under this category   * Stopping Early * Failure to conceal Allocation * Failure to blind * Loss to follow up * Stopping early for benefit * In appropriate controls * Selectively reporting outcomes. * Flawed measurement of outcome   The overall quality of evidence.  The extent to which a study contributes to the magnitude of effect. | Check for inconsistency in:   * Population * Intervention * Outcome * Study Methods * Point estimates vary widely across studies * Confidence intervals show minimal to no overlap. * The statistical tests for heterogeneity which test the null hypothesis that all studies in a meta-analysis have the same underlying magnitude of effect shows a low P-value * The I2 which quantifies the proportion of the variation in point estimates due to among study differences is large * Subgroups * Never rated up for consistency but always rated down | * Patients different from patients of interest * Intervention tested different from intervention of interest * Extraneous factors that might affect results biological/society * Outcomes of interest different from primary. Use of surrogates that might not necessarily be the same as patient. Surrogates need a lot of evidence to show that they are viable. * Comparison between interventions that have not had head to head comparison. * Do not grade down based on mechanism or study method. | * Small Sample size * Confidence interval narrow * Confidence interval exclude clinical decision threshold * Large sample size (>2000) small effect size * Rate down for confidence limits that are large compared to absolute values, not relative values. * Rate down CL cross threshold for recommend and not recommending treatment. * Rate down if data not with in Optimal Information Size http://www.stat.ubc.ca/|rollin/stats/ ssize/b2.html. * This one is really about how wide the confidence intervals are and how precise the data is in showing an effect. | This type of bias is more associated with conflicts of interest   * Small number of studies most of which have been commercially funded * Funnel plots * Studies with statistically significant results are more likely to be published * Systematic reviews preformed early will overestimate * Withholding of negative results by industry sponsors is common. * Be cautious about empirical measures of pub bias.   It can be hard to tell if there is publication bias for observation al studies. | * More than 140 participants * Large magnitude of effect (direct evidence, relative risk [RR] 5 2e 5 or RR 5 0.5e0.2 with no plausible confounders); very large with RR O 5 or RR ! 0.2 and no serious problems with risk of bias or precision (sufficiently narrow confidence intervals); more likely to rate up if effect rapid and out of keeping with prior trajectory; usually supported by indirect evidence | If there is a strong dose response relationship between the effect and the outcome. | If the study looked at the other factors that could have affected their study results. For example if a study looked at one thing they would also look at all the factors that could affected the study results. For example a study that looked at for profit and non profit hospitals also looked at insured status and how sick patients were before entering the hospital.  Spurious Effects  Instead of dose response we will look at if the study contains enumerated data | High – We are very confident that the true effect lies close to that of the estimate of the effect.  Moderate – Wear are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different from the estimate of effect.  Low- Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.  Very low – We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. |
| Modified GRADE for this this study | Observational Studies -> Low | * Flawed measurement of outcome. * Selectively reporting outcomes * Stopping early | * Subgroups * Point estimates vary widely across studies * If different methods were used for different parts. * Never rated up always down | * Extraneous factors that might affect results biological/society * Outcomes of interest different from primary. Use of surrogates that might not necessarily be the same as patient. * Surrogates need a lot of evidence to show that they are viable. * Do not grade down based on mechanism or study method. * Rated down for data from composite samples and not connected to individual samples. | * Small Sample size * Rate down for confidence limits that are large compared to absolute values, not relative values. | * Check for conflict of interest that might occur. | * More than 140 individual animals in a dataset. | * Rate up if there is enumerated data. | * Rate up if they checked for differences by animal characteristics. |  |
| Justification for Modifications | All the studies are observational so all of them will have a low GRADE  I decided to keep this to conform to GRADE standards also I decided to grade up in some areas. | These are the ones that I am going to keep the rest do not work since we are not looking at effects measures. | These are the ones that I am keeping since they are part of GRADE Standards | These are the ones I am keeping the others don’t work because they would have been filtered out in the systematic review, because they are what I want and I was not as concerned with the study. | The following modifications will be made: to keep imprecision based on sample size but we will ignore effect size since it is expected to be different for animal/ pathogen/ method categories.  Many of the examples are for a treatment effect and we have none so we are ignoring that part.  We are not using optimal information size since all studies would be down graded since our positive rate is low and data size is low so almost everything would be downgraded.  We are not going to grade down for imprecision for censored data since all data has it and showing it is more and effect of showing it instead of keeping it hidden. | Publication bias is one of those things that is hard to measure so I am just going to do it on a case by case basis. | For this I am going to not use the large effect size since there is nothing comparable. Also from what I have seen large effects or with large pathogen concentrations tend to be for studies that would be considered more biased or would be marked down due to inconsistency. | Instead of dose response we will look at if the study contains enumerated data since this is the closest we come to dose response. | The way that this is going to be interpreted is the study will be rated up if they seperated their data set by age, location, or other animal characteristics. | We are going to keep these the same as for everything else |
| Things that apply to everything | * When down grading be conservative and only down grade when it is a “serious” issue. * When synthesizing for multiple studies use the lowest quality among all studies * If there is a close call to rate down for multiple areas then pick one to rate down, acknowledge both cases. * Mention if something for a category is unclear or uncertain.   Things to keep in mind   * What we did can almost look like many different separate meta analysis. * This is subject to change as I go through articles. | | | | | | | | | |