* Intro material
  + Resistance to antibiotics may be acquired by spontaneously occurring genetic mutations, and be passed vertically by selection to daughter cells. More commonly, resistance is acquired by the horizontal transfer of mobile DNA elements from a donor cell, often from another bacterial species (Chambers, 2001; Sefton, 2002). The two main factors involved in the development of antibiotic resistance in bacteria are the selective pressure by the use of antibiotics and the presence of resistance genes (Levy, 1997; Witte, 2000).
  + There is growing evidence and little doubt that resistance genes can be spread and exchanged between different bacterial populations (McDermott et al., 2002; O’Brien, 2002; Teale, 2002). Resistance that is acquired by horizontal transfer of resistance genes can become rapidly and widely disseminated either by clonal spread of the resistant strain itself or by further genetic exchanges between the resistant strain and other susceptible strains (Chambers, 2001)
* Literature showing AB usage = selection pressure
  + - *“Antibiotic resistance is equally likely to diminish in prevalence when antibiotic use is decreased or discontinued. Although individual bacterial strains may retain resistance genes, they are often (gradually) replaced by susceptible strains when the selective pressure is removed”*
      * Phillips I, Casewell M, Cox T, et al. Does the use of antibiotics in food animals pose a risk to human health? A critical review of published data. J Antimicrob Chemother 2004;53:28 –52.
    - *“Generally, percentages of antimicrobial resistance before (conventional) were significantly higher than after (organic) the transition. Overall, percentages of antimicrobial resistant mastitis pathogens decreased after 6 months operating as an organic farm system. An 8-month study was conducted in Thailand to investigate the effects of antimicrobial-resistant patterns of mastitis pathogens during an experimental farm’s 6-month transition from conventional to organic farming. Antimicrobial resistance of mastitis pathogens in the before (conventional) and after (organic) transition periods were compared for 7 antimicrobial drugs used to treat mastitis.”*
      * Suriyasathaporn W. Milk quality and antimicrobial resistance against mastitis pathogens after changing from a conventional to an experimentally organic dairy farm. Asian Austral J Anim Sci May 1, 2010
    - Erskine RJ, Walker RD, Bolin CA, et al. Trends in antibacterial susceptibility of mastitis pathogens during a seven-year period. J Dairy Sci 2002;85:1111– 8
      * Not much evidence that ***AMR increasing over time,*** which is a different question
      * 7-year study of Michigan dairy herds; the proportion of bacterial isolates susceptible to antibiotics did not change for the majority of tests
      * Overall, the prevalence of AMR over a 7-year period did not change (1994–2000). The prevalence of S. aureus isolates resistant to ampicillin, penicillin and erythromycin declined during this period. Streptococcus uberis isolates became more susceptible to oxacillin, sulfa-trimethoprim gentamicin, and pirlimycin while becoming more resistant to penicillin. Linear declines in AMR were also reported for Streptococcus dysgalactiae, Streptococcus agalactiae, E. coli and Klebsiella pneumoniae. Overall, the authors concluded that there was no indication of increased resistance among mastitis clinical isolates for antimicrobials used commonly to treat mastitis
    - Nam HM, Lim SK, Kang HM, et al. Prevalence and antimicrobial susceptibility of gram-negative bacteria isolated from bovine mastitis between 2003 and 2008 in Korea. J Dairy Sci 2009;92:2020 – 6. 31.
    - Nam HM, Lim SK, Kang HM, et al. Antimicrobial resistance of streptococci isolated from mastitic bovine milk samples in Korea. J Vet Diagn Invest 2009;21:698 –701.
* BUT support for using AB
  + Call 2008: decreasing animal health could increase the probability of a higher pathogen load in these animals with commensurate increased risk of exposing humans to genuine pathogens (Cox and Popken, 2006) (also see Claycamp (2006)).
  + It reduces the suffering of animals and prevents pathogenesis in humans via consumption of milkborne/foodborne mastitis pathogens that are potential human pathogens
  + Danger of consumption of raw milk
    - Oliver SP, Boor KJ, Murphy SC, et al. Food safety hazards associated with consumption of raw milk. Foodborne Pathog Dis 2009;7:793– 806.
  + Find papers about pain/inflammation associated with mastitis
    - An Update on the Effect of Clinical Mastitis on the Welfare of Dairy Cows and Potential Therapies
    - Christina S Petersson-Wolfe 1, Kenneth E Leslie 2, Turner H Swartz 3
    - Assessment and Management of Pain in Dairy Cows with Clinical Mastitis Kenneth E. Leslie, DVM, MSca,\*, Christina S. Petersson-Wolfe
    - Ginger L, Ledoux D, Bouchon M, Rautenbach I, Bagnard C, Lurier T, Foucras G, Germon P, Durand D, de Boyer des Roches A. Using behavioral observations in freestalls and at milking to improve pain detection in dairy cows after lipopolysaccharide-induced clinical mastitis.
* Overall significance
  + Many MIC below clinical breakpoints – so, techinically still susceptible – so, what is clinical significance? Not really sure. BUT keeping an eye on it; and reporting MIC numbers, not just lumping in as SIR bc those cut points change over time
    - bacteriological cure rates may not differ between isolates of differing MIC
* Summarize studies
  + Start out with weaker, smaller ones
  + Describe results of largest, most rigorous analysis ones
    - Ruegg
    - Mcdougall
  + Other short communications that aren’t in the table
    - Studies on transitioning
      * Park 2012
      * Can compare to Erskine one which was long term
    - Walther 2007, org farm with MRSA epi – maybe this goes with point in cicconi hogan about org status doesn’t matter in regards to being source for MRSA
    - Rajala-schultz
      * Not organic, but cows exposed to dry terat and not
        + Age has so many other affects on animals though
        + Type of NAS, immune function, SCC
    - Fecal papers
      * Whole other body of work, different system
        + Different exposures, different pathogen behavior, different pathogen community interactions
* Limitations of some of the studies
  + Enumeration/standardization of drug usage
  + Europe vs. US
  + Complicated to compare between
    - Sampling strategies
    - Methodology of determination of antibiograms
      * agar diffusion, broth microdilution
      * the interpretive criteria used for categorizing isolates as susceptible or resistant are based on human data for the majority of compounds tested (Watts and Yancey, 1994; Thornsberry et al., 1997). They cannot be used to predict clinical efficacy and they may not accurately reflect the efficacy of the drug in treatment of bovine mastitis
  + Summarized in Call 2008
    - post-hoc analysis of individual studies is highly problematic due to differences in methods used (e.g. disc diffusion versus serial broth dilution and changing criteria) (Klement et al., 2005); failure to speciate the organisms under study when there can be considerable variation between species and strains (Rossitto et al., 2002); changes in management practices; differences in sample collection and culture methods can bias recovery of organisms; differences in sampling frame (independence between isolates; random, opportunistic, or clinical sampling) can also introduce bias; stochastic events (e.g. heterogeneous clonal dissemination) could easily bias interpretation of smaller studies; even well-organized, large-scale, and centralized studies encounter deviations in study protocols and unequal reporting efforts that make comparisons between countries tenuous (Hendriksen et al., 2008).
      * Clinical cases: analyses of clinical isolates, it is important to acknowledge that resistant isolates may be amplified by therapeutic treatments that are administered to sick animals prior to isolation of resistant organisms; this may bias prevalence estimates for AMR pathogens compared with a random sampling design
    - as with all correlation studies readers should be cautious about inferring causation when there are limited controls for confounding variables or when conclusions are drawn from a limited number of independent observations
  + *“variation among herds in MIC may in part be due to introduction of resistant isolates, rather than selection for, or perpetuation of, such isolates within a herd. Additionally, other mastitis management practices may affect the probability that resistant isolates remain in the herd. For example, selection criteria for culling of cows may remove cows infected with resistant isolates”* McDougall 2021
* What else explains degree of AMR carriage? Herd effect – clonality, esp. of contagious organisms
  + Dominant strain aureus may have resistance
  + Different strains associated with carrying resistance?
    - Find literature
  + So, dominant strain in one herd may carry resistance
  + Strain associated with resistance – phylogeny and not just env. pressures
    - From Call 2008: Walk et al. (2007) found that on average organic and conventional dairies have different representation of phylogenetic groupings of E. coli, suggesting there are differences between lineages of E. coli in their ability or probability of assimilating resistance genes
* What else explains degree of AMR carriage? Species effect – carriage of AMR likely associated with species of CNS
  + Older studies not differentiating
  + Literature showing AMR difference by species of NASM?
    - Strep: Rossitto PV, Ruiz L, Kikuchi Y, Glenn K, Luiz K, Watts JL and Cullor JS (2002). Antibiotic susceptibility patterns for environmental streptococci isolated from bovine mastitis in central California dairies. Journal of Dairy Science 85: 132–138.
* Why is AMR maintained in organic systems at all?
  + Call 2008: “*transient expansion of resistant populations can lead to genetic linkage with other selective traits that permit long-term persistence of AMR subpopulations in production environments”*
    - Example of persistence, chloramphenicol banned but still finding resistance 20 years later:
      * One study found that bacteria from retail ground beef from conventional operations had a higher prevalence of chloramphenicol and ceftiofur resistant bacteria, but there were no differences for nine other antimicrobials (LeJeune and Christie, 2004). It should be noted that chloramphenicol has been banned from use in US food animals since 1986 because of the risk of aplastic anemia and elevated risk of lymphoma in humans (Settepani, 1984), and thus the mechanism allowing persistence of chloramphenicol resistance in fecal bacteria is unclear for US cattle populations