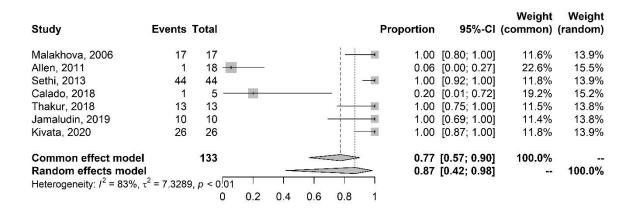
The frequency of mutations in the *penA*, *mtrR*, *gyrA* and *parC* genes of *Neisseria gonorrhoeae*, the presence of *tet*M gene and antibiotic resistance/susceptibility: a systematic review and meta-analyses

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FIGURES-SUPPLEMENTARY MATERIAL

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0 , 1									05% 01	Weight	
Study	Events 1	otal					Pro	oportion	95%-01	(common)	(random)
Allen, 2011	18	18				8	-	1.00	[0.81; 1.00]	17.5%	17.5%
Calado, 2018	1	1 —						1.00	[0.03; 1.00]	13.5%	13.5%
Thakur, 2018	13	13				1	i II	1.00	[0.75; 1.00]	17.3%	17.3%
Jamaludin, 2019	10	10					-	1.00	[0.69; 1.00]	17.2%	17.2%
Kivata, 2020	25	26				0	-	0.96	[0.80; 1.00]	34.6%	34.6%
Common effect model	l	68				V	\Rightarrow	0.95	[0.86; 0.98]	100.0%	
Random effects mode	5			~		V	\diamond	0.95	[0.86; 0.98]		100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	² = 0, <i>p</i> = 0.8	30	1	2	1	1	1				
		0	0.2	0.4	0.6	0.8	1				

Figure 1. Meta-analysis of the proportion of gene mutations in isolates resistant to the antibiotic penicillin. (A) *penA*. (B) *mtr*R. The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

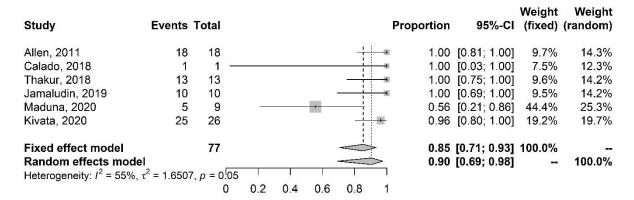


Figure. 2. Meta-analysis of the proportion of gene mutations in isolates resistant to penicillin and *mtr*R gene. The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

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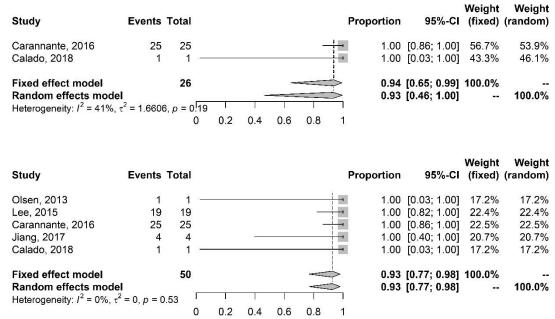
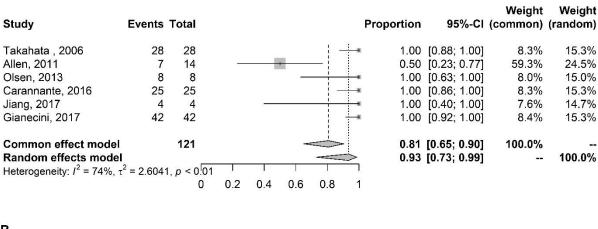


Figure. 3. Meta-analysis of the proportion of gene mutations in cefixime-resistant isolates. (A) *mtr*R. (B) *penA*. The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

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Study	Events Tot	al					1	Proportion	95%-CI	Weight (common)	Weight (random)
Allen, 2011 Olsen, 2013 Carannante, 2016	8	14 8 25			_	_	- - - - - -	1.00	[0.66; 1.00] [0.63; 1.00] [0.86; 1.00]		32.7% 16.7% 17.3%
Jiang, 2017 Gianecini, 2017	4 42	4 42							[0.40; 1.00] [0.92; 1.00]	15.9% 17.4%	15.9% 17.4%
Common effect mode Random effects mode Heterogeneity: $I^2 = 0\%$,	el	93 0	0.2	0.4	0.6	0.8	-∲-∲ 1		[0.88; 0.99] [0.88; 0.99]	100.0% 	 100.0%

Figure 4. Meta-analysis of the proportion of gene mutations in isolates with reduced susceptibility to cefixime. (A) *penA*. (B) *mtrR*. The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

Study	Events ⁻	Total					Pro	oportion	95%-Cl	Weight (common)(Weight random)
Allen, 2011	13	14			-			0.93	[0.66; 1.00]	32.7%	32.7%
Olsen, 2013	8	8			×	8			[0.63; 1.00]	16.7%	16.7%
Carannante, 2016	25	25				-	<u> </u>	1.00	[0.86; 1.00]	17.3%	17.3%
Jiang, 2017	4	4					-	1.00	[0.40; 1.00]	15.9%	15.9%
Gianecini, 2017	42	42						1.00	[0.92; 1.00]	17.4%	17.4%
Common effect model Random effects model		93				-			[0.88; 0.99] [0.88; 0.99]	100.0% 	 100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p = 0.	75	T		1	1					
and an		0	0.2	0.4	0.6	0.8	1				

Figure. 5. Meta-analysis of the proportion of gene mutations in isolates with reduced susceptibility to cefixime (*mtr*R gene). The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

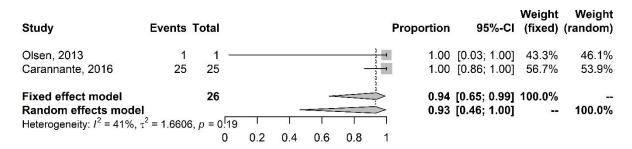


Figure. 6. Meta-analysis of the proportion of gene mutations in cefixime resistant isolates (*mtr*R gene). The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

A	Study	Events	Total					Proportion	95%-CI	Weight (fixed)	Weight (random)
	Olsen, 2013	5	5		-			→ 1.00	[0.48; 1.00]	12.6%	12.6%
	Chen, 2014	15	15					- 1.00	[0.78; 1.00]	13.3%	13.3%
	Lee, 2015	7	7			-		1.00	[0.59; 1.00]	12.9%	12.9%
	Claire de Curraize, 2016	2	2	-				- 1.00	[0.16; 1.00]	11.4%	11.4%
	Jiang, 2017	13	13					- 1.00	[0.75; 1.00]	13.2%	13.2%
	Zhao, 2017	2	2						[0.16; 1.00]	11.4%	11.4%
	Peng, 2017	3	3	1				- 1.00	[0.29; 1.00]	12.0%	12.0%
	Yan, 2019	12	12				\rightarrow	1.00	[0.74; 1.00]	13.2%	13.2%
	Fixed effect model		59				\sim	> 0.93	[0.82; 0.97]	100.0%	
	Random effects model						\sim	> 0.93	[0.82; 0.97]		100.0%
_	Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0\%$	= 0, <i>p</i> = 0			1	Party and a second	1. 	1			
в			0	0.2	0.4	0.6	0.8	1			
	Chudu	Events	Total					Duonontion	05% 01	Weight	Weight
	Study	Events	Total					Proportion	95%-CI	(fixea)	(random)
	Olsen, 2013	5	5		-			1.00	[0.48; 1.00]	20.7%	20.7%
	Chen, 2014	15						- 1.00	[0.78; 1.00]	21.9%	21.9%
	Claire de Curraize, 2016	2 3	2	6.5				- 1.00	[0.16; 1.00]	18.8%	18.8%
	Peng, 2017	3	3					- 1.00	[0.29; 1.00]	19.8%	19.8%
	Zhao, 2017	2	2	-				1.00	[0.16; 1.00]	18.8%	18.8%
	Fixed effect model		27				-	> 0.90	[0.72; 0.97]	100.0%	
	Random effects model						-	> 0.90	[0.72; 0.97]		100.0%
	Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0\%$	= 0, p = 0	.90	1			L				
			0	0.2	0.4	0.6	0.8	1			

Figure. 7. Meta-analysis of the proportion of gene mutations in ceftriaxone-resistant isolates. (A) *penA*. (B) *mtr*R. The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

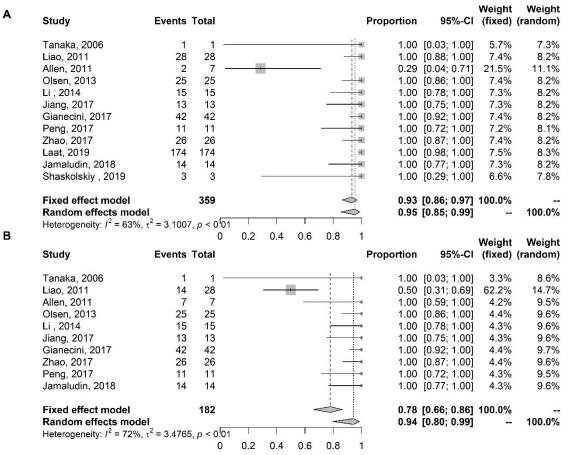


Figure. 8. Meta-analysis of the proportion of gene mutations in isolates with reduced susceptibility to ceftriaxone. (A) *penA*. (B) *mtrR*. The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

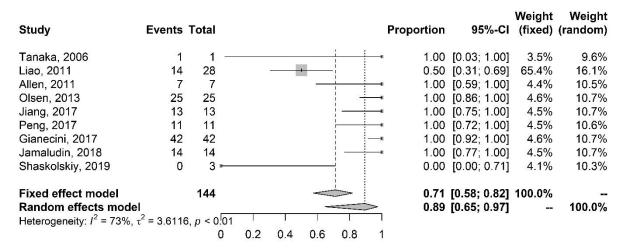


Figure. 9. Meta-analysis of the proportion of gene mutations in isolates with reduced susceptibility to ceftriaxone (*mtr*R gene). The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

Study	Events Total		Proportion	95%-CI (c	Weight Weight common) (random)
Olsen, 2013 Shen, 2014 Peng, 2017	5 5 15 15 3 3			[0.48; 1.00] [0.78; 1.00] [0.29; 1.00]	33.2%33.2%35.1%35.1%31.7%31.7%
Common effect model Random effects model Heterogeneity: $l^2 = 0\%$, τ^2		0.2 0.4 0.6		[0.72; 0.99] [0.72; 0.99]	100.0% 100.0%

Figure. 10. Meta-analysis of the proportion of gene mutations in isolates resistant to ceftriaxone (*mtr*R gene). The results are presented in forest plots. In its first column ("study") are the citations of the selected studies. The second column ("events") contains the number of isolates with mutations in the evaluated gene, while the third column ("total") shows the total number of samples analyzed in that study. The fourth column presents the proportion estimate followed by their confidence intervals. The sixth and seventh columns present, respectively, the weights for the fixed and random models of the meta-analysis.

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