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APPENDIX I. Search strategy

Databases: Evidence-Based Medicine Reviews (EBM Reviews) – Cochrane Database of Systematic Reviews <2005 to 26 June 2020>, EBM Reviews – ACP Journal Club <1991 to May 2020>, EBM Reviews – Database of Abstracts of Reviews of Effects <1st Quarter 2016>, EBM Reviews – Cochrane Clinical Answers <June 2020>, EBM Reviews – Cochrane Central Register of Controlled Trials <May 2020>, EBM Reviews – Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews – Health Technology Assessment <4th Quarter 2016>, EBM Reviews – NHS Economic Evaluation Database <1st Quarter 2016>, Embase Classic and Embase <1947 to 26 June 2020>, Ovid MEDLINE® and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versi®(R) <1946 to 26 June 2020>

Search Strat-----

- 1 exp ketamine/ (54265)
- 2 (ketamine adj5 (us* or abus* or addict*)).tw. (8914)
- 3 (ketamine or esketamine).tw. (49787)
- 4 1 or 2 or 3 (68577)
- 5 exp urinary tract/ or exp bladder/ or exp ureter/ or exp kidney/ or exp urothelium/ (1102649)
- 6 (ureter* or kidney* or urothel* or renal or urinary or cyst*).tw. (3734342)
- 7 5 or 6 (4037920)
- 8 (uroflow* or urodynamic* or UDS or void* or cyst*).tw. (1065264)
- 9 (bladder nglish apacit* or compliance or empty* or diar*)).tw. (20986)
- 10 (urin* adj4 (symptom* or discomfort* or sign* or problem*)).tw. (109320)
- 11 ((bladder or suprapubic) adj5 pain*).tw. (9390)
- 12 8 or 9 or 10 or 11 (1158156)
- 13 ((ketamine or esketamine or ketamine-induced or ketamine-associated or ketamine-related) adj5 uro*).tw. (167)
- 14 4 and 7 (2954)
- 15 4 and 12 (959)
- 16 13 or 14 or 15 (3056)
- 17 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.) (11389475)
- 18 16 not 17 (2076)
- 19 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt. or "Journal: Conference Abstract".pt. (4121095)
- 20 18 not 19 (1736)
- 21 limit nglishnglish [Limit not valid in DARE,CLCMR,CLEED; records were retained] (1365)
- 22 remove duplicates from 21 (*****

APPENDIX 2. Forest plots showing pooled prevalence of clinical manifestations in patients with ketamineassociated uropathy

a. Pooled prevalence of frequency: 77.1% (95% CI=56.9%-92.2%)



b. Pooled prevalence of urgency: 69.9% (95% CI=48.8%-87.3%)



APPENDIX 2. (cont'd)

Studies Estimate (95% C.I.) Ev/Trt Yek 2015 0.75 (0.28, 1.00) 3/4 62/127 Suppiah 2016 0.49 (0.40, 0.57) Zeng 2017 0.31 (0.17, 0.46) 11/36 Yee 2019 0.26 (0.11, 0.46) 6/23 0.77 (0.59, 0.91) Lee 2017 20/26 Huang 2014 0.74 (0.56, 0.89) 20/27 Shahani 2007 0.67 (0.14, 1.00) 2/3 Chen 2011 0.90 (0.53, 1.00) 4/4 Misra 2014 0.99 (0.92, 1.00) 34/34 Jhang 2017 0.68 (0.49, 0.84) 17/25 0.82 (0.66, 0.94) Jhang 2017 23/28 Ng 2013 0.25 (0.00, 0.72) 1/4Pal 2013 0.09 (0.07, 0.10) 94/1083 Overall (I^2=9747 % , P< 0.01) 0.60 (0.35, 0.83) 297/1424 0.25 0.5 0.75 Arcsine of Square Root Proportion

c. Pooled prevalence of suprapubic pain: 60.4% (95% CI=35.3%-82.9%)

d. Pooled prevalence of nocturia: 58.0% (95% CI=38.5%-76.2%)



e. Pooled prevalence of dysuria: 49.8% (95% CI=28.5%-71.1%)



APPENDIX 2. (cont'd)

Estimate (95% C.I.) Ev/Trt Studies Yek 2015 0.50 (0.08, 0.92) 2/4 0.67 (0.28, 0.95) Wang 2017 4/6 Zeng 2017 0.12 (0.02, 0.26) 3/26 Yee 2019 0.09 (0.01, 0.23) 2/23 Huang 2014 0.30 (0.14, 0.48) 8/27 0.20 (0.10, 0.33) Sihra 2018 9/44 Shahani 2007 0.33 (0.00, 0.86) 1/3 Hung 2019 0.37 (0.09, 0.71) 3/8 0.50 (0.25, 0.75) Chung 2014 7/14 Misra 2014 0.99 (0.92, 1.00) 34/34 0.48 (0.29, 0.67) Jhang 2017 : 12/25 0.32 (0.16, 0.50) Jhang 2017 9/28 Ng 2012 0.68 (0.55, 0.80) 34/50 0.95 (0.76, 1.00) Chu 2007 10/10 Lai 2012 0.93 (0.64, 1.00) 6/6 Pal 2013 0.02 (0.01, 0.03) 18/1083 🗖 Overall (I^2=9728 % , P< 0.01) 0.46 (0.23, 0.71) 162/1391 0.25 0.5 0.75 Arcsine of Square Root Proportion

f. Pooled prevalence of haematuria: 46.3% (95% CI=22.6%-71.0%)

g. Pooled prevalence of incontinence: 43.9% (95% CI=21.0%-68.2%)



APPENDIX 2. (cont'd)

Studies Estimate (95% C.I.) Ev/Trt Lin 2016 0.22 (0.10, 0.37) 8/36 Wu 2016 0.37 (0.09, 0.71) 3/8 Yeung 2012 0.28 (0.15, 0.43) 10/36 0.51 (0.38, 0.63) Chu 2008 30/59 Wang 2017 0.67 (0.28, 0.95) 4/6 Tsai 2009 0.56 (0.24, 0.85) 5/9 Wu et al 2016 0.30 (0.20, 0.41) 23/77 0.17 (0.14, 0.20) Yee 2017 96/572 Lee 2017 0.35 (0.18, 0.54) 9/26 0.44 (0.27, 0.63) Huang 2014 12/27 Sihra 2018 0.14 (0.04, 0.29) 4/28 0.37 (0.09, 0.71) Hung 2019 3/8 Chung 2014 0.64 (0.38, 0.86) 9/14 Chen 2011 0.10 (0.00, 0.47) 0/4 Misra 2014 _ 0.11 (0.01, 0.29) 2/18 Jhang 2017 0.14 (0.03, 0.31) 3/22 Jhang 2017 0.29 (0.14, 0.46) 8/28 Ng 2012 0.23 (0.12, 0.37) 10/43 0.01 (0.00, 0.07) Cheung 2011 0/40 Lee 2015 0.95 (0.74, 1.00) 9/9 Lai 2012 0.17 (0.00, 0.54) 1/6 Overall (I^2=8387 % , P< 0.01) 0.30 (0.22, 0.39) 249/1076 0 0.25 0.5 0.75 Arcsine of Square Root Proportion

h. Pooled prevalence of hydronephrosis: 30.2% (95% CI=22.0%-39.2%)

i. Pooled prevalence of ureteral stricture: 19.4% (95% CI=7.3%-35.5%)



j. Pooled prevalence of impaired renal function: 8.3% (95% CI=4.8%-12.6%)



APPENDIX 3. Forest plots showing pooled symptom scores in patients with ketamine-associated uropathy

a. Pooled mean International Prostate Symptom Score (IPSS) score: 11.61 (n=1366)



b. Pooled mean Interstitial Cystitis Symptom Index (ICSI) score: 11.11 (n=1263)



c. Pooled mean Interstitial Cystitis Problem Index (ICPI) score: 10.24 (n=1263)



APPENDIX 3. (cont'd)

Estimate (95% C.I.) Studies Chu 2008 24.700 (21.699, 27.701) Wu et al 2016 23.000 (21.955, 24.045) Yee 2017 21.000 (20.377, 21.623) Yee 2019 17.800 (14.776, 20.824) Ng 2012 21.400 (19.321, 23.479) Overall (I^2=8050 %, P< 0.001) 21.662 (20.123, 23.202) 16 18 20 22 24 26

d. Pooled mean Pelvic Pain and Urgency/Frequency (PUF) score: 21.66 (n=750)

e. Pooled mean Visual Analogue Scale (VAS) score: 6.46 (n=161)



APPENDIX 4. Forest plots showing bladder assessment in patients with ketamine-associated uropathy

a. Pooled mean functional bladder capacity: 95.23 mL (n=717)



b. Pooled mean cystometric capacity: 97.37 mL (n=491)



c. Pooled mean maximum cystometric capacity: 202.09 mL (n=140)



APPENDIX 4. (cont'd)

d. Pooled mean voided volume: 113.31 mL (n=630)



e. Pooled maximum urine flow rate: 8.69 mL/s (n=451)



f. Pooled prevalence of detrusor overactivity: 63.9% (95% CI=45.6%-80.3%)



APPENDIX 4. (cont'd)



g. Pooled prevalence of vesicoureteral reflux: 22.0% (95% CI=12.4%-33.5%)

E-reference list for the Appendices

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