Table 18.1A. GRADE evidence profile comparing assisted partner notification (provider referral) to passive referral

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http://journals.lww.com/aidsonline/fulltext/2017/08240/Improving_HIV_test_uptake_and_case_finding_with.12.aspx
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Question: Should assisted partner notification services (provider referral) be implemented as part of HIV testing services?

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Assisted partner notification (provider referral) versus passive referral	Control	Relative (95% CI)	Absolute		
Uptake of HIV testing among partners (assessed with: HIV testing and return to clinic; meta-analysis using all identified partners as denominators[1])												
3[2]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	152/372 (40.9%)	97/346 (28%)	RR 1.48 (1.22 to 1.8)	135 more per 1000 (from 62 more to 224 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Uptake of HIV testing among partners (assessed with: HIV testing and return to clinic; meta-analysis using locatable partners as denominators[1])												
3[2]	randomised trials	serious[3]	no serious inconsistency[4]	no serious indirectness	no serious imprecision	none	152/260 (58.5%)	97/232 (41.8%)	RR 1.39 (0.93 to 2.06)[5]	163 more per 1000 (from 29 fewer to 443 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Uptake of HIV testing among male partners (assessed with: Visiting clinic for counseling and testing)												
1	randomised trials	serious[6]	no serious inconsistency[7]	no serious indirectness	serious[8]	reporting bias[9]	-	-	Adjusted RR 3.30 (1.59 to 6.85)	-[10]	⨁◯◯◯ VERY LOW	CRITICAL
Uptake of HIV testing among female partners (assessed with: Visiting clinic for counseling and testing)												
1	randomised trials	serious[6]	no serious inconsistency[7]	no serious indirectness	serious[8]	reporting bias[9]	-	-	Adjusted RR 1.50 (0.90 to 2.50)	-[10]	⨁◯◯◯ VERY LOW	CRITICAL
Uptake of HIV testing among main partners (assessed with: Visiting clinic for counseling and testing)												
1	randomised trials	serious[6]	no serious inconsistency[7]	no serious indirectness	serious[8]	reporting bias[9]	-	-	Adjusted RR 2.00 (1.32 to 3.04)	-[10]	⨁◯◯◯ VERY LOW	CRITICAL
Uptake of HIV testing among casual partners (assessed with: Visiting clinic for counseling and testing)												
1	randomised trials	serious[6]	no serious inconsistency[7]	no serious indirectness	very serious[11]	reporting bias[9]	-	-	Adjusted RR 3.90 (0.49 to 31.25)	-[10]	⨁◯◯◯ VERY LOW	CRITICAL
Proportion of partners who tested and were diagnosed HIV positive (assessed with: Meta-analysis using all identified partners as denominators)												
3[2]	randomised trials	serious[3]	no serious inconsistency[12]	no serious indirectness	no serious imprecision	none	88/372 (23.7%)	56/346 (16.2%)	RR 1.47 (1.12 to 1.92)	76 more per 1000 (from 19 more to 149 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Proportion of partners who tested and were diagnosed HIV positive (assessed with: Meta-analysis using all locatable partners as denominators)												
3[2]	randomised trials	serious[3]	no serious inconsistency[13]	no serious indirectness	no serious imprecision	none	88/260 (33.8%)	56/232 (24.1%)	RR 1.49 (1.14 to 1.95)[14]	118 more per 1000 (from 34 more to 229 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Proportion of partners who tested and were newly diagnosed HIV positive (assessed with: Meta-analysis using all locatable partners)												

3	randomised trials	serious[15]	no serious inconsistency	no serious indirectness	serious[16]	none	63/260 (24.2%)	43/232 (18.5%)	RR 1.37 (0.98 to 1.93)[17]	69 more per 1000 (from 4 fewer to 172 more)	⨁⨁◯◯ LOW	CRITICAL
New linkage to care among HIV positive partners												
2	randomised trials	serious[6]	no serious inconsistency[18]	no serious indirectness	serious[19]	none	-	-	Rate Ratio 3.76 (2.41 to 5.86)	-[10]	⨁⨁◯◯ LOW	CRITICAL
Adverse events assessed with Intimate Partner Violence or abandonment using locatable partners as denominator												
3	randomised trials	serious[3]	no serious inconsistency[20]	no serious indirectness	very serious[21]	none	5/807 (0.62%)	2/862 (0.23%)	RR 1.86 (0.37 to 9.5)	2 more per 1000 (from 1 fewer to 20 more)	⨁◯◯◯ VERY LOW	IMPORTANT

[1] Some studies measured actual uptake of HIV testing among partners while others measured return to clinic by partners; we considered these similar enough to merge with the assumption that most partners who returned to the clinics would be expected to uptake HIV testing.

[2] The meta-analysis included three RCTs: Brown et al., 2011 (general population in Malawi); Landis et al., 1992 (general population in the United States, but 35% of participants reported intravenous drug use and 76% of male participants reported bisexuality or homosexuality); Rosenberg et al., 2015 (women attending ANC and male partners in Malawi). Cherutich et al. 2016 (a cluster RCT of the general population in Kenya) also measured this outcome but presented the results as Incidence Rate Ratios accounting for the clustering.

[3] Risk of Bias: Down-graded once. Studies were generally considered low or uncertain risk of bias across measures; most uncertainty was due to non-reporting of risk of bias measures. We observed a high risk of bias due to the lack of blinding across studies which may have introduced performance bias as staff and participants may have been influenced by group allocation; detection bias was rated as unclear in most studies as returning partners were given coded cards, but it is not clear if the group allocation was identifiable in those cards; if so, staff recording the outcome of return may have been influenced by this knowledge. In Landis 1992, attrition (defined as proportion of identified partners who were located) was high (59%); for Brown overall attrition was 16% and for Rosenberg the proportion of identified partners who were located was only provided for those partners in the contact tracing arm (12%). Due to the potential for risk of performance bias in all three trials, and the high attrition in Landis, we downgraded once for risk of bias.

[4] When the denominator of locatable partners was used the meta-analysis showed high heterogeneity (Chi squared = 8.34; df = 2; p = 0.02 and I squared 76%). This is likely to be driven by Landis. This may be due to the difference in study populations compared to the African studies (Brown and Rosenberg) or the difference in the interventions and timing of the trial which was conducted more than 20 years prior to Brown and Rosenberg. Given the potential for explaining the heterogeneity on these grounds, we did not mark down for indirectness.

[5] Cherutich et al., 2016 reported on this outcome. The number of partners tested in the immediate PN arm was 392/550 (rate per index=0.713) and in the delayed arm was 85/569 (rate per index=0.1049). Accounting for clustering in the study design, an IRR comparing immediate to delayed arm was 4.83 (95% CI: 3.66, 6.39). A combined meta-analysis was conducted using the generic inverse variance (GIV) to allow combination with relative risks from the other studies and to account for clustering in the Cherutich et al., 2016 study as the trials seemed similar enough to combine methodologically and clinically, However, a large statistical heterogeneity driven by the cluster-randomized trial could not be explained, so this trial was removed from the overall analysis. However, results go in the same direction with an overall RR = 1.91 (95% CI: 0.93; 3.93) I2 = 95%).

[6] Risk of Bias: We marked down once for risk of bias due to the lack of blinding and risk of performance and detection bias.

[7] Inconsistency: Not downgraded but noted that this is a single study only and consistency is not applicable.

[8] Imprecision: Down-graded once. The 95% Confidence Interval is wide and the event rate very low at less than 62 (the number of events in the trial overall; the numbers for the sub-groups are not provided, only the % of events within the groups).

[9] The results are from a sub-group of a single study and should be treated with caution.

[10] Cannot be calculated as adjusted estimate entered using the Generic inverse variance data option.

[11] Imprecision: Down-graded twice. The 95%CI is extremely wide.

[12] Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.14$, df = 2 (P = 0.93); $I^2 = 0\%$.

[13] Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.87$, df = 2 (P = 0.65); $I^2 = 0\%$

[14] Cherutich et al., 2016 reported on this outcome. The number of partners diagnosed with HIV in the immediate PN arm was 392/550 (rate per index=0.713) and in the delayed arm was 85/569 (rate per index=0.1049). Accounting for clustering in the study design, an IRR comparing immediate to delayed arm was 4.83 (95% CI: 3.66, 6.39). A combined meta-analysis was conducted using the generic inverse variance (GIV) to allow combination with relative risks from the other studies and to account for clustering in the Cherutich et al., 2016 study as the trials seemed similar enough to combine methodologically and clinically, However, a large statistical heterogeneity driven by the cluster-randomized trial could not be explained, so this trial was removed from the overall analysis. However, results go in the same direction with an overall RR = 1.91 (95% CI: 0.93; 3.93) I2 = 95%).

[15] Risk of Bias: Down-graded once. Studies were generally considered low or uncertain risk of bias across measures; most uncertainty was due to non-reporting of risk of bias measures. We observed a high risk of bias due to the lack of blinding across studies which may have introduced performance bias as staff and participants may have been influenced by group allocation; detection bias was likely to be low as outcome of new HIV diagnoses were likely to be done in a laboratory. In Landis 1992, attrition (defined as proportion of identified partners who were located) was high (59%); for Brown overall attrition was 16% and for Rosenberg the proportion of identified partners who were located was only provided for those partners in the contact tracing arm (12%). Due to the potential for risk of performance bias in all three trials, and the high attrition in Landis, we downgraded once for risk of bias.

[16] Imprecision: Down-graded once. The 95% CI is wide and crosses the line of no effect and appreciable benefit.

[17] Cherutich et al., 2016 reported on this outcome. The number of partners newly diagnosed with HIV in the immediate PN arm was 136/550 (rate per index=0.247) and in the delayed arm was 28/569 (rate per index=0.049). Accounting for clustering in the study design, an IRR comparing immediate to delayed arm was 5.00 (95% CI: 3.18, 7.86). A combined meta-analysis was conducted using the generic inverse variance (GIV) to allow combination with relative risks from the other studies and to account for clustering in the Cherutich et al., 2016 study as the trials seemed similar enough to combine methodologically and clinically, However, a large statistical heterogeneity driven by the cluster-randomized trial could not be explained, so this trial was removed from the overall analysis. However, results go in the same direction with an overall RR = 1.97 [0.91, 4.24].

[18] Inconsistency: Statistical heterogeneity was low ($Chi^2 = 1.48$, df = 1 (P = 0.22); $I^2 = 33\%$).

[19] Imprecision: Down-graded once. The 95% CI is very wide. This is a sub-group analysis of the whole sample and should be viewed with caution.
[20] Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.17$, df = 2 (P = 0.56); $I^2 = 0\%$
[21] Imprecision: Down-graded twice. The 95% CI was very wide and the event rate was very small (8 overall).