# SUPPLEMENTARY MATERIAL

# **Table S1.** Search query CAB Abstracts

|  |  |  |
| --- | --- | --- |
| # | Query | Results |
| S25 | S24 (Limiters - Publication Year: 20100101-) | 435 |
| S24 | S11 AND S12 AND S17 AND S20 NOT S23 | 920 |
| S23 | S21 OR S22 | 11,429 |
| S22 | TX "dry period" | 9,543 |
| S21 | TX "dry cow\*" | 3,041 |
| S20 | S18 OR S19 | 2,179,355 |
| S19 | TX "therap\*" | 824,150 |
| S18 | TX "treatment\*" | 1,651,863 |
| S17 | S13 OR S14 OR S15 OR S16 | 992,634 |
| S16 | TX "targeted" | 70,674 |
| S15 | TX "rapid test\*" | 2,985 |
| S14 | TX "cultur\*" | 836,772 |
| S13 | TX "selective" | 102,301 |
| S12 | S6 OR S7 OR S8 OR S9 OR S10 | 633,779 |
| S11 | S1 OR S2 OR S3 OR S4 OR S5 | 35,610 |
| S10 | DE "cattle" | 524,631 |
| S9 | DE "dairy cattle" | 66,195 |
| S8 | DE "cow" | 10,614 |
| S7 | TX "cow\*" | 326,138 |
| S6 | TX "cattle" | 566,928 |
| S5 | DE "summer mastitis" | 155 |
| S4 | DE "mycotic mastitis" | 172 |
| S3 | DE "bovine mastitis" | 20,670 |
| S2 | DE "mastitis" | 25,606 |
| S1 | TX "mastitis" | 35,610 |

# Table S2. Search query Medline

|  |  |  |
| --- | --- | --- |
| # | Query | Results |
| 1 | "mastitis".mp. | 16645 |
| 2 | Mastitis, Bovine/ | 8114 |
| 3 | "treatment\*".mp. | 5535812 |
| 4 | "therap\*".mp. | 6631069 |
| 5 | "cultur\*".mp. | 1851763 |
| 6 | "selective".mp. | 546356 |
| 7 | "rapid test\*".mp. | 6413 |
| 8 | "targeted".mp. | 406855 |
| 9 | "cattle".mp. | 378685 |
| 10 | "cow\*".mp. | 81169 |
| 11 | Cattle/ | 359989 |
| 12 | "dry cow\*".mp. | 976 |
| 13 | "dry period".mp. | 1715 |
| 14 | 1 or 2 | 16645 |
| 15 | 3 or 4 | 9175407 |
| 16 | 5 or 6 or 7 or 8 | 2704591 |
| 17 | 9 or 10 or 11 | 407082 |
| 18 | 12 or 13 | 2431 |
| 19 | (14 and 15 and 16 and 17) not 18 | 458 |
| 20 | limit 19 to yr="2010 -Current" | 268 |

# Table S3. Search query Web of science

|  |  |  |
| --- | --- | --- |
| # | Query | Results |
| 17 | #16 (publication date 2010-01-10 to 2021-12-01) | 337 |
| 16 | (#1 AND #4 AND #9 AND #12) NOT #15 | 482 |
| 15 | #13 OR #14 | 6,603 |
| 14 | ALL = (“dry period”) | 5,442 |
| 13 | ALL = (“dry cow\*”) | 1,510 |
| 12 | #10 OR #11 | 419,455 |
| 11 | ALL = (“cow\*”) | 272,590 |
| 10 | ALL = (“cattle”) | 190,520 |
| 9 | #5 OR #6 OR #7 OR #8 | 4,280,415 |
| 8 | ALL = (“targeted\*”) | 522,862 |
| 7 | ALL = (“rapid test\*”) | 7,431 |
| 6 | ALL = (“selective”) | 926,498 |
| 5 | ALL = (“cultur\*”) | 2,938,837 |
| 4 | #2 OR #3 | 8,3221,055 |
| 3 | ALL = (“therap\*”) | 4,226,528 |
| 2 | ALL = (“treatment\*”) | 5,692,080 |
| 1 | ALL = (“mastitis”) | 21,418 |

# Table S4. Search query Scopus (371 results)

( ( TITLE-ABS-KEY ( mastitis ) ) AND ( ( TITLE-ABS-KEY ( treatment\* ) ) OR ( TITLE-ABS-KEY ( therap\* ) ) ) AND ( ( TITLE-ABS-KEY ( cultur\* ) ) OR ( TITLE-ABS-KEY ( "rapid test\*" ) ) OR ( TITLE-ABS-KEY ( targeted ) ) OR ( TITLE-ABS-KEY ( selective ) ) ) AND ( ( TITLE-ABS-KEY ( cattle ) ) OR ( TITLE-ABS-KEY ( cow\* ) ) ) AND ( PUBYEAR > 2009 ) ) AND NOT ( ( TITLE-ABS-KEY ( "dry cow\*" ) ) OR ( TITLE-ABS-KEY ( "dry period" ) ) )

# Table S5. Summary of outcome measures reported in studies comparing selective with blanket CM treatment protocols

|  |  |  |  |
| --- | --- | --- | --- |
| Study and outcome | Additional information | Reported values, displayed as either mean ± SD (n) or % (n) | Source |
| Selective | Blanket |
| **Bacteriological cure (absence of original pathogen)** |  |  |  |
| Lago et al. (2011a) | Both 14 + 21 d sample | 60 (85) | 71 (97) | M |
| MacDonald (2011) | Both 14 + 21 d sample | 54 (306) | 70 (324) | M |
| Mansion-de Vries et al. (2016) | Both 14 + 21 d sample | 68 (144) | 65 (121) | M |
| Lago et al. (2016a) | Both 14 + 21 d sample | 69 (105) | 66 (134) | C |
| Lago et al. (2016b) | Both 14 + 21 d sample | 77 (52) | 83 (48) | C |
| Kock et al. (2018) | Both 14 + 21 d sample | 63 (48) | 67 (54) | M |
| Bates et al. (2020) | 21 d sample | 89 (276) | 88 (259) | M |
| Schmenger et al. (2020) | Both 14 + 21 d sample | 78 (153) | 75 (182) | M |
| Bazzanella et al. (2020) | 21 d sample | 89 (83) | 78 (72) | M + C |
| Griffioen et al. (2021) | 21 d sample | 67 (57) | 92 (26) | M |
|  |  |  |  |  |
| **Clinical cure, proportion cured** |  |  |  |  |
| MacDonald (2011) | At 14 d | 77 (327) | 78 (347) | M |
| Mansion-de Vries et al. (2016) | At 5 d | 63 (236) | 54 (230) | M |
| Kock et al. (2018) | At 5 d | 43 (69) | 22 (69) | M |
| Bazzanella et al. (2020) | At 7 d | 54 (86) | 26 (77) | M + C |
| Bazzanella et al. (2020) | At 21 d | 77 (83) | 46 (72) | M + C |
| Griffioen et al. (2021) | At 21 d | 83 (78) | 78 (32) | M |
|  |  |  |  |  |
| **Clinical cure, days till cure** |  |  |  |  |
| Lago et al. (2011a) |  | 3.2 ± 1.7 d (163) | 2.7 ± 1.5 d (196) | M |
| MacDonald (2011) |  | 3 (327) | 3 (347) | M |
| Lago et al. (2016a) |  | 4.0 ± 3.2 d (211) | 3.6 ± 2.5 d (262) | C |
| Lago et al. (2016b) |  | 3.5 ± 3.2 d (117) | 3.1 ± 2.8 d (159) | C |
| Vasquez et al. (2017) |  | 5.3 ± 2.7 d (150) | 5.1 ± 4.8 d (219) | M + C |
|  |  |  |  |  |
| **New IMI (different pathogen isolated)** |  |  |  |
| Lago et al. (2011a) | 14 or 21 d sample | 50 (160) | 50 (163) | M |
| Lago et al. (2016a) | 14 or 21 d sample | 22 (170) | 21 (215) | C |
| Lago et al. (2016b) | 14 or 21 d sample | 20 (99) | 25 (118) | C |
| Schmenger et al. (2020) | Both 14 + 21 d sample | 8.7 (287) | 10 (252) | M |
|  |  |  |  |  |
| **Recurrence, proportion with new CM case (same quarter unless stated otherwise)** |  |
| Lago et al. (2011b) | Remainder of lactation | 43 (210) | 35 (220) | M + C |
| MacDonald (2011) | Within 4 mo | 4.2 (309) | 6.7 (328) | M |
| MacDonald (2011) | Within 4 mo (same pathogen) | 0.6 | 1.2 | M |
| Mansion-de Vries et al. (2016) | Within 100 d  | 35 (236) | 35 (230) | M |
| Lago et al. (2016a) | Within 60 d (different pathogen) | 20 (211) | 23 (262) | C |
| Lago et al. (2016b) | Within 60 d (different pathogen) | 13 (117) | 25 (159) | C |
| Kock et al. (2018) | Within 100 d  | 21 (43) | 6.5 (31) | M + C |
| McDougall et al. (2018) | Remainder of lactation, cow level | 20 (211) | 29 (207) | M |
| Bates et al. (2020) | Within 60 d  | 2.5 (276) | 3.4 (259) | M |
| Schmenger et al. (2020) | Within 90 d  | 11 (398) | 8.9 (395) | M |
| Griffioen et al. (2021) | Within 21 d (same pathogen) | 31 (65) | 31 (32) | M |
|  |  |  |  |  |
| **Recurrence, days till new CM case in same quarter** |  |
| Lago et al. (2011b) |  | 82 ± 73 d (83) | 78 ± 83 d (68) | M + C |
|  |  |  |  |  |
| **SCS** |  |  |  |  |
| Lago et al. (2011b) | Remainder of lactation | 4.4 ± 1.8 (178) | 4.2 ± 1.8 (178) | M + C |
| Vasquez et al. (2017) | 43 d  | 4.3 ± 2.3 (196) | 4.2 ± 2.3 (200) | M + C |
| Kock et al. (2018) | 14 d | 6.7 ± 2.9 (69) | 6.8 ± 2.5 (71) | C |
| Kock et al. (2018) | 21 d | 5.3 ± 3.0 (69) | 6.4 ± 2.7 (71) | C |
| Lago et al. (2019)1 | 150 d | 1.1 ± 0.6 (232) | 2.3 ± 0.8 (241) | C |
| Lago et al. (2019)2 | 150 d | 2.1 ± 0.6 (140) | 2.1 ± 0.6 (136) | C |
| Bates et al. (2020) | 30-35 d before dry-off | 4.1 ± 1.9 (174) | 4.2 ± 1.9 (176) | M + C |
| Schmenger et al. (2020) | 14 d | 6.5 ± 2.7 (300) | 5.8 ± 2.9 (289) | C |
| Schmenger et al. (2020) | 21 d | 6.0 ± 3.0 (300) | 5.7 ± 2.9 (289) | C |
| Bazzanella et al. (2020) | 14 d | 4.7 ± 2.7 (89) | 4.5 ± 2.6 (73) | C |
| Bazzanella et al. (2020) | 21 d | 4.0 ± 2.5 (83) | 4.1 ± 2.8 (71) | C |
| Borchardt et al. (2022) | 43 d  | 4.6 ± 2.4 (202) | 4.4 ± 2.3 (187) | M + C |
|  |  |  |  |  |
| **Proportion low SCC (cells/mL)** |  |  |  |  |
| Kock et al. (2018) | <200,000, 14 + 21 d | 14 (69) | 10 (71) | M |
| Schmenger et al. (2020) | <200,000, 14 + 21 d | 17 (300) | 19 (289) | M |
| Bazzanella et al. (2020) | <200,000, 14 d | 39 (89) | 45 (73) | C |
| Bazzanella et al. (2020) | <200,000, 21 d | 55 (83) | 49 (71) | M + C |
| Griffioen et al. (2021) | <100,000, 21 d | 27 (82) | 28 (36) | M |
|  |  |  |  |  |
| **Culling, proportion culled** |  |  |  |  |
| Lago et al. (2011b) | Remainder of lactation | 32 (195) | 28 (195) | M |
| Mansion-de Vries et al. (2016) | Within 100 d (due to mastitis) | 9.3 (236) | 10.4 (230) | M |
| Lago et al. (2016a) | Within 21 d | 15 (191) | 15 (234) | C |
| Lago et al. (2016b) | Within 21 d | 7 (98) | 14 (125) | C |
| Vasquez et al. (2017) | Within 30 d | 4 (225) | 6 (226) | M |
| Vasquez et al. (2017) | Within 60 d | 10 (225) | 12 (226) | M |
| Kock et al. (2018) | Within 100 d (due to mastitis) | 2.9 (69) | 5.6 (71) | M + C |
| Borchardt et al. (2022) | Within 30 d | 6.5 (232) | 8.9 (236) | M |
| Borchardt et al. (2022) | Within 60 d | 12 (232) | 19 (236) | M |
|  |  |  |  |  |
| **Culling, days to culling** |  |  |  |  |
| Lago et al. (2011b) | Remainder of lactation | 137 ± 99 d (61) | 160 ± 109 d (54) | M + C |
|  |  |  |  |  |
| **Days out of the tank** |  |  |  |  |
| Lago et al. (2011a) | Days out of the tank | 5.2 ± 3.5 d (184) | 5.9 ± 2.9 d (183) | M + C |
| Lago et al. (2016a) | Days out of the tank | 7.1 ± 3.0 d (191) | 6.7 ± 2.1 d (234) | C |
| Lago et al. (2016b) | Days out of the tank | 5.7 ± 3.0 d (98) | 6.7 ± 2.2 d (125) | C |
| Vasquez et al. (2017) | Hospital days | 6.3 ± 3.2 d (166) | 8.6 ± 3.2 d (222) | M + C |
| Kock et al. (2018) | Withdrawal period | 6.1 ± 2.5 d (69) | 6.2 ± 1.1 d (69) | M + C |
| Bates et al. (2020) | Days milk withheld | 5.7 ± 1.9 d (273) | 5.4 ± 0.5 d (262) | M + C |
| Borchardt et al. (2022) | Hospital days | 6.7 ± 5.0 d (230) | 6.6 ± 5.0 d (233) | M + C |
|  |  |  |  |  |
| **Secondary treatments** |  |  |  |  |
| Lago et al. (2011a) |  | 19 (208) | 36 (214) | M |
| MacDonald (2011) |  | 14.3 | 14.4 | M |
| Kock et al. (2018) |  | 9 (69) | 13 (71) | M + C |
|  |  |  |  |  |
| **Milk production** |  |
| Lago et al. (2011b) | Remainder of lactation  | 31 ± 8.5 kg (178) | 30 ± 8.4 kg (178) | M + C |
| Lago et al. (2019)1 | 150 d | 38 ± 12 kg (232) | 40 ± 12 kg (241) | C |
| Lago et al. (2019)2 | 150 d | 38 ± 13 kg (140) | 37 ± 12 kg (136) | C |
| Vasquez et al. (2017) | Remainder of lactation | 36 ± 11 kg (202) | 34 ± 10 kg (206) | M + C |
| Borchardt et al. (2022) | 43 d | 25 ± 11 kg (202) | 34 ± 11 kg (187) | M + C |

M = manuscript, C = author contacted

1 Corresponding to Lago et al. (2016a)

2 Corresponding to Lago et al. (2016b)

# Table S6. Calculated non-inferiority margins (M) using estimates of risk ratios (RR) or mean differences (MD) when comparing blanket antimicrobial clinical mastitis treatment with no antimicrobial treatment protocols. Assumed percentage of effect retained (α) was 50%.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Outcomes | Included studies | RR/MD(95% CI) | M | Remark |
| Proportion not reaching bacteriological cure | Roberson et al. (2004)Hektoen et al. (2004)Werner et al. (2010)Suojala et al. (2010)1Schukken et al. (2011)1Persson et al. (2015)1Fuenzalida et al. (2019)1 | RR 0.50 (0.36 – 0.70) | 1.42 | Removing studies that only included Gram-negative or *E. coli* cases (indicated by 1) did not change estimate |
| Proportion not reaching clinical cure | Roberson et al. (2004)Hektoen et al. (2004)Schukken et al. (2011)1Persson et al. (2015)1 | RR 0.90 (0.74 – 1.09) | NA2 | Removing studies that only included Gram-negative or *E. coli* cases (indicated by 1) did not change estimate |
| Days to clinical cure | Fuenzalida et al. (2019)1 | MD 0.60(0.47 – 0.74) | *Not calculated3* |  |
| New IMI | Suojala et al. (2010)1 | RR 0.72 (0.21 – 2.50) | *Not calculated3* |  |
| Recurrence  | Fuenzalida et al. (2019)1 | RR 1.06 (0.60 – 1.82) | *Not calculated3* |  |
| SCS | Schukken et al. (2011)1Persson et al. (2015)1 | MD 1.18(0.63 – 1.73) | NA2 | Only studied in Gram-negative or *E. coli* cases |
| High SCC | Roberson et al. (2004)Persson et al. (2015)1 | RR 0.89 (0.63 – 1.27) | NA2 |  |
| Culling | Suojala et al. (2010)1Schukken et al. (2011)1Persson et al. (2015)1Fuenzalida et al. (2019)1 | RR 0.95 (0.63 – 1.42) | NA2 | Only studied in Gram-negative or *E. coli* cases |
| Milk yield | Persson et al. (2015)1Fuenzalida et al. (2019)1 | MD 0.17 (-1.08 – 1.42) | NA2 | Only studied in Gram-negative or *E. coli* cases |

1Study with only Gram-negative or *E. coli* cases

2RR/MD shows no effect of antimicrobial treatment, or effect in favor of no antimicrobial treatment

3Only 1 study was available.

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