**Table S1:** Quality scores of observational studies in the meta-analysis based on NOS scoring system

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Study ID | Study Type | Selection | Comparability | Outcome/Exposure | Total Scores |
| Oltmanns2014 | Cohort | ★★★★ | ★ | ★★ | 7 |
| Bonella2013 | Cohort | ★★★★ | ★ | ★★ | 7 |
| Mao2018 | Cohort | ★★★★ | ★ | ★★★ | 7 |
| Ma2018 | Cohort | ★★★★ | ★★ | ★★ | 8 |
| Sakamoto2014 | CC | ★★★ | ★ | ★★ | 6 |

Abbreviations: NOS: Newcastle-Ottawa quality assessment scale, Cohort: Cohort study, CC: Case-control study



**Figure S1** Forest plot of efficacy profile (outcomes: the predicted decline in FVC% (Figure S1-a) and DLco% (Figure S1-b)) between the combined pirfenidone and acetylcysteine group and the pirfenidone alone group with only oral NAC studies. FVC: forced vital capacity, PFD: pirfenidone, NAC: N-acetylcysteine.



**Figure S2** Forest plot of the safety profile (outcome measure: at least one side effect, Figure S2-a) and tolerability profile (outcome measure: intolerable side effects leading to treatment discontinuation, Figure S2-b) between the combined pirfenidone and acetylcysteine group and the pirfenidone alone group with only oral NAC studies. PFD: pirfenidone, NAC: N-acetylcysteine.



**Figure S3** Forest plot of the specific safety profile (outcome measure: gastrointestinal side effects (Figure S3-a) and skin side effects (Figure S3-b)) between the combined pirfenidone and acetylcysteine group and the pirfenidone alone group with only oral NAC studies. PFD: pirfenidone, NAC: N-acetylcysteine.