

Supporting materials

Efficacy of the XEN-implant and a meta-analysis of the literature

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Table S1. Summary of the retrieved studies from the systematic review.

	Study	Design	<i>n</i> (eyes) per Group	Diagnosis	Intervention*	Follow-up months	IOP Reduction mmHg Mean ± s.d. (%)	Needling (%)	Secondary Surgeries (%)	Hypotony (%)	Choroideal Effusion/Detachment (%)	Macular Edema/ Hypotone Maculopathy (%)	
1	Smith et al 2019 [30]	R	Case series	68	(P)OAG	XEN + MMC (+ CE <i>n</i> = 10)	12	(33)	38.2	10.3	7.4	1.5	NA
2	Reitsamer et al. 2019 [28]	P	Multicenter clinical study	202	(P)OAG	XEN + MMC (+ CE <i>n</i> = 79)	24	6.2 ± 4.9 (27.8)	41.1	6.4	2.3	1.8	0.5
3	Heidinger et al. 2019 [21]	R	Cohort study	199	Glaucoma	XEN + MMC	18	(22.7)	22	14	8	0	NA
4	Karimi et al. 2019 [23]	R	Case series	259	Glaucoma	XEN + MMC (+ CE <i>n</i> = 72)	12	(26.4)	27	6	23.7	1.5	1.9
5	Widder, et al. 2018 [32]	R	Cohort study	261	Glaucoma	XEN + MMC (+ CE <i>n</i> = 49)	12	7.5 ± 10.1 (30.9)	NA	34	NA	3.4	1.7
6	Ozal, et al. 2017 [26]	R	Cohort study	15	(P)OAG, PEG/PEX	XEN (+ CE <i>n</i> = 6)	12	(53.6)	0	6.6	0	0	NA
7	Tan, et al. 2017 [31]	R	Cohort study	39	Glaucoma	XEN + MMC (+ CE, <i>n</i> = 2)	12	10.4 ± 8.5 (41.8)	17.0	2.6	20.5	NA	NA
8	Grover, et al. 2017 [7]	P	Cohort study	52	(P)OAG, PEG/PEX	XEN + MMC	12	9.1 ± 1.6 (35.6)	32.3	13.8	24.6	3.1	1.5
9	De Gregorio, et al. 2017 [16]	P	Cohort study	41	(P)OAG, PEG/PEX	XEN + MMC + CE	12	9.4 ± 4.4 (41.8)	2.4	2.4	2.4	2.4	NA
10	Galal, et al. 2017 [20]	P	Cohort study	13	(P)OAG	XEN + MMC (+ CE <i>n</i> = 10)	12	4 ± 5 (29.4)	30.7	15.4	15.4	15.4	0.
11	Başer et al. 2020 [15]	R	Case series	29	Glaucoma	XEN + MMC (+ CE <i>n</i> = 6)	36	(31.6)	27	NA	17	17	NA
12	Fernández et al. 2020 [18]	R	Observational study	63	(P)OAG	XEN + MMC	36	(24.5)	5.4	NA	NA	NA	NA
13	Fea et al. 2020 [17]	P	Multicenter clinical trial	298	GLaucoma	XEN + MMC (+ CE <i>n</i> = 56)	12	7.4 ± 7.9 (35.2)	46.2	7	NA	9.4	NA
14	Olgun et al. 2020 [25]	R	Multicenter clinical study	114	Glaucoma	XEN (+ CE <i>n</i> = 45)	24	(57.9)	31.5	4.4	0	NA	NA
15	Mansouri et al. 2019 [24]	P	Interventional study	149	Glaucoma	XEN + MMC (+ CE <i>n</i> = 109)	24	14.1±3.7 (28.7)	44.4	11.4	2	2.7	0.7
16	Hengerer, et al. 2019 [22]	R	Cohort study	148	(P)OAG	XEN + MMC	12	(53–58)	33.1	7.4	4.7	0	0
17	Gabbay et al. 2019 [19]	R	Cohort study	151	Glaucoma	XEN + MMC (+ CE <i>n</i> = 57)	24	(34.6)	36.8	4.6	NA	3	0.6
18	Rauchegger et	R	Observational	60	Glaucoma	XEN + MMC (+	24	(29)	62	16	2.4	2.4	NA

	al. 2020 [27]		study			CE <i>n</i> = 23)							
19	Scheres et al. 2020 [29]	R	Comparative study	41	(P)OAG	XEN + MMC (+ CE <i>n</i> = 15)	24	(28)	20	14	24	2	NA

* = in brackets the number of eyes from the total study population that underwent a combined procedure; P = prospective; R = retrospective; MMC = Mitomycin C; POAG = primary open angle glaucoma; s.d. = standard deviation; Glaucoma = mixture of different types of glaucoma; PEG = pigment dispersion glaucoma; PEX = pseudoexfoliation glaucoma; OAG = open-angle glaucoma; CE = cataract extraction.

Table S2. Quality assessment of the included non-randomized studies according to the Newcastle-Ottawa Scale.

	Author	Selection	Comparability	Outcome (Cohort)/ Exposure (Case- Control)	Total Score (max.9)
1	Smith et al. 2019 [30]	4	2	2	8
2	Reitsamer et al. 2019 [28]	4	2	2	8
3	Heidinger et al. 2019 [21]	3	2	3	8
4	Karimi et al. 2019 [23]	3	2	2	7
5	Widder, et al. 2018 [32]	4	2	2	8
6	Ozal, et al. 2017 [26]	3	2	2	7
7	Tan, et al. 2017 [31]	3	2	2	7
8	Grover, et al. 2017 [7]	3	2	2	7
9	De Gregorio, et al. 2017 [16]	3	2	3	8
10	Galal, et al. 2017 [20]	3	2	2	7
11	Başer et al. 2020 [15]	4	2	2	8
12	Fernández et al. 2020 [18]	3	2	3	8
13	Fea et al. 2020 [17]	4	2	3	9
14	Olgun et al. 2020 [25]	4	2	3	9
15	Mansouri et al. 2019 [24]	4	2	2	8
16	Hengerer, et al. 2019 [22]	4	2	3	9
17	Gabbay et al. 2019 [19]	4	2	2	8
18	Rauchegger et al. 2020 [27]	3	2	2	7
19	Scheres et al. 2020 [29]	4	2	3	9

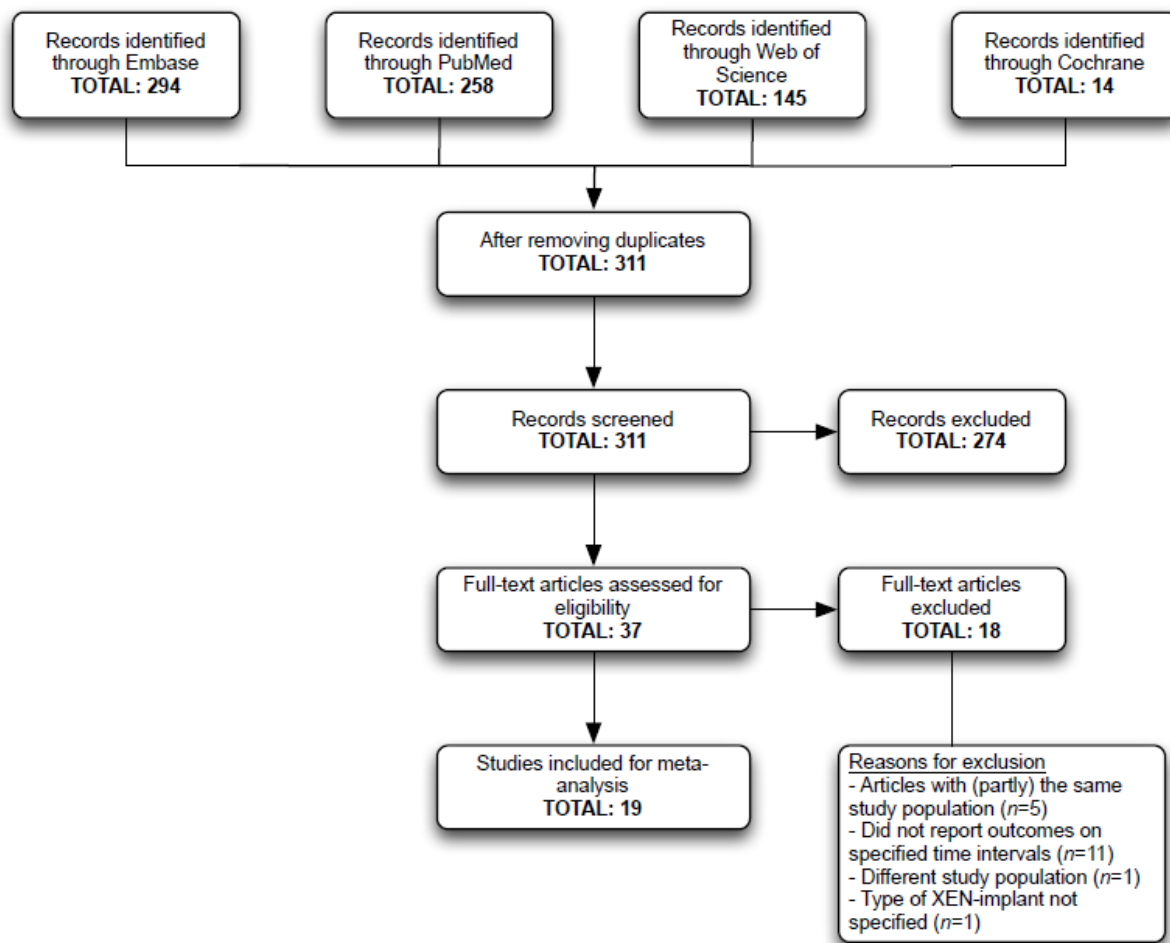
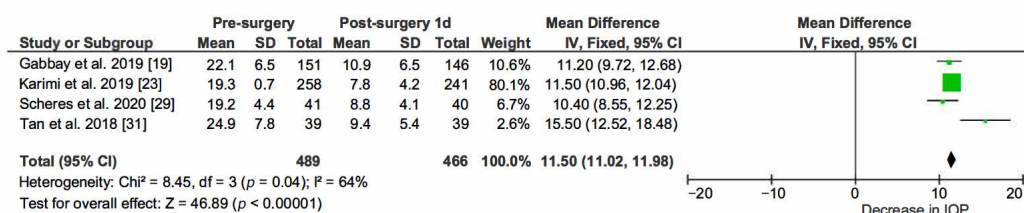
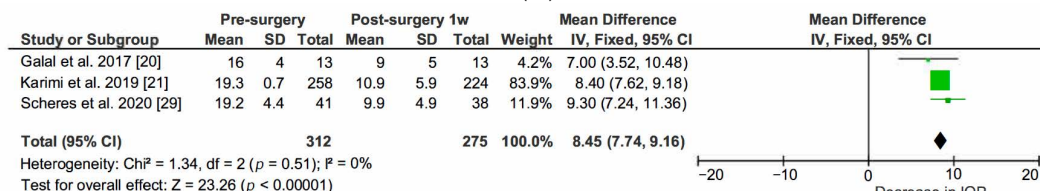


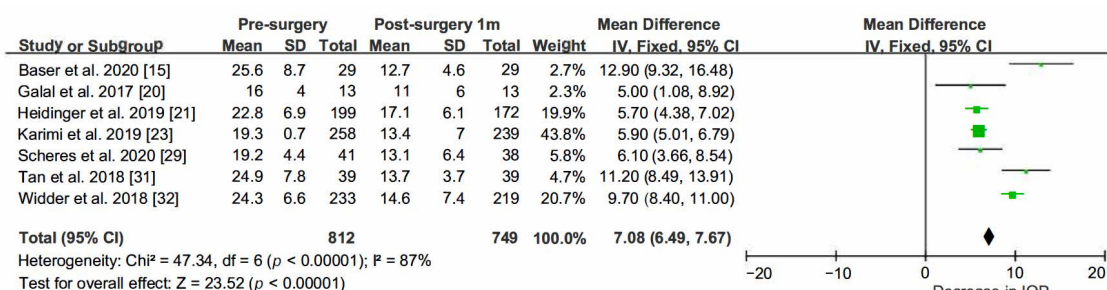
Figure S1. Flowchart (according to PRISMA) showing the selection process for inclusion of studies from our searches*. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; * = Search strings: **Embase:** ('xen'/de OR XEN45/de OR (((xen OR ab-interno) NEAR/3 (stent* OR microstent* OR implant* OR microimplant*)) OR xen45 OR xen-45):ab,ti,kw,dn) OR ((xen OR gelstent* OR gel-stent* OR gelatin*-stent*):ab,ti,kw,dn AND ('glaucoma drainage implant'/de OR 'glaucoma'/exp OR (glaucoma*):ab,ti,kw)) AND [English]/lim NOT [conference abstract]/lim. **Medline ALL Ovid (PubMed):** (((((xen OR ab-interno) ADJ3 (stent* OR microstent* OR implant* OR microimplant*)) OR xen45 OR xen-45).ab,ti,kf.) OR ((xen OR gelstent* OR gel-stent* OR gelatin*-stent*) ab,ti,kf. AND (Glaucoma Drainage Implants / OR Glaucoma / OR (glaucoma*) ab,ti,kf.)) AND english.la. **Web of Science (SCI-EXPANDED & SSCI, 1975-):** TS = (((((xen OR ab-interno) NEAR/2 (stent* OR microstent* OR implant* OR microimplant*)) OR xen45 OR xen-45)) OR ((xen OR gelstent* OR gel-stent* OR gelatin*-stent*) AND ((glaucoma*)))) AND DT = (article) AND LA = (english). **Cochrane CENTRAL register of Trials:** (((((xen OR ab NEXT interno) NEAR/3 (stent* OR microstent* OR implant* OR microimplant*)) OR xen45 OR xen NEXT 45) ab,ti) OR ((xen OR gelstent* OR gel NEXT stent* OR gelatin* NEXT stent*):ab,ti AND ((glaucoma*):ab,ti))



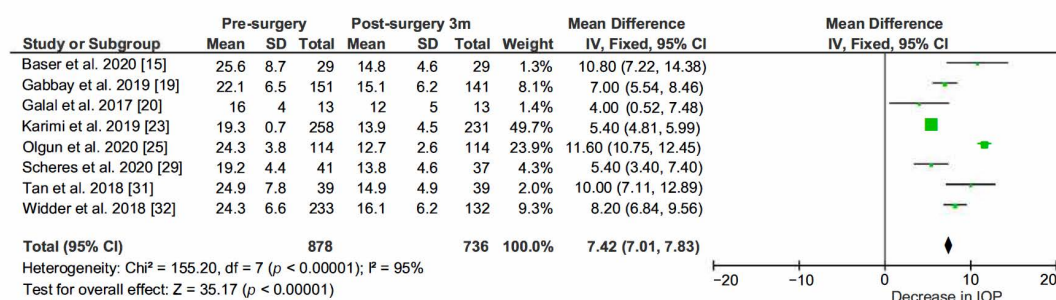
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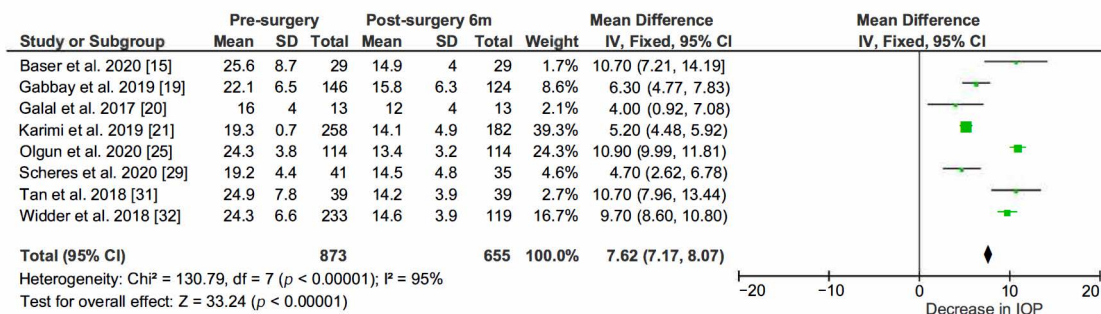
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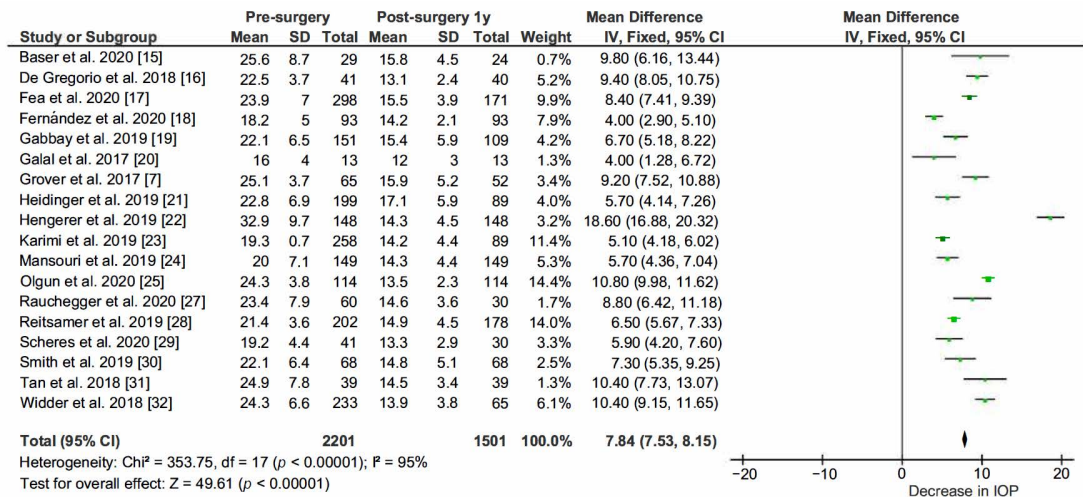
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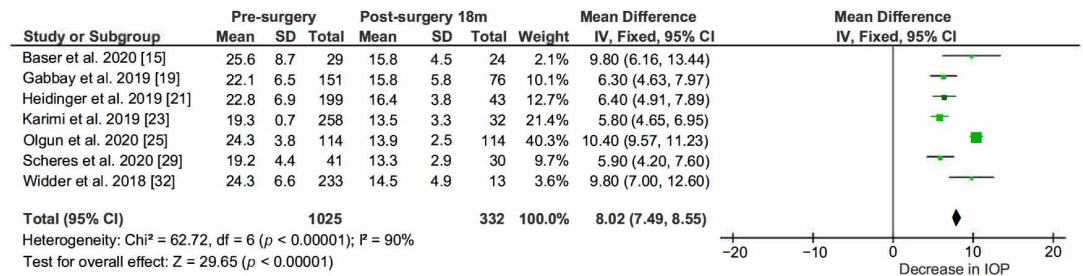
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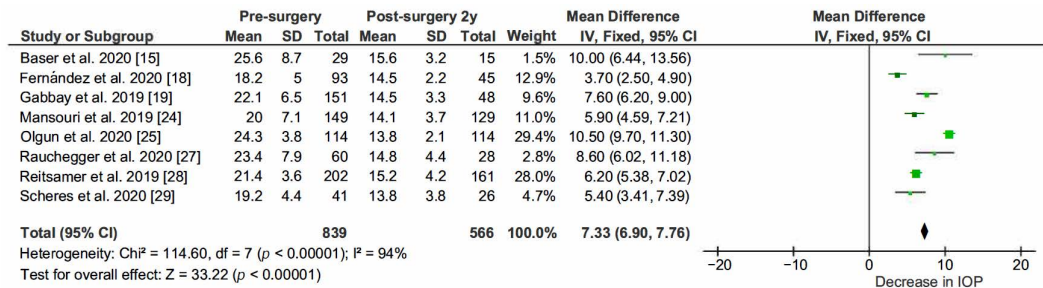
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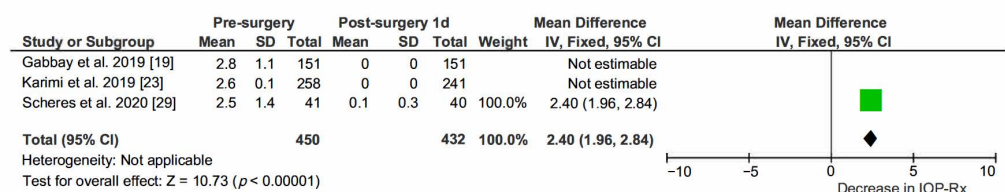


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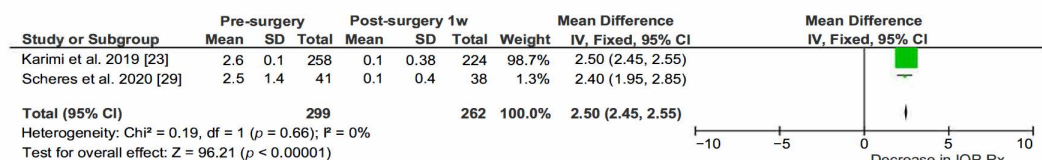


(H)

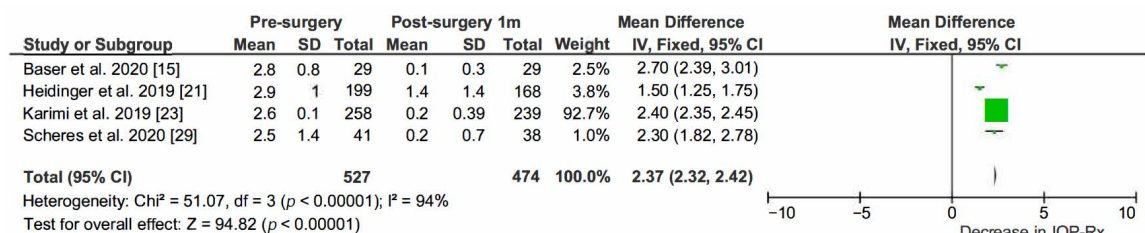
Figure S2. Meta-analyses for the effect of XEN-implant on IOP for all specified time-intervals*. * = Presented as mean decrease in IOP at 1 day (A), 1 week (B), 1 month (C), 3 months (D), 6 months (E), 1 year (F), 1.5 years (G) and 2 years (H) follow-up. Black diamonds indicate the overall weighted mean difference (WMD). The size of the green box is inversely proportional to the variance. Horizontal lines indicate 95% confidence interval (CI). The dashed vertical line in each panel shows the value for no effect (WMD = 0) compared to the pre-surgery IOP. IOP = intraocular pressure; CI = confidence interval; SD = standard deviation; IV = inverse variance.



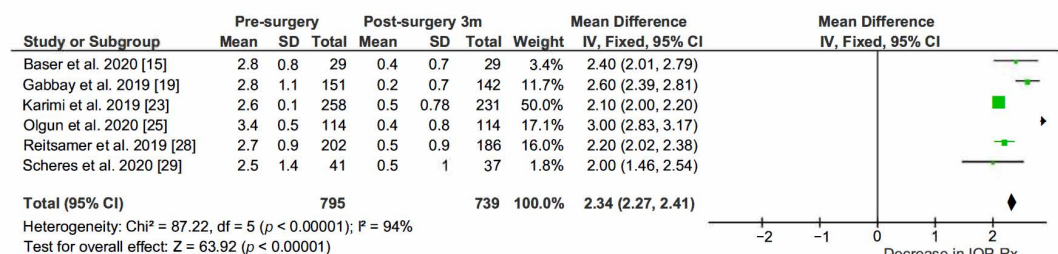
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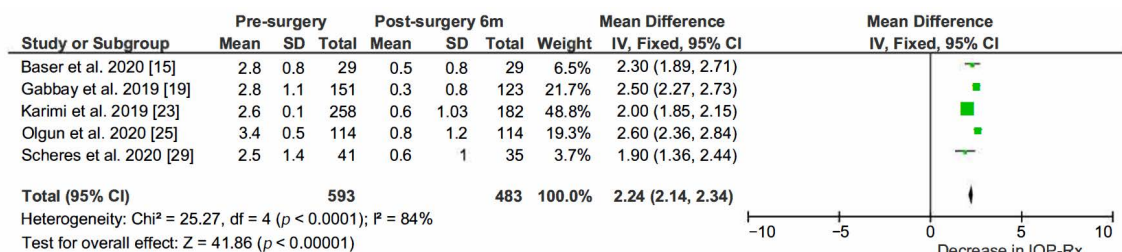
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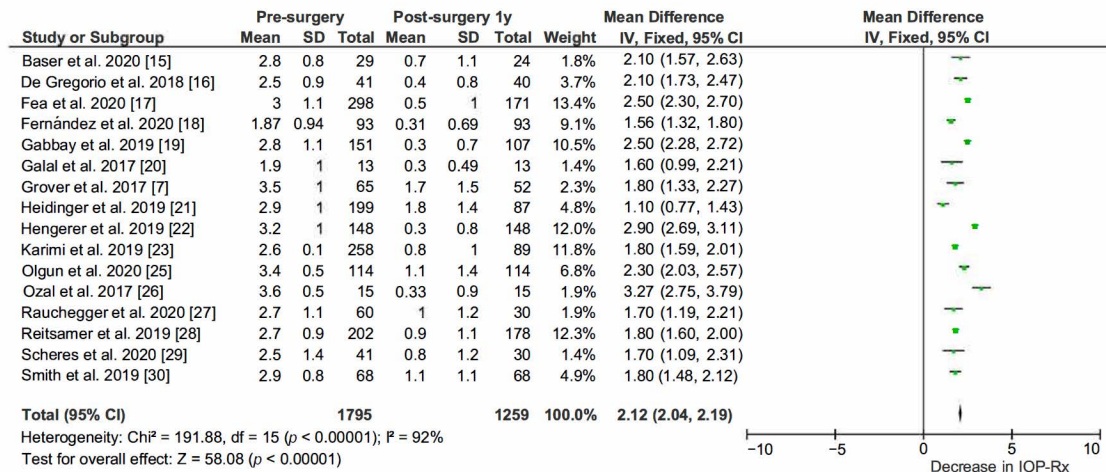
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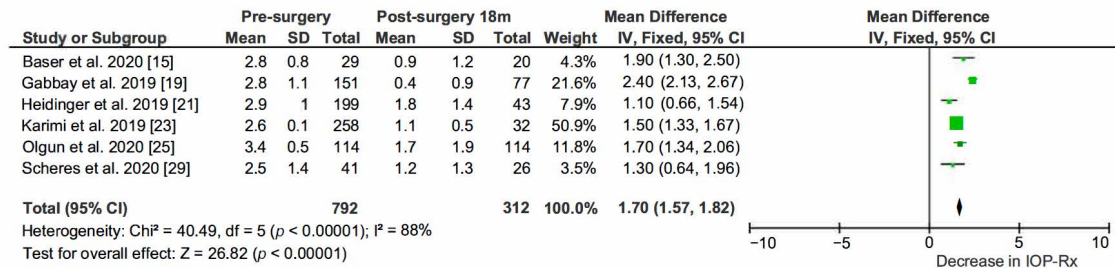
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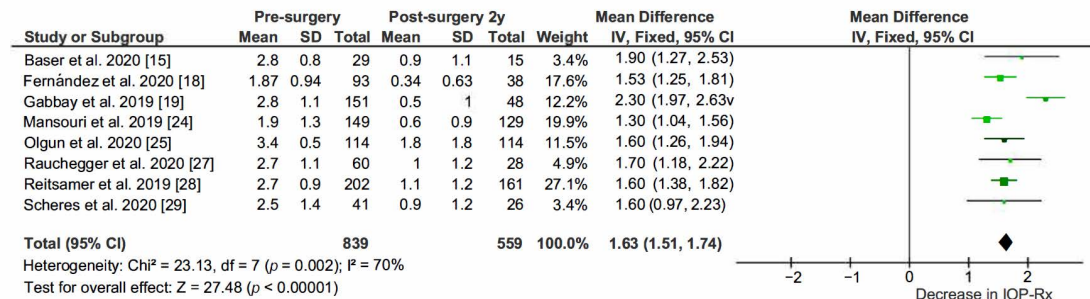
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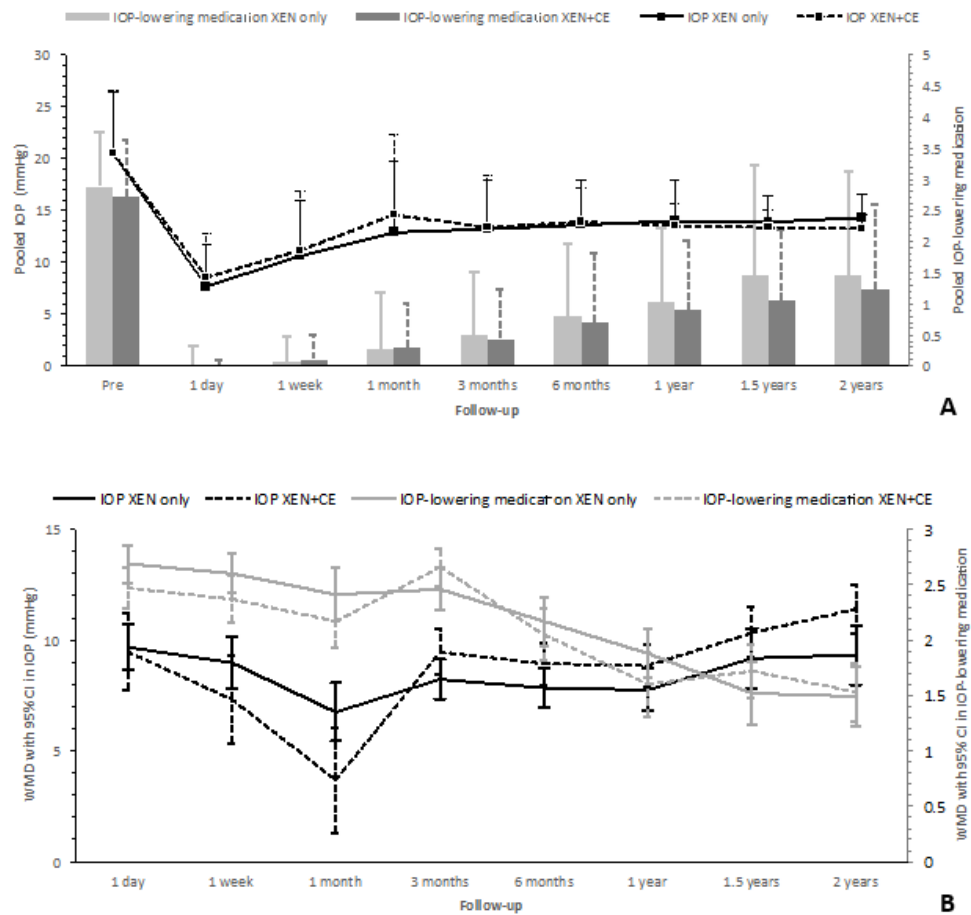


(G)



(H)

Figure S3. Meta-analyses for the effect of XEN-implant on IOP-lowering medication for all specified time-intervalls. *. * = Presented as mean decrease in IOP-lowering medication at 1 day (A), 1 week (B), 1 month (C), 3 months (D), 6 months (E), 1 year (F), 1.5 years (G) and 2 years (H) follow-up. Black diamonds indicate the overall weighted mean difference (WMD). The size of the green box is inversely proportional to the variance. Horizontal lines indicate 95% confidence interval (CI). The dashed vertical line in each panel shows the value for no effect (WMD = 0) compared to the pre-surgery IOP-lowering medication. IOP = intraocular pressure; CI = confidence interval; SD = standard deviation; IV = inverse variance.



XEN		Pre	1 day	1 week	1 month	3 months	6 months	1 year	1.5 years	2 years
standalone	N (IOP)	263	205	191	204	238	209	141	67	67
combined	N (IOP)	132	76	71	73	126	104	74	55	55
standalone	N (IOP-lowering medication)	191	140	132	129	175	178	167	151	153
combined	N (IOP-lowering medication)	148	102	99	96	142	139	137	134	130

Figure S4. Meta-analyses for the postoperative change in intraocular pressure (IOP) and number of IOP-lowering medications for XEN-implant as a standalone and as a combined procedure for all specified time-intervals. Presented as pooled mean with standard deviation (**A**) and weighted mean difference (WMD) with corresponding 95% confidence intervals (**B**). CE = cataract extraction (i.e., combined procedure).