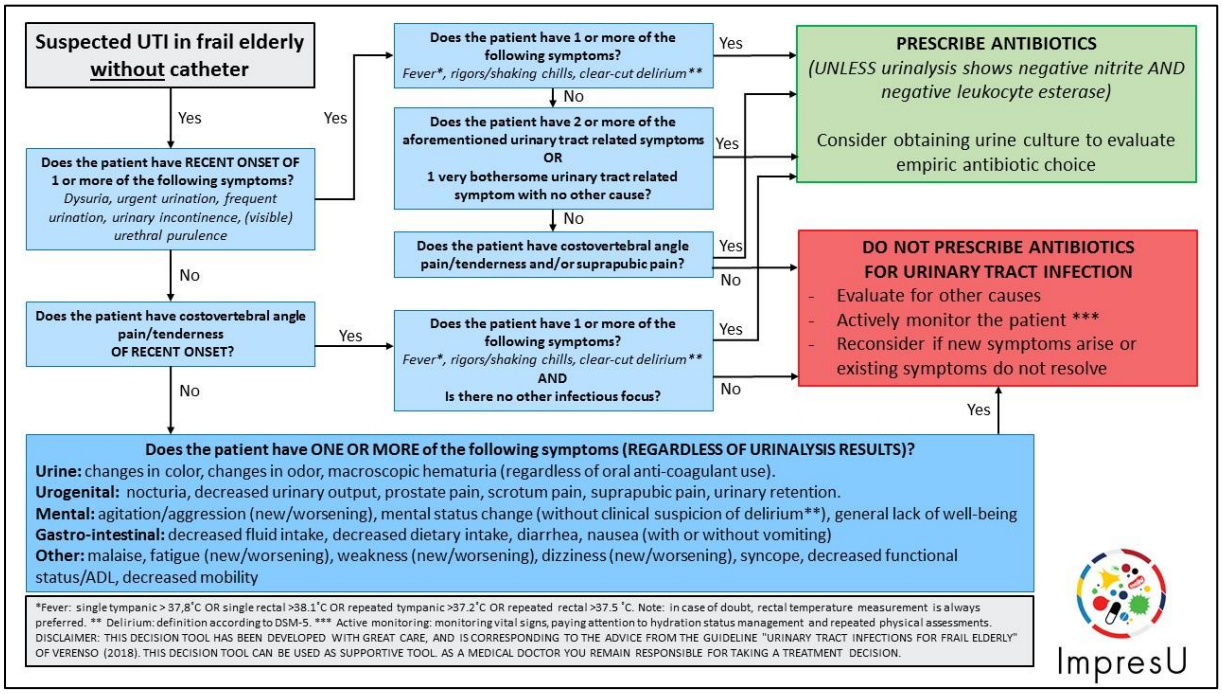
The effect of a multifaceted antibiotic stewardship intervention to improve antibiotic prescribing for suspected urinary tract infections in frail older adults (ImpresU): a pragmatic cluster randomised controlled trial in four European countries

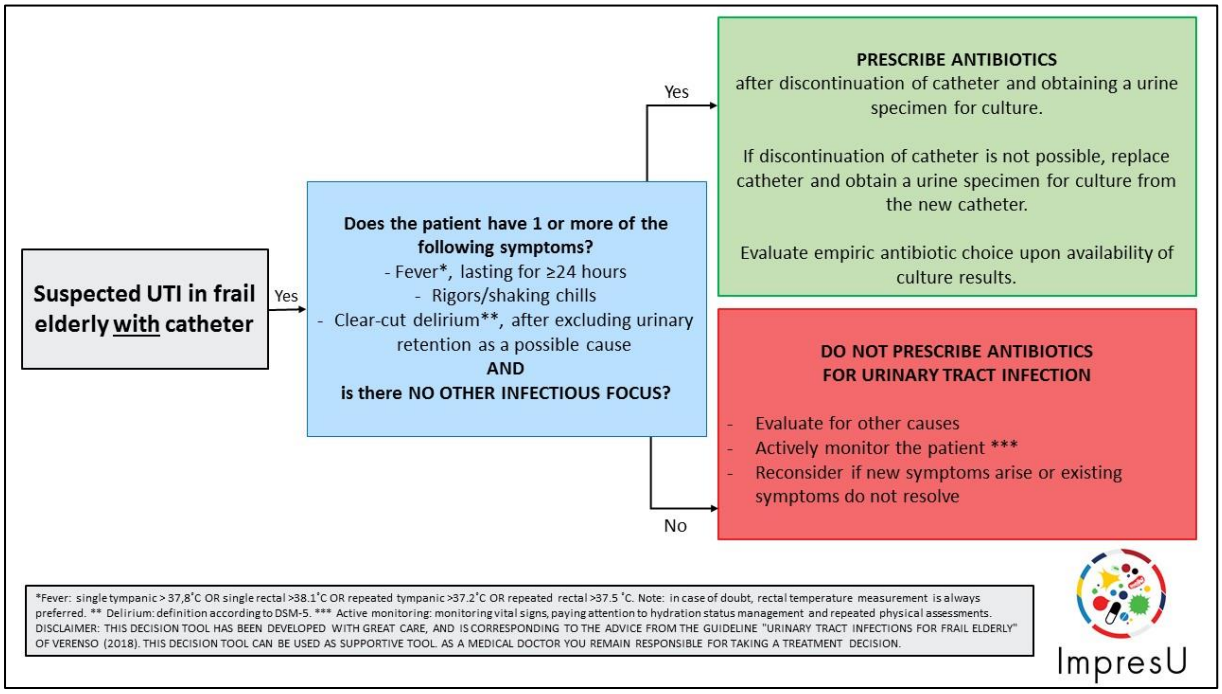
Data Supplement

Contents

Supplementary material S1:
Decision-tool and an example of toolbox materials

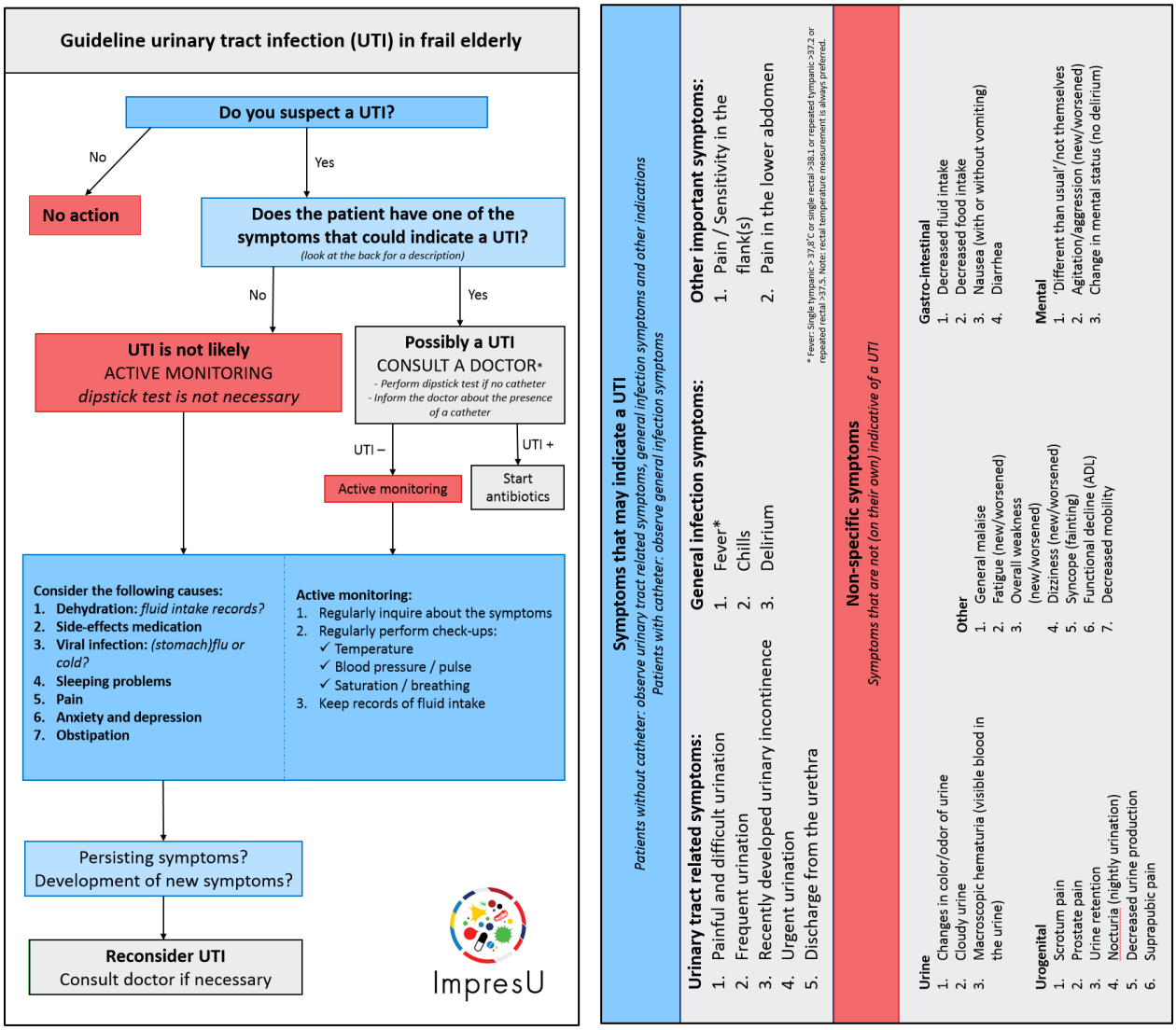
Decision-tool for suspected UTIs in patients with and without catheter (Van Buul et al. 2018):





Reference: van Buul LW, Vreeken HL, Bradley SF, et al. The Development of a Decision Tool for the Empiric Treatment of Suspected Urinary Tract Infection in Frail Older Adults: A Delphi Consensus Procedure. J Am Med Dir Assoc. 2018;19(9):757-6

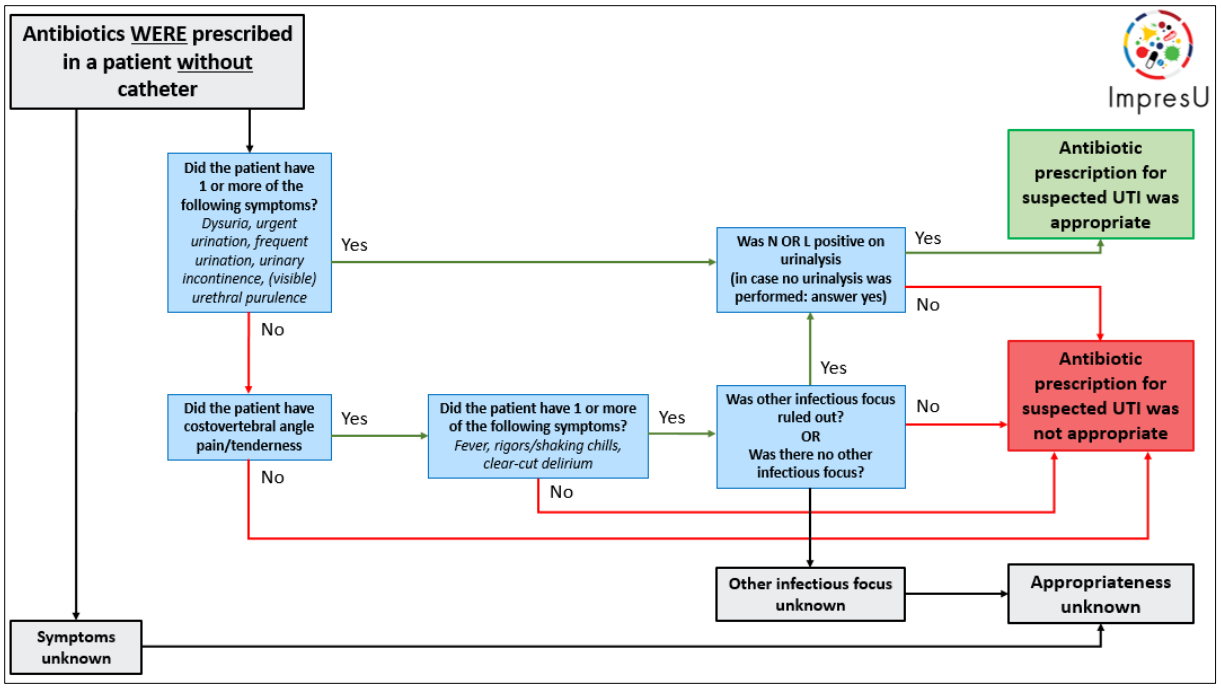
Example pocket card for nursing staff:



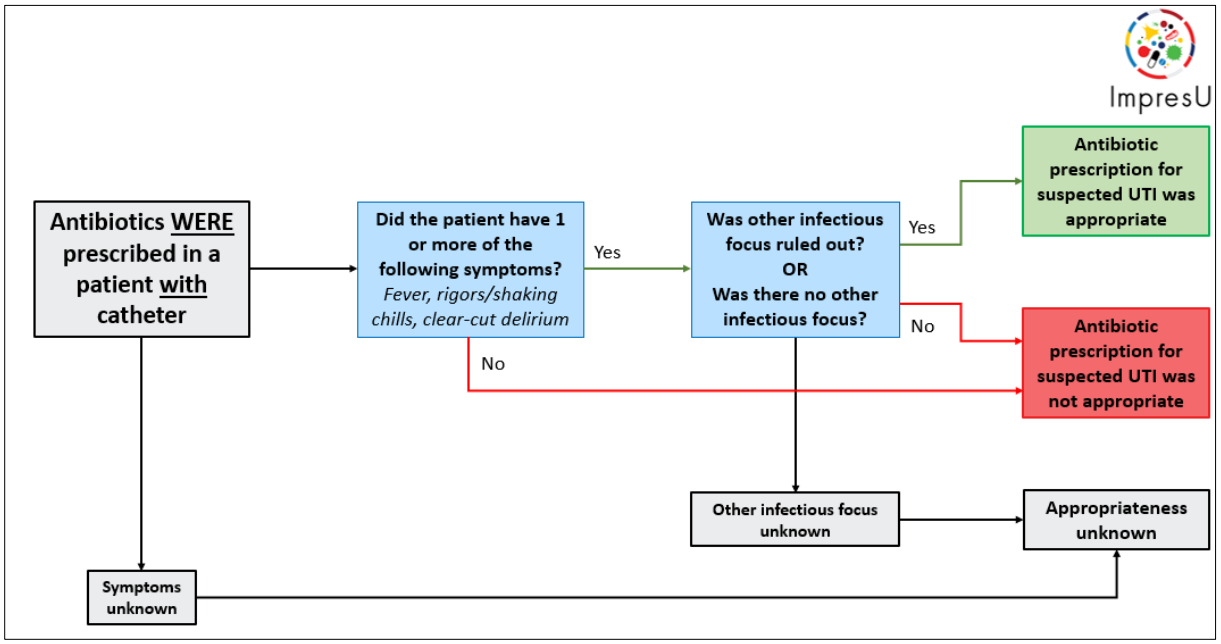
Supplementary material S2:
Reverse decision-tools

For scoring the appropriateness of antibiotic prescriptions, the decision-tool was reversed: that is, starting with the antibiotic prescription instead of ending with it.

Evaluation of the appropriateness of antibiotic prescriptions in patients without catheter

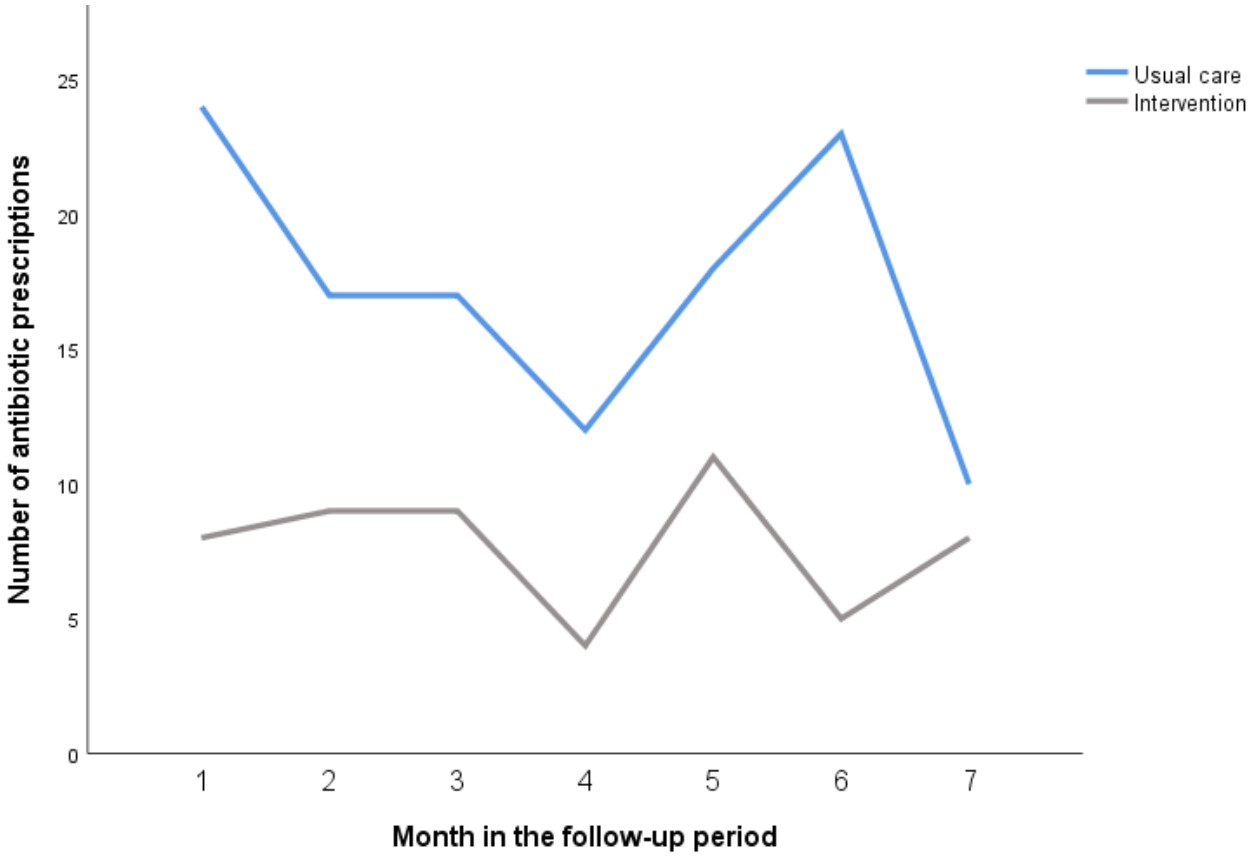


Evaluation of the appropriateness of antibiotic prescriptions in patients with catheter



Supplementary material S3:

Number of antibiotic prescriptions in the follow-up period



Supplementary table S1: Cluster size in randomisation

Table S1 | Cluster size in November 2019 used for randomisation procedure, Numbers of included patients corresponding with cluster sizes.				
Cluster size[1]	**Poland**	**The Netherlands**	**Norway**	**Sweden**
Small (≤7%)	≤ 25	≤ 9	≤ 14	≤ 12
Medium (8-14%)	26-41	10 – 17	15 – 23	13-22
Large ≥15%	≥ 42	≥ 18	≥ 24	n/a
[1]Based on the percentage of included participants within the country in November 2019 (N participants cluster / N participants country).				

Supplementary table S2: Participant characteristics per country

Table S2 | Baseline characteristics of participants in each country.
Values are numbers (percentages) unless stated otherwise.

	Poland (n=325)	The Netherlands (n=233)	Norway (n=276)	Sweden (n=207)	Total (n=1041)
Study arm					
Intervention	150 (46)	123 (53)	128 (46)	101 (49)	502 (48)
Usual care	175 (54)	110 (47)	148 (54)	106 (51)	539 (52)
Mean (SD) age (years)	82.9 (7.4)	87.7 (6.6)	88.4 (7.0)	87.3 (7.5)	86.3 (7.5)
Female	234 (72)	154 (66)	206 (75)	144 (70)	738 (71)
Site of residence					
Nursing home	325 (100)	0 (0)	276 (100)	207 (100)	808 (78)
Residential care home	0 (0)	198 (85)	0 (0)	0 (0)	198 (19)
Home care	0 (0)	35 (15)	0 (0)	0 (0)	35 (3)
Comorbidity					
Cardiovascular illness	232 (71)	176 (76)	163 (59)	149 (72)	720 (69)
Pulmonary illness	62 (19)	59 (25)	41 (15)	28 (14)	190 (18)
Diabetes mellitus	66 (20)	51 (22)	31 (11)	39 (19)	187 (18)
Immunosuppression	0 (0)	10 (4)	5 (2)	24 (12)	39 (4)
Disorders of kidney / urinary tract	86 (26)	55 (24)	46 (17)	39 (19)	226 (22)
Dementia	153 (47)	73 (31)	187 (68)	49 (24)	462 (44)
Mild Cognitive Impairment	129 (40)	37 (16)	51 (18)	60 (29)	277 (27)
Recurrent urinary tract infections (≥ 3 yearly)	58 (18)	27 (12)	30 (11)	15 (7)	130 (12)
Indwelling urinary catheter	11 (3)	24 (10)	25 (9)	18 (9)	78 (7)
Urinary incontinence	184 (57)	118 (51)	159 (58)	141 (68)	602 (58)
Faecal incontinence	94 (29)	31 (13)	100 (36)	57 (28)	282 (27)
Mean (SD) Katz-ADL score (range 0-6 from independent to dependent)	2.6 (2.0)	3.0 (1.7)	3.4 (2.1)	3.1 (2.0)	2.8 (2.0)

Supplementary table S3: UTI episodes

Table S3 | Characteristics of UTI episodes in the intervention and usual care group in the follow-up period
Values are numbers (percentages) unless stated otherwise.

	Intervention (n=65)	Usual care (n=150)	Total (n=215)
Country			
Poland	14 (22)	76 (51)	90 (42)
The Netherlands	17 (26)	30 (20)	47 (22)
Norway	17 (26)	36 (24)	53 (25)
Sweden	17 (26)	8 (5)	25 (12)
At least one recent onset genitourinary symptoms	35 (54)	99 (66)	134 (62)
Dysuria	23 (36)	73 (49)	96 (45)
Urgent/frequent urination	28 (44)	77 (51)	105 (49)
Urinary incontinence	16 (25)	56 (37)	72 (34)
Urethral purulence	2 (3)	9 (6)	11 (5)
Costovertebral angle pain/tenderness	12 (19)	41 (27)	53 (25)
Suprapubic pain	19 (30)	82 (55)	101 (47)
Systemic signs			
Fever	7 (11)	32 (21)	39 (18)
Rigors/shaking chills	1 (2)	12 (8)	13 (6)
Delirium	1 (2)	3 (2)	4 (2)
Indwelling urinary catheter	10 (15)	32 (21)	42 (20)
Antibiotic prescription for suspected UTI	54 (83)	121 (81)	175 (81)
Inappropriate antibiotic prescription (of total antibiotic prescriptions)	23 (43)	41 (34)	64 (37)
List of antibiotics prescribed at day 1 of UTI suspicion (of total at day 1)*	45 (100)	84 (100)	129 (100)
Nitrofurantoin / Furazidine	14 (31)	24 (29)	38 (29)
Pivmecillinam	10 (22)	15 (18)	25 (19)
Trimethoprim	5 (11)	5 (6)	10 (8)
Fosfomycin	0 (0)	9 (11)	9 (7)
Ciprofloxacin	5 (11)	15 (18)	20 (16)
Cotrimoxazol	6 (13)	7 (8)	13 (10)
Amoxicillin clavulanic acid	4 (9)	1 (1)	5 (4)
Amoxicillin	0 (0)	2 (2)	2 (2)
Ceftriaxone	0 (0)	1 (1)	1 (1)
Norfloxacin	1 (2)	3 (4)	4 (3)
Other	1 (2)	4 (5)	5 (4)

*Numbers do not add up as multiple antibiotics were given simultaneously in a small number of episodes.
List per country: Poland (total 32): 12 nitrofurantoin/furazidine, 1 trimethoprim, 11 ciprofloxacin, 1 cotrimoxazol, 2 amoxicillin clavulanic acid, 4 norfloxacin, 1 other | The Netherlands (total 37): 16 nitrofurantoin, 2 trimethoprim, 9 fosfomycin, 5 ciprofloxacin, 3 amoxicillin clavulanic acid, 1 amoxicillin, 1 ceftriaxone, 1 other | Norway (total 43): 4 nitrofurantoin, 18 pivmecillinam, 7 trimethoprim, 12 cotrimoxazole, 1 amoxicillin, 1 other | Sweden (total 17): 6 nitrofurantoin, 7 pivmecillinam, 4 ciprofloxacin, 2 other

Supplementary table S4: Subgroup analyses

Table S4: | Primary outcome in planned subgroups										
		Intervention		Usual care		Rate ratio's				LR test[1]
	Period	Count / person-years	per person-year	Count / person-years	per person-year	Unadjusted RR (95% CI)	p-value	Adjusted RR (95% CI)	p-value	
Overall effect	Baseline	87 / 174	0.50	77 / 174	0.44	0.41 (0.25 to 0.65)	<0.001	0.42 (0.26 to 0.68)	<0.001	n/a
	Follow-up	54 / 202	0.27	121 / 209	0.58					
Poland	Baseline	17 / 57	0.30	26 / 61	0.43	0.29 (0.11 to 0.74)	0.01	0.28 (0.11 to 0.73)	0.009	0.02
	Follow-up	9 / 66	0.14	50 / 74	0.68					
The Netherlands	Baseline	39 / 45	0.87	24 / 36	0.68	0.33 (0.13 to 0.85)	0.02	0.32 (0.12 to 0.82)	0.02	
	Follow-up	13 / 53	0.24	27 / 46	0.58					
Norway	Baseline	19 / 40	0.48	14 / 45	0.31	0.35 (0.14 to 0.88)	0.02	0.40 (0.16 to 1.03)	0.06	
	Follow-up	15 / 43	0.35	36 / 53	0.68					
Sweden	Baseline	12 / 33	0.37	13 / 33	0.39	2.27 (0.55 to 9.41)	0.26	2.25 (0.57 to 8.88)	0.25	
	Follow-up	17 / 41	0.42	8 / 35	0.23					
Female patients	Baseline	68 / 120	0.57	55 / 127	0.43	0.40 (0.23 to 0.67)	0.001	0.43 (0.25 to 0.73)	0.002	0.78
	Follow-up	43 / 141	0.30	89 / 154	0.58					
Male patients	Baseline	19 / 54	0.36	22 / 46	0.47	0.39 (0.14 to 1.12)	0.08	0.40 (0.15 to 1.06)	0.07	
	Follow-up	11 / 61	0.18	32 / 55	0.58					
Patients with dementia	Baseline	43 / 61	0.70	35 / 91	0.38	0.32 (0.16 to 0.61)	0.001	0.33 (0.17 to 0.64)	0.001	0.09
	Follow-up	25 / 68	0.37	64 / 100	0.64					
Patients without dementia	Baseline	44 / 111	0.39	42 / 79	0.53	0.57 (0.29 to 1.13)	0.11	0.56 (0.28 to 1.12)	0.10	
	Follow-up	29 / 134	0.22	57 / 108	0.53					
Patients with urinary incontinence	Baseline	49 / 96	0.51	46 / 108	0.43	0.51 (0.28 to 0.92)	0.03	0.53 (0.29 to 0.96)	0.04	0.09
	Follow-up	39 / 103	0.38	70 / 117	0.60					
Patients without urinary incontinence	Baseline	36 / 75	0.48	31 / 66	0.47	0.25 (0.11 to 0.56)	0.001	0.24 (0.11 to 0.54)	0.001	
	Follow-up	14 / 96	0.15	51 / 92	0.56					
Patients with catheter[2]	Baseline	15 / 11	1.31	16 / 15	1.07	0.39 (0.12 to 1.28)	0.12	0.37 (0.11 to 1.21)	0.10	0.92
	Follow-up	7 / 12	0.60	15 / 12	1.22					
Patients without catheter	Baseline	72 / 162	0.44	61 / 159	0.38	0.40 (0.24 to 0.67	0.001	0.43 (0.26 to 0.74)	0.002	
	Follow-up	47 / 190	0.25	106 / 197	0.54					
	Baseline	14 / 37	0.37	16 / 40	0.41					

Patients aged below 80	Follow-up	11 / 46	0.24	34 / 53	0.64	0.41 (0.15 to 1.14)	0.09	0.38 (0.14 to 1.08)	0.07	0.87
Patients aged 80 and older	Baseline	73 / 136	0.54	61 / 134	0.45	0.42 (0.25 to 0.72)	0.001	0.44 (0.26 to 0.75)	0.002	
	Follow-up	43 / 156	0.28	87 / 156	0.56					

1: For each model, the p-value is provided of a likelihood ratio test compared the adjusted model to the same model where interaction terms (intervention*subgroup, period*subgroup, intervention*period*subgroup) were added.
2: In the analysis with the unadjusted analysis for patients with an indwelling catheter, the random intercept at organizational level is omitted. Otherwise, the model did not converge.

Supplementary table S5: Number of clusters with a COVID-19 outbreak

Table S5 | Numbers of clusters with a COVID-19 outbreak in the follow-up period per total number of clusters.
An outbreak is defined as 3 or more registered COVID-19 cases in a month in an older adult care organization.

	Poland	The Netherlands	Norway	Sweden
Intervention	4/4	3/6	0/4	3/5
Usual care	3/4	2/5	0/5	0/5
Total	7/8	5/11	0/9	3/10