Appendix 1. Systematic Review Methods

The Netherlands

PubMed and Embase were searched using the search terms shown in Appendix 3, resulting in 242 and 136 articles respectively. The removing of duplicates in Endnote and Rayyan resulted in a final set of 296 articles for title/abstract screening. In this stage, articles were included that reported Dutch studies on UTI or bacteraemia, that potentially contained data for both susceptible and resistant UTIs, but had not necessarily reported these data or did not mention the specific pathogen. In the case where, for example, testing for resistance had been mentioned but specific data were not separately reported for AMR and AMS *E. coli*, the authors were emailed. After full-text screening of 43 articles, a total of 18 were retained, and the authors were requested more data. If there was no response after a month, a follow-up email was sent.

We excluded case studies and studies that were carried out in a specific vulnerable population (elderly persons, children), or in highly-specific clinical patient populations. Inclusion criteria applied to the final set of articles were : a Dutch study, published in 2017 or later, UTI caused by resistant and/or susceptible *E. coli*, and estimates for of one or more of parameters needed for the OTs. Following this systematic literature search, further relevant articles were possibly identified during correspondence with authors.

Given the almost null yield of the first search, a second literature search was undertaken to locate relevant studies specifically informing the model parameters involving bacteraemia (i.e., $P(\text{Bact}|\text{UTI})$, $DD(\text{Bact})$, $P(\text{Death}|\text{Bact})$) (Appendix 3). This produced 24 hits, due to the limited number of hits, we performed full-text screening for all. Inclusion criteria were only that the study reported suitable data on cases of bacteraemia in which *E. coli* had been isolated.

Following this search, further relevant articles were possibly identified in correspondence with authors of retained articles. We then applied the following algorithm to the set of identified articles: (i) if no eligible Dutch population studies were found reporting parameter values involving bacteraemia due to susceptible/resistant *E. coli* UTI, then (ii) Dutch studies reporting parameter values involving bacteraemia with susceptible/resistant *E. coli from any infection site* were used. (iii) If still no eligible studies found, then *EU* studies reporting parameter values due to bacteraemia with AMR/AMS *E. coli* from any infection site were considered eligible.

A third systematic literature search was conducted to attempt to find relevant studies specifically to inform $P(\text{Bact}|\text{UTI})$, with restriction to studies of resistant *E. coli* UTIs (Appendix 1). This produced 13 hits; 10 articles were eliminated based on abstract screening and the remaining three after full-text screening. A PRISMA diagram for all three searches together is shown in Figure S1.

Italy

PubMed and Embase were searched using the search term in Appendix 4, and yielded 231 and 176 results respectively. After removing duplicates in EndNote and Rayan, 290 articles remained. After title/abstract screening 56 articles were screened full text and 32 articles potentially contained parameter estimates relevant for the Italian population.

Given the almost null yield of the first search, we performed new separate searches for the incidence, progression from UTI to bacteraemia, DD(UTI) and LOS due to bacteraemia. For LOS(UTI) a third search was conducted (Appendix 4). Eventually, three articles from the search and one article recommended to the authors which fell outside the initial search criteria

of articles published from 2017 or later were used to estimate the parameters. A PRISMA diagram for all searches on Italian parameters together is shown in Figure S2.

Appendix 2 – Systematic review to identity Dutch parameter estimates

Search 1

4th of February 2019

PubMed: (("2017/01/01"[Date - Publication] : "3000"[Date - Publication])) AND (((((urinary[Title/Abstract] AND tract[Title/Abstract]) AND (infection[Title/Abstract] OR infections[Title/Abstract])) OR urinary tract infection[MeSH] OR UTI[Title/Abstract]) AND (Netherlands OR Netherlands[MeSH] OR Dutch) AND (english[Language] OR dutch[Language])) AND ("2017/01/01"[PDat] : "3000/12/31"[PDat]))

242 results

4th of February 2019

Embase: ('urinary':ab,ti AND 'tract':ab,ti AND ('infection':ab,ti OR 'infections':ab,ti) OR 'uti':ab,ti) AND ('netherlands' OR 'dutch') AND [article]/lim AND ([dutch]/lim OR [english]/lim) AND [humans]/lim AND [embase]/lim AND [2017-2019]/py

136 results

Search 2

10th of February, 2020

PubMed: *((bacteraemia[Title/Abstract]) OR (bacteremia[Title/Abstract])) AND ((Netherlands[Text Word]) AND Dutch[Text Word])*.

24 results

13th of February, 2020

PubMed:((((((urinary tract[Title/Abstract]) AND infection[Title/Abstract])) OR

UTI[Title/Abstract])) AND ((Netherlands[Text Word]) OR Dutch [Text Word])) AND ((lenght of stay[Text Word]) OR LOS[Text Word])

3 results

Search 3 –

13th of February, 2020

PubMed: (((bacteraemia[Text Word]) OR (bacteremia[Text Word])) AND resist*[Text Word] AND (E coli[MeSH] OR E coli[Text Word]) AND ((urinary tract infection[MeSH]) OR (UTI[Text Word])) AND (("probability of"[Text Word]) OR (progress*[Text Word]) OR ("risk of "[Text Word]))).

13 results

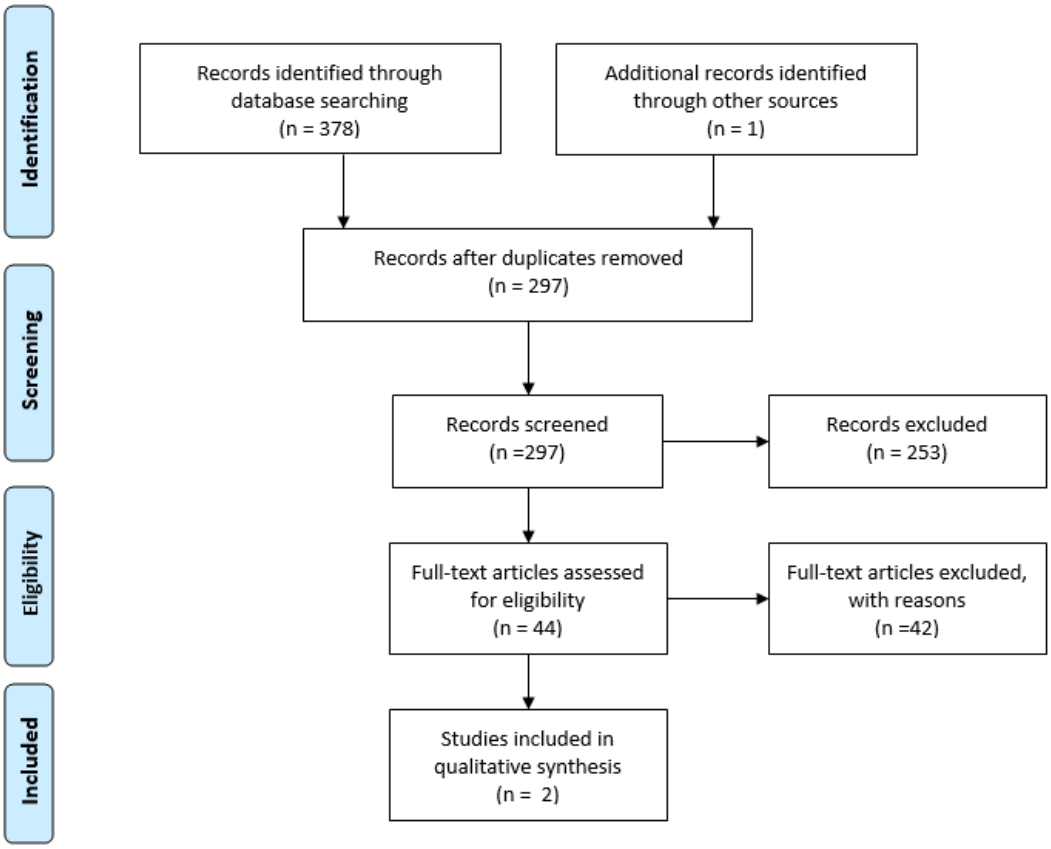

Figure S1

PRISMA flowchart of the first literature search on Dutch parameter estimates

Appendix 3 – Systematic review to identify Italian parameter estimates

Search 1

4th of February, 2019

Pubmed: ((("2017/01/01"[Date - Publication] : "3000"[Date - Publication])) AND (((((urinary[Title/Abstract] AND tract[Title/Abstract]) AND (infection[Title/Abstract] OR infections[Title/Abstract])) OR urinary tract infection[MeSH] OR UTI[Title/Abstract]) AND (Italy OR Italy[MeSH] OR Italian) AND (english[Language] OR dutch[Language])) AND ("2017/01/01"[PDat] : "3000/12/31"[PDat])))

231 results

('urinary':ab,ti AND 'tract':ab,ti AND ('infection':ab,ti OR 'infections':ab,ti) OR 'uti':ab,ti) AND ('italy' OR 'italian') AND [article]/lim AND ([dutch]/lim OR [english]/lim) AND [humans]/lim AND [embase]/lim AND [2017-2019]/py

176 results

Search 2

3th of June, 2020

Incidence - PubMed: ("2019/01/01"[Date - Publication] : "3000"[Date - Publication]) AND Italy AND ((urinary[Title/Abstract] AND tract [Title/Abstract] AND infection [Title/Abstract]) OR UTI [Title/Abstract]) AND incidence.

35 results

3th of June, 2020

LOS UTI - PubMed ("2019/01/01"[Date - Publication] : "3000"[Date - Publication]) AND Italy AND ((urinary[Title/Abstract] AND tract [Title/Abstract] AND infection [Title/Abstract]) OR

UTI [Title/Abstract]) AND (LOS [Title/Abstract] OR (length [Title/Abstract] AND stay [Title/Abstract])).

5 results

18th of June, 2020

UTI to bacteraemia – PubMed: (("2019/01/01"[Date - Publication] : "2020/06/18"[Date - Publication])) AND ((Italy[Text Word]) AND ((UTI[Title/Abstract]) OR (((urinary[Title/Abstract]) AND (tract[Title/Abstract])) AND (infection[Title/Abstract])))).

21 results

31st of August, 2020

LOS Bacteraemia – PubMed: (("2005/01/01"[Date - Publication] : "3000"[Date - Publication])) AND ((Italy[Text Word]) AND (((((bacteraemia[Title/Abstract]) OR (bacteraemias[Title/Abstract])) OR (bacteremia[Title/Abstract])) OR (bacteremias[Title/Abstract])) AND (((days[Title/Abstract]) OR (((length[Title/Abstract]) AND (of[Title/Abstract])) AND (stay[Title/Abstract]))) OR (LOS[Title/Abstract]))))

24 results

Search 3

16th of June, 2020

LOS UTI– Pubmed (("2015/01/01"[Date - Publication] : "3000"[Date - Publication]) AND Italy AND ((urinary[Title/Abstract] AND tract [Title/Abstract] AND infection [Title/Abstract]) OR UTI [Title/Abstract]) AND (LOS [Title/Abstract] OR disability duration [Title/Abstract] OR (length [Title/Abstract] AND stay [Title/Abstract]))) NOT (("2019/01/01"[Date - Publication] : "2020/06/02"[Date - Publication]) AND Italy AND ((urinary[Title/Abstract] AND tract [Title/Abstract] AND infection [Title/Abstract]) OR UTI [Title/Abstract]) AND (LOS

[Title/Abstract] OR (length [Title/Abstract] AND stay [Title/Abstract]))).

7 results

2nd of September, 2020

(((general practitioner) OR (general practice)) AND (((urinary tract infection) OR (UTI)) AND (Italy))) AND ((out-patient) OR (outpatient))

10 results, 1 included

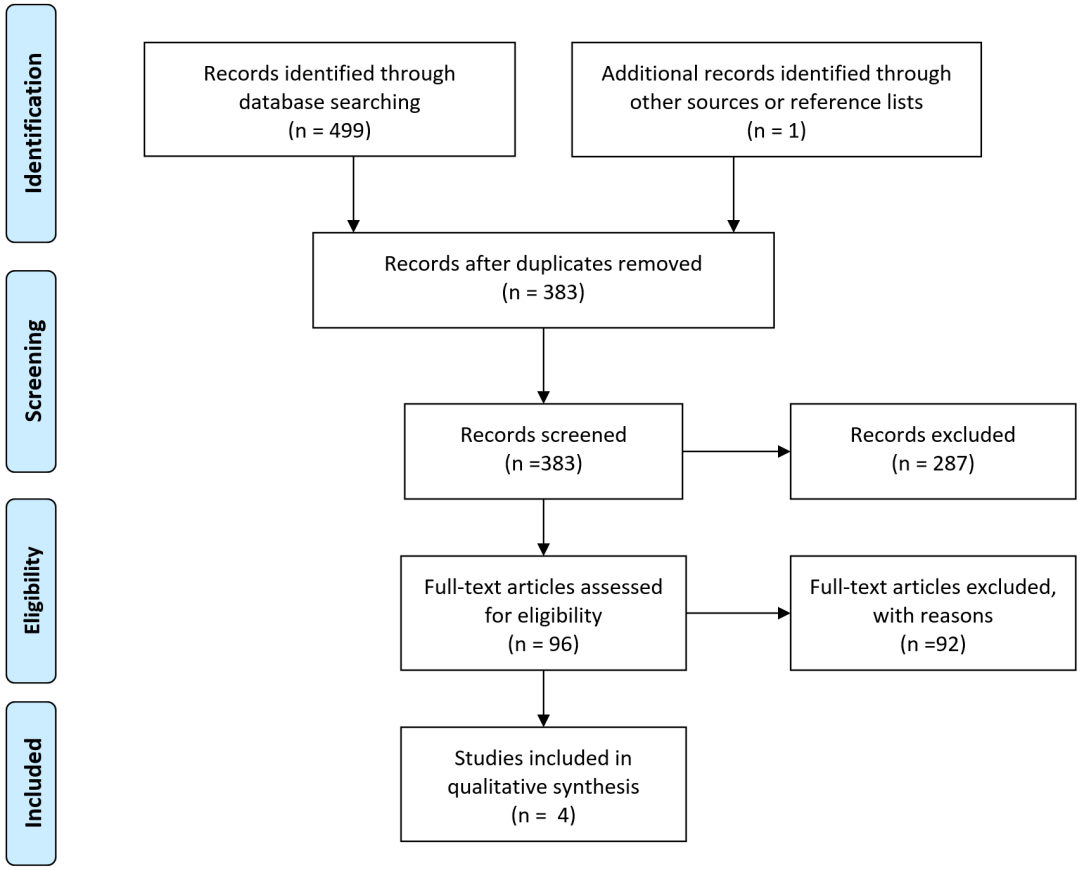

Figure S2

PRISMA flowchart of the literature search on Italian parameter estimates

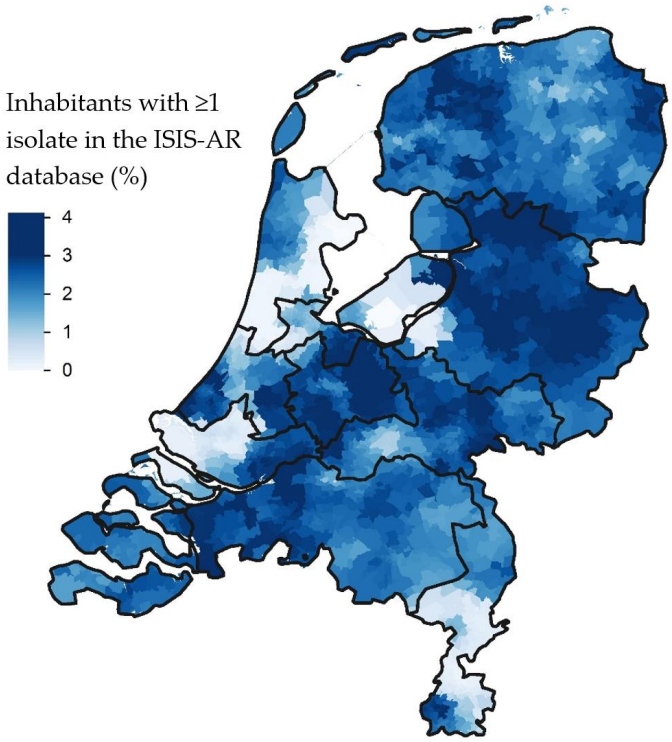

Figure S3

smoothed geographical distribution of the percentage of inhabitants for whom at least 1 urinary isolate was found in the ISIS-AR database in 2018, by 4-digit postal code area and with regional cooperative network borders

Appendix 4.

Systematic review results

The Netherlands

The first systematic literature review yielded only two articles, both providing an estimate of DD(UTI). In the first study the Netherlands was one of four countries on which analysis was based, and bacteria species and AMS vs. AMR infections were not distinguished. Correspondence with the authors yielded a more appropriate citation (1), which was carried out in England and Wales in 2002-2004 and reported DD(UTI) for *E. coli* UTIs separately for AMS and AMR infection. (In Figure S1 this article is indicated as an additional record identified through other sources). We justified this choice as the analysis in (2) did not find any between-country difference in DD(UTI).

The second review resulted in one suitable study for P(Death|Bact), which was a Dutch study that reported 30-day mortality in bacteraemia patients with either resistant *E. coli* or susceptible *E. coli* in 2014–2016 (3). The study population had a median age of 69 years (*IQR* 57 to 77); it is plausible that a lower mortality rate would be observed for younger age-groups. We could only locate a single study reporting age-group specific values for 30-day mortality due to bacteraemia (4). This study was conducted in Iceland among patients with bacteraemia caused by *S. aureus.* We took the simple approach of setting the parameter values for P(Death|Bact) for the age-groups 55 years and older to the value from study (3), and then scaling the parameter values for the younger age-groups according to the ratio of 30-day mortality risks between the 'reference' age-group, 55-74 years, and the <35 years and 35-54 years age-groups from the Icelandic study (4). This meant P(Death|Bact) was zero for <35

years (since mortality risk was 0% for <35 years (4)), and a scaling factor of 0.54 (from 3.8%/7.1%) was applied to 35-54 years.

For the parameter DD(Bact), the literature reviews did not yield any eligible studies. We decided to adopt values from (5), which is a large well-conducted multi-country study that was carried out in 2007/8, and that reported patient characteristic-adjusted LOS values for both AMS and 3rd generation cephalosporin-resistant *E. coli* bloodstream infections (BSIs). All selected parameter values are provided in Table 1.

As the third systematic literature review, which was specifically aimed at P(Bact|UTI), did not yield any studies. We relied on a previous pooled analysis [24] which we identified through citation search. This study did not distinguish between AMR and AMS infections, and the contributing studies were all carried out in the USA in the 1980s.

Italy

We found one article providing estimates on P(Death|Bact). The study of Palacios-Baena et al. (6) found a 30-day mortality of 26.2% of ESBL blood stream infections (BSI), 34 of the 130 Italian BSI patients died. We calculated the mortality for susceptible BSI using the ratio of susceptible vs. resistant mortality reported in another, less recent, Italian study by Tumbarello et al. (7) and estimated a 30-day mortality of 5.47% for susceptible BSI.

Furthermore, for DD(UTI) and DD(BACT) we only found an Italian study amongst elderly (*Mdn* = 77, *IQR* = 65–83*)* with UTIs or urosepsis which reported a mean LOS of 10 [7-17] days (8) and a median LOS of 9.5 days for Italian patients with complicated UTIs in Italy (9). Of the UTIs 58% was caused by *E. coli.* Unfortunately, no studies were identified which specified LOS for ESBL *E. coli* and *E. coli* UTIs. Because the lack of better studies on DD(UTI) and

DD(BACT) amongst adults, we used the estimate of Covino et al. (8) in elderly and Vallejo-Torres et al. (9) on complicated UTIs.

Moreover, we searched the citations of Cassini et al. (10) for relevant Italian studies and found that Tumbarello et al. (7) reported LOS for resistant BSI of 20 ± 17 days and 13 ± 9 days for non-AMR BSI.

For P(Bact|UTI) we were unable to locate a parameter and, therefore, we used the same value as the Dutch parameter. For the health outcomes following bacteremia, other than death, we used the same values as Cassini et al. (10).

Regarding the incidence of resistant *E. coli,* we did not locate any direct estimates; therefore, we estimated incidence (see Methods).

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Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis [Internet]. 2019 Jan 1;19(1):56–66. Available from: https://doi.org/10.1016/S1473-3099(18)30605-4

Table S1. *Number and incidence of resistant E. coli UTI per age- and sex category in the Netherlands in 2018*

	Males					Females				
Age category	**Male inhabitants**	**Number of resistant *E. coli* UTIs**	**Resistant *E.coli* UTIs incidence**	**Recurrent* resistant *E. Coli* UTIs**	**Average resistant *E. coli* UTIs per patient**	**Female inhabitants**	**Number of resistant *E. coli* UTIs**	**Resistant *E. coli* UTIs incidence**	**Recurrent* resistant *E. coli* UTIs**	**Average resistant *E. coli* UTIs per patient**
0	87001	12	0.000137929	0	1.00	82565	10	0.000121117	0	1.00
1-4	358019	25	5.86561E-05	4	1.19	340514	117	0.000323041	7	1.06
5-9	475503	19	2.10304E-05	9	1.90	452563	148	0.000287253	18	1.14
10-14	494511	11	1.61776E-05	3	1.38	471948	62	0.000122895	4	1.07
15-19	536852	20	2.79407E-05	5	1.33	511180	60	0.000105638	6	1.11
20-24	542817	19	2.76336E-05	4	1.27	525964	140	0.000230054	19	1.16
25-29	560319	36	5.53256E-05	5	1.16	545838	155	0.000283967	0	1.00
30-34	530554	38	6.59688E-05	3	1.09	522235	136	0.000250845	5	1.04
35-39	512925	26	3.70425E-05	7	1.37	512431	114	0.000204906	9	1.09

40-44	516723	53	6.77346E-05	18	1.51	521589	125	0.000191722	25	1.25
45-49	634188	92	0.000108801	23	1.33	634635	198	0.000272598	25	1.14
50-54	644223	143	0.000176957	29	1.25	635623	270	0.00035713	43	1.19
55-59	606130	211	0.000268919	48	1.29	605380	441	0.000597972	79	1.22
60-64	537540	287	0.000401831	71	1.33	542198	445	0.000671341	81	1.22
65-69	495875	460	0.000703806	111	1.32	503662	473	0.000770358	85	1.22
70-74	424486	633	0.001036548	193	1.44	447439	613	0.001115236	114	1.23
75-79	273902	621	0.001595461	184	1.42	314838	689	0.001715168	149	1.28
80-84	172825	487	0.002065673	130	1.36	235430	683	0.002229962	158	1.30
≥ 85	122648	495	0.003000457	127	1.35	248011	1056	0.00033063	236	1.29
Total	8527041	3688	0.000432506	974	1.36	8654043	5935	0.000685807	1063	1.22

**Defined as a UTI occurring more than 14 days after another UTI*

Table S2. *Number and incidence of E. coli UTI per age- and sex category in the Netherlands in 2018*

	Males					Females				
Age category	**Male inhabitants**	**Number of *E. coli* UTIs**	***E.coli* UTIs incidence**	**Recurrent * *E. Coli* UTIs**	**Average *E. coli* UTIs per patient**	**Female inhabitants**	**Number of *E. coli* UTIs**	***E. coli* UTIs incidence**	**Recurrent * *E. coli* UTIs**	**Average *E. coli* UTIs per patient**
0	87001	453	0.0052	0	1.00	82565	413	0.0044	52	1.14
1-4	358019	598	0.0015	74	1.14	340514	4079	0.0105	518	1.15
5-9	475503	351	0.0006	45	1.15	452563	6336	0.0115	1111	1.21
10-14	494511	260	0.0005	34	1.15	471948	2766	0.0049	473	1.21
15-19	536852	315	0.0005	41	1.15	511180	2651	0.0047	260	1.11
20-24	542817	318	0.0005	30	1.10	525964	3499	0.0061	316	1.10
25-29	560319	492	0.0008	60	1.14	545838	3745	0.0069	0	1.00
30-34	530554	500	0.0009	25	1.05	522235	3714	0.0069	102	1.03
35-39	512925	731	0.0012	106	1.17	512431	3638	0.0063	432	1.13
40-44	516723	968	0.0016	147	1.18	521589	3608	0.0060	497	1.16

45-49	634188	1630	0.0022	242	1.17	634635	5053	0.0068	742	1.17
50-54	644223	2224	0.0029	331	1.17	635623	6648	0.0089	1022	1.18
55-59	606130	3154	0.0044	498	1.19	605380	8686	0.0120	1418	1.20
60-64	537540	4166	0.0065	672	1.19	542198	10635	0.0161	1880	1.21
65-69	495875	6022	0.0099	1113	1.23	503662	12863	0.0210	2296	1.22
70-74	424486	7930	0.0149	1598	1.25	447439	16474	0.0297	3201	1.24
75-79	273902	7017	0.0203	1465	1.26	314838	15964	0.0407	3162	1.25
80-84	172825	6148	0.0280	1312	1.27	235430	16251	0.0548	3340	1.26
≥ 85	122648	6251	0.0411	1213	1.24	248011	22890	0.0747	4355	1.23
Total	**8527041**	**49528**	**0.0058**	**9006**	**1.22**	**8654043**	**149913**	**0.0173**	**25177**	**1.20**

**Defined as a UTI occurring more than 14 days after another UTI*

Table S3. *Sensitivity analysis of the number and incidence of resistant E. coli UTI per age- and sex category in the Netherlands in 2018*

	Males					Females				
Age category	**Male inhabitants**	**Number of resistant *E. coli* UTIs**	**Resistant *E.coli* UTIs incidence**	**Recurrent* resistant *E. Coli* UTIs**	**Average resistant *E. coli* UTIs per patient**	**Female inhabitants**	**Number of resistant *E. coli* UTIs**	**Resistant *E. coli* UTIs incidence**	**Recurrent* resistant *E. coli* UTIs**	**Average resistant *E. coli* UTIs per patient**
0	87001	12	0.000137929	0	1.00	82565	10	0.000121117	0	1.00
1-4	358019	21	5.86561E-05	0	1.00	340514	111	0.000323041	1	1.01
5-9	475503	10	2.10304E-05	0	1.00	452563	137	0.000287253	7	1.05
10-14	494511	8	1.61776E-05	0	1.00	471948	58	0.000122895	0	1.00
15-19	536852	16	2.79407E-05	1	1.07	511180	54	0.000105638	0	1.00
20-24	542817	16	2.76336E-05	1	1.07	525964	121	0.000230054	0	1.00
25-29	560319	32	5.53256E-05	1	1.03	545838	155	0.000283967	0	1.00
30-34	530554	35	6.59688E-05	0	1.00	522235	132	0.000250845	1	1.01
35-39	512925	19	3.70425E-05	0	1.00	512431	107	0.000204906	2	1.02

40-44	516723	38	6.77346E-05	3	1.09	521589	100	0.000191722	0	1.00
45-49	634188	75	0.000108801	6	1.09	634635	178	0.000272598	5	1.03
50-54	644223	118	0.000176957	4	1.04	635623	231	0.00035713	4	1.02
55-59	606130	169	0.000268919	6	1.04	605380	377	0.000597972	15	1.04
60-64	537540	227	0.000401831	11	1.05	542198	382	0.000671341	18	1.05
65-69	495875	368	0.000703806	19	1.05	503662	409	0.000770358	21	1.05
70-74	424486	488	0.001036548	48	1.11	447439	526	0.001115236	27	1.05
75-79	273902	477	0.001595461	40	1.09	314838	581	0.001715168	41	1.08
80-84	172825	379	0.002065673	22	1.06	235430	563	0.002229962	38	1.07
≥ 85	122648	400	0.003000457	32	1.09	248011	879	0.003306305	59	1.07
Total	**8527041**	**2908**	**0.000341**	**194**	**1.07**	**8654043**	**5111**	**0.000591**	**239**	**1.05**

**Defined as a UTI occurring more than 3 months after another UTI*