*From de buck review*

* S. chromogenes have relatively low phenotypic and genotypic prevalence of AMR when compared to other NAS species isolated from the udder (82)
  + *Nobrega DB, Naushad S, Naqvi SA, Condas LAZ, Saini V, Kastelic JP,et al. Prevalence, genetic basis of antimicrobial resistance in non-aureusStaphylococciisolated from Canadian dairy herds.Front Microbiol.(2018)9:256*
* Another study demonstrated that S. epidermidis had increased resistance rates against penicillin when compared to S. chromogenes (94).
  + *Sampimon OC.Coagulase-Negative Staphylococci Mastitis in Dutch DairyHerds. Utrecht: Utrecht University (2009)*
* Additionally, researchers reported presence of β-lactamase in S. chromogenes is relatively low when compared to either S. haemolyticus or S. Epidermidis (61)
  + *Persson Waller K, Aspán A, Nyman A, Persson Y, Grönlund Andersson U.CNS species and antimicrobial resistance in clinical and subclinical bovine mastitis.Vet Microbiol.(2011) 152:112–6.*
* In Canada, higher numbers of AMR genes, with a strong correlation between AMR genotype and phenotype, were identified in NAS rather than S. aureus originating from the same dairy herds (82)
  + *Nobrega DB, Naushad S, Naqvi SA, Condas LAZ, Saini V, Kastelic JP,et al. Prevalence, genetic basis of antimicrobial resistance in non-aureusStaphylococciisolated from Canadian dairy herds*
* This is in agreement with previous reports where S. aureus isolated from SCM and CM cases were less resistant than NAS against commonly used antimicrobials (60,75,95,96)
  + *Taponen S, Pyörälä S. Coagulase-negative staphylococci as cause ofbovine mastitis — Not so different fromStaphylococcus aureus?*
  + *Wald R, Hess C, Urbantke V, Wittek T, Baumgartner M. Characterization ofStaphylococcusspecies isolated from bovine quarter milk samples.Animals.(2019)*
  + *Kot B, Piechota M, Wolska KM, Frankowska A, Zdunek E, Binek T, et al.Phenotypic and genotypic antimicrobial resistance of staphylococci frombovine milk.Pol J Vet Sci.(2012)*
  + *de Jong Garch FE, Simjee S, Moyaert H, Rose M, Youala M, SiegwartE.Monitoring of antimicrobial susceptibility of udder pathogens recoveredfrom cases of clinical mastitis in dairy cows across Europe: VetPathresults.Vet Microbiol.(2018)*
* In addition, studies have demonstrated that NAS could serve as reservoirs for AMR genes for major mastitis pathogens including S. Aureus (97,98)
  + *Fišarová L, Pantuˇcek R, Botka T, Doškar J. Variability of resistanceplasmids in coagulase-negative staphylococci and their importance as areservoir of antimicrobial resistance.Res Microbiol.(2019) 170:105–11.doi: 10.1016/j.resmic.2018.11.00498.*
  + *Argudín MA, Vanderhaeghen W, Butaye P. Diversity of antimicrobialresistance and virulence genes in methicillin-resistant non-Staphylococcusaureus staphylococci from veal calves.Res Vet Sci*
* A study (60) investigated the association between AMR and antimicrobial use in NAS. An association was present when penicillins, third-generation cephalosporins or macrolides were administered systemically, but not when antimicrobials were administered via the intrauterine and intramammary route
  + *Taponen S, Pyörälä S. Coagulase-negative staphylococci as cause ofbovine mastitis — Not so different fromStaphylococcus aureus?*
  + *(99)*
  + *Nobrega DB, De Buck J, Barkema HW. Antimicrobial resistance in non-aureus staphylococci isolated from milk is associated with systemicbut notintramammary administration of antimicrobials in dairy cattle.J Dairy Sci.(2018)*
* It was hypothesized that antimicrobials administered systemically for conditions other than mastitis, if partitioning to the udder, could cause prolonged bacterial exposure to sub-therapeutic antimicrobial concentrations in the udder.
* Similarly, one study suggested that increasing systemic administration resulted in a decrease of antimicrobial susceptibility of NAStoβ-lactams, as opposed to intramammary treatment of SCM. Systemic administration was expressed as antimicrobial treatment incidence, with units of the number of defined daily doses animal used per 1,000 cow-days (100). In addition, there isa higher likelihood of NAS being present in the udder compared S. aureus, which would therefore result in an increased window of exposure of NAS to antimicrobials used in dairy herds
  + *Stevens M, Piepers S, Supré K, De Vliegher S. Antimicrobial consumptionon dairy herds and its association with antimicrobial inhibition zonediameters of non-aureusstaphylococci andStaphylococcus aureusisolated from subclinical mastitis.J Dairy Sci.(2018)*
* Methicillin-resistant NAS were an important reservoir of AMR and virulence genes in a Belgian study (98). Most cases saw an association between presence of AMR genes and phenotypic resistance, and only a few cases had a negative correlation between presence of AMR genes and resistance. This study also identified some isolates which did not carry any of the investigated AMR genes yet still displayed a non-wildtype (epidemiologically resistant) phenotype (98).Staphylococcus sciuri appeared resistant to fusidic acid but this phenotype was not correlated to any of the known fusidic acid resistance genes (98)
  + *Argudín MA, Vanderhaeghen W, Butaye P. Diversity of antimicrobialresistance and virulence genes in methicillin-resistant non-Staphylococcusaureus staphylococci from veal calves.Res Vet Sci*
* In a Swiss study (98) in vitro phenotypic resistance to several antimicrobials such as erythromycin, clindamycin and streptomycin was not explained by the presence of any tested genes (102), suggesting development of new resistance mechanisms.
  + *Frey Y, Rodriguez JP, Thomann A, Schwendener S, Perreten V. Geneticcharacterization of antimicrobial resistance in coagulase-negativestaphylococci from bovine mastitis milk.J Dairy Sci.(2013*
* Previous studies have also characterized associations between resistance determinants and AMR in NAS. These includeβ-lactam resistance being associated with blaZ and mecA genes, and chloramphenicol resistance having a correlation with the FexA transporter. Daptomycin resistance was explained by the presence of the mprF gene, whereas tetK and tetL genes were associated with tetracycline resistance (82). Even though bovine NAS isolates may acquire resistance to these antimicrobials, it has been suggested through phenotypic AMR patterns that intrinsic mechanisms of AMR may be present for a subset of NAS species as well (82). It is worth noting that many of these antimicrobials are not labeled for use in lactating dairy cows. For example in North America and Europe chloramphenicol is illegal for use in food-producing animals, suggesting the absence of selective pressures
  + *Nobrega DB, Naushad S, Naqvi SA, Condas LAZ, Saini V, Kastelic JP,et al. Prevalence, genetic basis of antimicrobial resistance in non-aureusStaphylococciisolated from Canadian dairy herds.Front Microbiol.(2018)*
* A study in Portugal characterized the AMR profile of methicillin-resistant staphylococci (MRS) isolates from bovine SCM and CM cases, identifying 9.3% of isolates as being MRS and associated with the mecA virulence gene (101). Despite the low percentage of MRS detected, the majority of isolates still had a multi-resistance profile (101)
  + *Seixas R, Santos JP, Bexiga R, Vilela CL, Oliveira M. Short communication:antimicrobial resistance and virulence characterization of methicillin-resistant staphylococci isolates from bovine mastitis cases in Portugal.J DairySci.(2014) 97:340–4.*
* This study, in addition to a Swedish one (61), revealed that AMR and **virulence gene profiles are species dependent**. The Swedish study revealed that the prevalence ofβ-lactamase varied among NAS species and was more common in isolates originating from SCM cases than from CM cases (61).β-lactamase is the most common resistance mechanism in staphylococci, and while the prevalence was high in S. epidermis and S. haemolyticus, there was little to no detection in S. chromogenes and S. simulans(61). In this study, S. chromogenes and S. epidermis were the most commonly isolated species in SCM cases
  + *Persson Waller K, Aspán A, Nyman A, Persson Y, Grönlund Andersson U.CNS species and antimicrobial resistance in clinical and subclinical bovinemastitis.Vet Microbiol.(2011) 152:112–6. doi:*
* In a Dutch study, 70% of S. Epidermis isolates and 18% of S. chromogenes isolates were resistant to penicillin (94)
  + *Sampimon OC.Coagulase-Negative Staphylococci Mastitis in Dutch DairyHerds. Utrecht: Utrecht University (2009).*
  + *(Table 4), suggesting that a highprevalence of penicillin resistance in SCM was associated with thehigh prevalence ofS. Epidermis (61)*
  + *Persson Waller K, Aspán A, Nyman A, Persson Y, Grönlund Andersson U.CNS species and antimicrobial resistance in clinical and subclinical bovinemastitis.Vet Microbiol.(2011) 152:112–6. doi*
* These findings confirm the existence of inter-species variation in AMR profiles, emphasizing the need to continue monitoring co-resistance profiles among NAS populations associated with bovine mastitis cases. Coupled with the possible development of resistance mechanisms not associated with previously characterized virulence genes, additional studies analyzing AMR in NAS are needed alongside the characterization of bovine NAS specific clinical antimicrobial susceptibility breakpoints, as this presents a challenge in treating bovine mastitis cases

References from Table 4 from de buck “Summary of antimicrobial resistance profiles and prevalence of single gene resistance determinants of frequently isolated NAS species across several studies”

* 98 - Argudín MA, Vanderhaeghen W, Butaye P. Diversity of antimicrobialresistance and virulence genes in methicillin-resistant non-Staphylococcusaureus staphylococci from veal calves.Res Vet Sci.(2015) 99:10–16.do
* 101 – Seixas R, Santos JP, Bexiga R, Vilela CL, Oliveira M. Short communication:antimicrobial resistance and virulence characterization of methicillin-resistant staphylococci isolates from bovine mastitis cases in Portugal.J DairySci.(2014) 97:340–4.
* 94 - Sampimon OC.Coagulase-Negative Staphylococci Mastitis in Dutch DairyHerds
* 102 - Frey Y, Rodriguez JP, Thomann A, Schwendener S, Perreten V. Geneticcharacterization of antimicrobial resistance in coagulase-negativestaphylococci from bovine mastitis milk.J Dairy Sci.(2013) 96:2247–57.doi:
* 82 - Nobrega DB, Naushad S, Naqvi SA, Condas LAZ, Saini V, Kastelic JP,et al. Prevalence, genetic basis of antimicrobial resistance in non-aureusStaphylococciisolated from Canadian dairy herds.Front Microbiol.(2018)9:256
* 103 - Andreis SN, Perreten V, Schwendener S. Novelβ-lactamaseblaARLinStaphyloccocus arlettae.mSphere. (2017) 2:e00117-17