Table 37: Adverse Events and Harms of MIGS Versus Comparators in Adults With Glaucoma

Quality Assessment							Summary of Findings				Importance
							No. of Eyes		Effect	Quality	
No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	MIGS	Comparator			
MIGS Vs. Pharmacotherapy: 2x iStent Vs. Travoprost, or 2x iStent Inject Vs. Latanoprost + Timolol											
2	RCT[a]	Very serious risk of bias[b]	No serious inconsistency	Serious indirectness[c]	Serious imprecision[d]	None	2x iStent, 54 2x iStent Inject, 94	Travoprost, 47 Latanoprost + Timolol, 98	**MIGS [=] Pharmacotherapy:**[36,58] **Adverse events** were minor in all treatment groups. The incidence of all adverse events was < 2% each[36,58] except for progression of cataract, which was 20% and 17% in *2x* iStent and Travoprost groups respectively in one study.[58]	⊕OOO VERY LOW	CRITICAL
MIGS Vs. Laser Therapy: Hydrus Microstent Vs. SLT											
1	Prospective cohort[e]	Serious risk of bias[f]	No serious inconsistency	Serious indirectness[g]	Serious imprecision[h]	None	56	31	**MIGS [=] Laser Therapy:**[62] **Adverse events** were transient (<7 d) and minor in both treatment groups. Adverse event incidence ranged from 6.5% (IOP spike in the Hydrus Microstent group) to 40% (eye discomfort in the SLT group; not reported in the Hydrus Microstent group).[62]	⊕OOO VERY LOW	CRITICAL
MIGS Vs. Another MIGS: 1x Vs. 2x Vs. 3x iStent											
1	RCT[i]	Serious risk of bias[j]	No serious inconsistency	Serious indirectness[k]	Serious imprecision[l]	None	iStent, 38 2x iStent, 41 3x iStent, 40	NA[m]	**1 iStent [=] 2 iStents [=] 3 iStents:**[59,60] **Adverse events:** None in any group **Secondary cataract surgery required:** Up to 13% of eyes in each group by 42 mo follow-up; no numerical between-group	⊕OOO VERY LOW	CRITICAL

Quality Assessment							Summary of Findings				Importance
							No. of Eyes		Effect	Quality	
No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	MIGS	Comparator			
									differences (not tested statistically).		
MIGS Vs. Filtration Surgery: ECP Vs. Glaucoma Drainage Device											
2	Retrospective cohort and non-randomized controlled clinical trial[n]	Serious risk of bias[o]	No serious inconsistency	Serious indirectness[p]	Serious imprecision[q]	None	59	BGI, 48 AGI, 34	**Mixed Findings;[61,63] MIGS =/> Glaucoma Drainage Device:** ***Adverse events:*** No between-group differences[61,63] except for shallow anterior chamber (a minor complication) that occurred in significantly fewer eyes in the ECP vs. AGI group.[61] Major complications (failure of corneal graft, retinal detachment, tube exposure, endophalmitis, phthisis bulbi) occurred in both ECP and AGI groups in one study, with incidence ranging from 2.9% to 11.8%, but with no significant differences between groups.[61]	⊕OOO VERY LOW	CRITICAL
MIGS Vs. Filtration Surgery: Trabectome Vs. Trabeculectomy With MMC											
1	Retrospective cohort[r]	Serious risk of bias[s]	No serious inconsistency	Serious indirectness[t]	Serious imprecision[u]	None	115	102	**Mixed Findings;[64] Trabectome </> Trabeculectomy With MMC:** **Adverse events:** • including hyphema: Trabectome (100%) < Trabeculectomy (~38%) • excluding hyphema: Trabectome (~4%) > Trabeculectomy (~35%) • all minor, except for persistent hypotony (~5% of Trabeculectomy group) and bullous keratopathy (1% of Trabeculectomy group)	⊕OOO VERY LOW	CRITICAL

Quality Assessment							Summary of Findings				Importance
							No. of Eyes		Effect	Quality	
No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	MIGS	Comparator			
									Secondary glaucoma surgery required: • Trabectome (~44%) < Trabeculectomy (~11%)		
MIGS Vs. Filtration Surgery: Xen45 With MMC Vs. Trabeculectomy With MMC											
1	Retrospective cohort[v]	Serious risk of bias[w]	No serious inconsistency	Serious indirectness[x]	Serious imprecision[y]	None	185	169	**Mixed Findings;[65] Xen45 with MMC [>]/= Trabeculectomy with MMC:** **Adverse events:** • Xen45 (11.9%) [=] Trabeculectomy (17.8%) • Major complications (hypotony maculopathy, corneal decompensation, malignant glaucoma) occurred in both groups, with incidence ranging from 0% to 2.2% across groups; exposed Xen45 occurred in 1 eye (0.5%) **Post-operative interventions:** • Xen45 (63.2%) [>] Trabeculectomy (97.6%) **Secondary glaucoma surgery required:** • Xen45 (10.3%) = Trabeculectomy (5.3%)	⊕OOO VERY LOW	CRITICAL

= = not significantly different between groups; [=] = not compared statistically but tendency for no difference between groups; > = intervention more favourable than comparator; [>] = not compared statistically but tendency for intervention more favourable than comparator; < = intervention less favourable than comparator; 1x = one device; 2x = two devices; 3x = three devices; AGI = Ahmed glaucoma implant; BGI = Baerveldt glaucoma implant; d = days; ECP = endoscopic cyclophotocoagulation; ; IOP = intraocular pressure; MIGS = minimally invasive glaucoma surgery; MMC = mitomycin C; mo = months; NA = not applicable; no. = number; RCT = randomized controlled trial; SLT = selective laser trabeculoplasty; vs. = versus.

Note: Data were collected by RCT, non-randomized controlled clinical trial, retrospective or prospective cohort, with up to 42 months of follow-up. The method of measuring adverse events or harms was not reported in any study.

[a] Two RCTs.[36,58]

[b] Very serious risk of bias. Selection bias: no indication of allocation concealment.[36,58] Detection bias: method of measuring adverse events and harms not specified.[36,58] Attrition bias: low-risk at 12- and 24 -month follow-up; large amount of missing data at 36-month follow-up and reasons not reported.[58] Reporting bias: no statistical comparisons conducted;[58] no *P* values reported for between-group difference in adverse events.[36]

[c] Serious indirectness.[36,58] Method of measuring adverse events or harms was not specified; therefore, it is unclear whether direct or surrogate measures were used or whether data on all patient-important adverse events or harms were collected.

[d] Serious imprecision.[36,58] No measures of variability.

[e] One prospective cohort study.[62]

[f] Serious risk of bias.[62] Bias due to confounding: significant differences between groups at baseline were not controlled, and treatment arm was assigned by geographical location. Bias in measurement of outcome: method of measuring adverse events and harms not specified. Reporting bias: no statistical comparisons conducted.

[g] Serious indirectness.[62] Method of measuring adverse events or harms was not specified; therefore, it is unclear whether direct or surrogate measures were used or whether data on all patient-important adverse events or harms were collected.

[h] Serious imprecision.[62] Only a single study and no measures of variability.

[i] One RCT in two publications.[59,60]

[j] Serious risk of bias.[59,60] Selection bias: no indication of allocation concealment. Detection bias: method of measuring adverse events and harms not specified. Reporting bias: no statistical comparisons conducted.

[k] Serious indirectness.[59,60] Method of measuring adverse events or harms was not specified; therefore, it is unclear whether direct or surrogate measures were used or whether data on all patient-important adverse events or harms were collected.

[l] Serious imprecision.[59,60] Only a single study; no adverse events or harms, relatively few secondary surgical interventions (all cataract surgery), and no measures of variability.

[m] In this study, different numbers of iStents (all MIGS) were compared.[59,60]

[n] One retrospective cohort[63] and one non-randomized controlled clinical trial.[61]

[o] Serious risk of bias.[61,63] Bias due to confounding: different surgeons performed ECP and BGI surgery;[63] pseudorandomization (first patient randomized, followed by counterbalanced enrolment);[61] potential confounding variables not controlled for in analyses.[61,63] Bias in selection of participants: only those with two-year complete data were included and it is possible that those with complete data were systematically different from those without complete data (i.e., different from those in routine clinical practice).[63] Bias due to missing data: large loss to follow-up, amount of missing data not balanced across groups, and reasons for missing data not reported.[61,63] Bias in measurement of outcomes: method of measuring adverse events and harms not specified.[61,63]

[p] Serious indirectness.[61,63] Method of measuring adverse events or harms was not specified; therefore, it is unclear whether direct or surrogate measures were used or whether data on all patient-important adverse events or harms were collected.

[q] Serious imprecision.[61,63] No measures of variability.

[r] One retrospective cohort study.[64]

[s] Serious risk of bias.[64] Bias due to confounding: retrospective study and rationale for assigning treatments likely to be different between groups; significant differences between groups at baseline; potential confounding variables not controlled for in analyses. Bias due to deviations from intended interventions: important co-intervention not balanced between groups (number of medications significantly different between groups). Bias due to missing data: large loss to follow-up and reasons for missing data not reported; follow-up duration different between groups (i.e., mean follow-up of 7.4 months and 2.1 months in ECP + Phaco and Phaco alone groups, respectively) leading to a different likelihood of capturing adverse events. Bias in measurement of outcomes: method of measuring adverse events and harms not specified.

[t] Serious indirectness.[64] Method of measuring adverse events or harms was not specified; therefore, it is unclear whether direct or surrogate measures were used or whether data on all patient-important adverse events or harms were collected.

[u] Serious imprecision.[64] Only a single study and no measures of variability.

[v] One retrospective cohort study.[65]

[w] Serious risk of bias.[65] Bias due to confounding: significant differences between groups at baseline; potential confounding variables not controlled for in analyses. Bias in selection of participants: patients with < 1 month follow-up were excluded and it is possible that those with < 1 month follow-up were systematically different from those with ≥ 1 month follow-up (i.e., different from those in routine clinical practice). Bias due to missing data: no information on amount or nature of missing data was reported. Bias in measurement of outcomes: method of measuring adverse events and harms not specified. Bias in selection of the reported result: statistical comparisons not conducted for adverse events or harms.

[x] Serious indirectness.[65] Method of measuring adverse events or harms was not specified; therefore, it is unclear whether direct or surrogate measures were used or whether data on all patient-important adverse events or harms were collected.

[y] Serious imprecision.[65] Only a single study and no measures of variability.