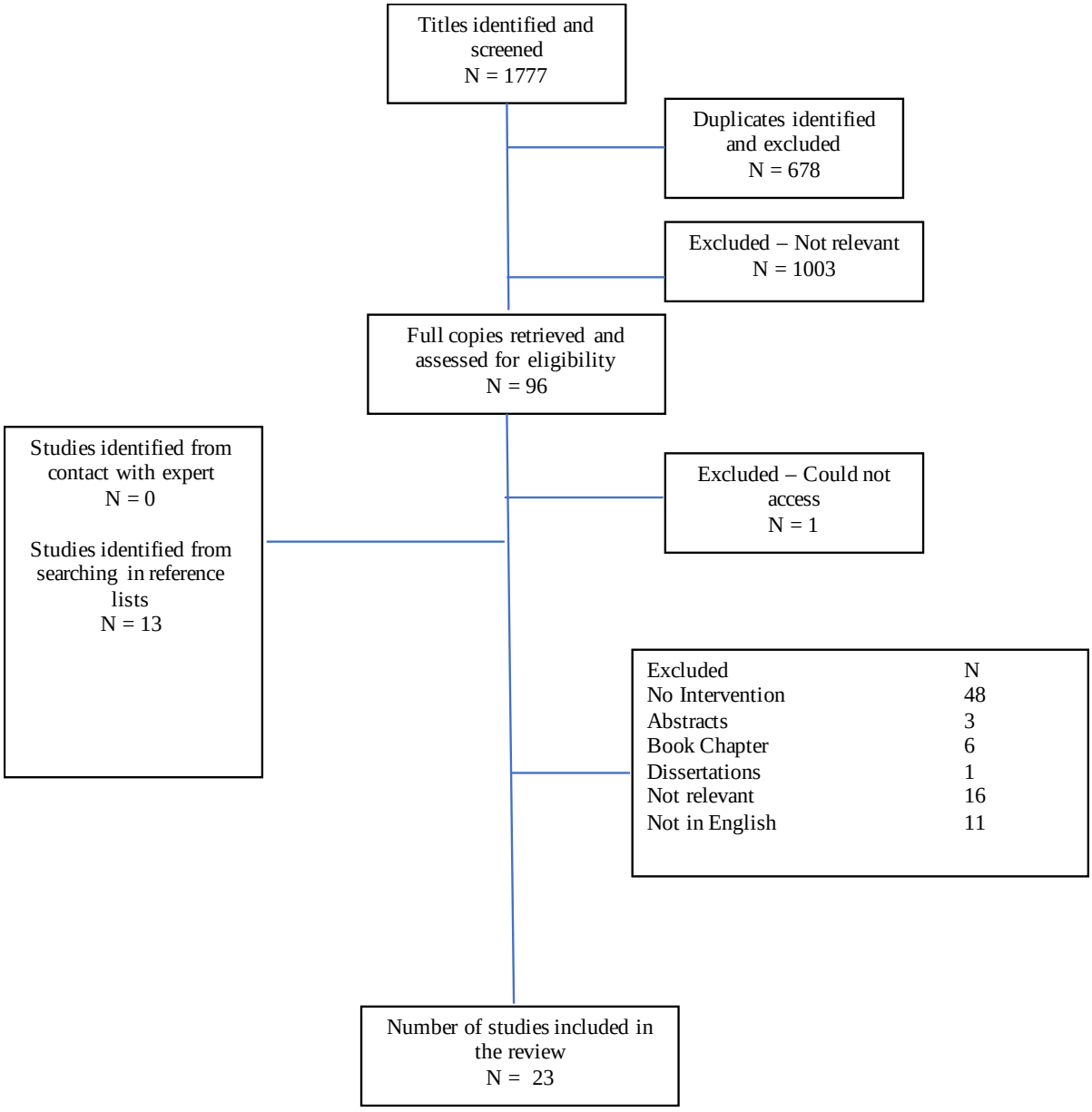
Online Supplement 1. Flow Diagram.



Online Supplement 2. Summary of Quantitative Findings.

Treatment outcomes for the quantitative studies investigating OD are summarised below. Studies are of low quality and high risk of bias which precludes conclusions about efficacy and further studies are required to evaluate the potential efficacy of OD. Findings have been grouped by service user outcomes, including hospitalisation, use of antipsychotic medication and incidence rates.

Therapeutic Outcomes

Symptom reduction.

Interpretation of the evidence from Seikkula and colleagues is hindered by the absence of randomisation methods, limited control group data and comparison of groups which all received some form of OD. An initial study (1) divided results into 'poor' and 'good' outcome groups where the entire sample received OD. The authors defined poor versus good outcomes based on occupational status and level of residual psychotic symptoms rated on the Strauss and Carpenter Scale (2) at two-year follow up. This study reports baseline data using the Brief Psychiatric Ratings Scale (BPRS; (3) and Global Assessment of Function Scale (GAF; (4), however, no follow-up data for the BPRS and GAF are reported. The authors concluded that the data's "bearing on the effectiveness of OD is encouraging" given that only 22% of service users were identified as having a poor outcome. The design of this study did not include a control group. The ratings of psychotic symptoms, and diagnosis (a key inclusion criteria) were scored jointly by the treatment team and the authors. The authors are noted as not being involved in the treatment process.

A second study (5) reported on outcomes of the API and ODAP1 groups compared to a small control group (N=14). The ODAP1 group showed a significant reduction in residual

psychotic symptoms when compared to the control group. The significance level of the comparison between the API group and control group is not reported. The API group was found to have a higher mean BPRS score than both the ODAP1 and control group, however this is accounted for by two possible outliers. The difference between the ODAP1 and API groups on the BPRS is reported as significant, the statistical outcome of the analysis of the API and ODAP1 groups against the control group is not reported.

Comparisons across API, ODAP1 and ODAP2 groups

The five-year follow-up data (6) from the API and ODAP1 groups did not report the control group data. The API and ODAP1 groups were compared to each other as the API group is described as an earlier phase in the development of OD. The authors describe the that the ODAP1 group recovered faster than the API group due to a significant reduction in symptoms on the BPRS at 2-years however these differences were not seen at the 5-year follow-up. The authors do not raise, as they did previously, the possibility of outliers driving this effect. The study reports that 82% in the ODAP1 and 72% in the API groups reported no residual psychotic symptoms at five-years. Both groups received OD, however as previously mentioned the API group received an earlier 'phase of OD' and there is no control group. A long-term follow-up study (7) found that although the ODAP2 group showed an improvement in symptoms on the BPRS at two-years, the improvements were not as large as those shown in the ODAP1 group at this time point. More than 80% of service users (API, ODAP1 and ODAP2) in the study had no remaining psychotic symptoms at two-years. The authors suggest that OD results in a reduction of symptoms, however it is important to note that the API, ODAP1 and ODAP2 groups all received OD in some form. Findings, while promising, are preliminary and evidence is of a low quality, and warrants further investigation.

Regions outside of Western Lapland

More recently, the Collaborative Pathway study (8) reported a significant positive change in psychotic symptoms and functioning as measured by the Revised Behavior and Symptom Identification Scale, and Strauss-Carpenter Level of Function Scale. Granö and colleagues (9) reported on suicidal ideation rates of 130 adolescent service users completing OD-informed treatment. A significant reduction in rates of suicidal ideation on a single item measure (item nine on the Beck Depression Inventory II; (10) in around 50% of the sample was reported with an average treatment length of around nine months. No control group was included in this study, and the analysis did not adjust for history of suicidality. The reduction in suicidality positively correlated with a change in auditory distortions and paranoia measured on the PROD screen (11).

Recent systematic reviews evaluating remission rates in psychosis note that as few studies use similar outcome measures it is difficult to define remission and recovery, and report estimated remission rates for schizophrenia ranging from 6% to 52% (12, 13). Again, this compounds the issues of interpreting findings of symptom reduction in the context of OD treatment without a control group and further investigation is needed. Additionally, duration of untreated psychosis (DUP) is predictive of improved remission rates in psychosis (14). It is important to consider that remission rates in these studies may reflect a high proportion of individuals with a relatively short DUP.

Antipsychotic medication use.

One principle of OD is to avoid the use of antipsychotic medication at the initial assessment and only if there is no improvement, antipsychotic medication is prescribed (5). The reviewed

studies suggest that this occurs in practice. At the original trial site, Seikkula and colleagues (1) describe significant differences between two groups, where all service users received OD, (defined by the authors as 'poor' versus 'good' outcomes) at two-years with fewer participants in the 'good outcomes' group starting antipsychotic medication. The authors suggest that the use of antipsychotic medication can be decreased in context of OD treatment without increasing the risk of poor outcomes (1, 15). At a two-year follow-up (5) there were significant differences in antipsychotic use between the API and ODAP1 samples and a small non-randomly allocated control group. Long-term follow up data (16) reported that antipsychotic treatment was used in 26% of cases at initial contact, and 55% of cases over the entire study period. The authors report that 71% of those who received antipsychotic medication at the start of treatment (n=17) were still on medication in 2015, which is between 10 and 23 years from initial entry. An important limitation of these findings is that the use of medication across the original Western Lapland studies were likely influenced by the varied nature of individual presentations across each treatment group. These studies included a range of presentations; non-specified psychosis, brief psychotic episode (BPE), schizophrenia, and schizophreniform (DSM III and DSM IV criteria) which is not adjusted for in the interpretation of these findings.

Regions outside of Western Lapland

Data from the Collaborative Pathway study (8) show that eight (57%) out of 14 service users entered OD treatment on antipsychotics, and, of these, four service users stopped medication during the study, and a further three participants of the six previously not on medication started on antipsychotics during the trial. A second US-based study (17) reported on anecdotal evidence, which suggested that from a clinician's perspective service users showed increased acceptance of medication and treatment plan changes. In summary, in line with the API project's initial aims, relatively low rates of antipsychotic medication were observed

across three studies (5, 6, 18). Interpretation of these findings is complex as the protocol of the study included that antipsychotic medication was not started within the first three weeks after admission whenever possible, and treatment was only started if there was no improvement in symptoms (19). The delay in starting antipsychotic use is therefore a feature of the intervention as opposed to an outcome of OD. No information is given regarding other types of medication used.

Overall, without a control group it is not possible to draw clear conclusions about antipsychotic use from these data and little evidence exists outside of the original OD project in Western Lapland that suggests antipsychotic use is reduced in OD treatment.

Hospitalisation admission rates and duration of stay.

Hospital admission and re-admission rates were a commonly used outcome in the reviewed studies. Seikkula and colleagues consistently reference lower than expected rates of hospitalisation to be associated with OD, however OD is only ever compared in a to a small comparison group (n=14) in a single study (5). In another study (30), the authors discuss the mean length hospitalisation in ODAP1 groups in the context of the outcomes of a completely separate Sweden-based study (20), which the authors suggest as a treatment as usual (TAU) comparison for mean hospitalisation stay (ODAP= 17, TAU= 110). The aim of OD is to reduce hospitalisation and deliver treatment in the community and therefore low hospitalisation rates are expected to be associated with the treatment. When considering the low hospitalisation days reported it is important to consider that this may be tied to the explicit aim of the system change to reduce hospitalization. This is contrasted to a more packaged version of OD which does not explicitly aim to reduce hospitalisation as part of the

system redesign but rather uses this as a measurement of treatment outcome. It is important to clarify between intervention characteristics and outcomes.

A further Finish-based study (21) reports a reduction in long-term hospital admissions in an analysis that included cases from two periods, a historical control group using pre-OD period (1985 to 1989) and a post OD period (1990 to 1994.) However, it is not clear whether this analysis included some of the cases used in the sample for previous studies (1, 5, 6, 18). Furthermore, the authors (21) refer to 1990 to 1994 as a period when OD was in full operation, a period previously referred to as 'pre-open dialogue approach'. The API project took place between 1 April 1992 and 31 January 1993. A study (19) reporting long-term follow up data from 10-23 years for the samples API, ODAP1 and ODAP2, with no control group, concludes that the majority of service users were treated with only one hospital admission, or with no hospital treatment (54%), and 95% spent less than a year as an inpatient over the entire period.

Regions outside of Western Lapland

The Collaborative Pathway (8) feasibility study reports one-year outcomes for 14 out of 16 service users and shows that four individuals (25%) had short term hospitalisations, however duration of stay was not reported. Rosen and Stoklosa (17) interviewed 20 staff and 30 service users and reported positive outcomes, including increased voluntary over involuntary admissions and reduced use of restraint. Interpretations of these findings are limited by small sample sizes and lack of control group data.

Although authors from all of these studies purport that OD is associated with low rates of relapse, few hospital admissions, and short hospital stays it is not possible to confirm these

conclusions because of the descriptive nature of these studies. Further research is needed to address this question.

Incidence rates across the Western Lapland sites.

One of the more contentious claims in relation to the evidence for OD is that it may reduce the incidence of psychosis in the region where it was established. An examination of the data suggests these statements are not as solid as some may claim (22, 23). It seems that the positive increase in early intervention has improved access to treatment at the prodromal stage which may in turn reduce conversion to schizophrenia. This is not the same as a reduction in overall incidence but rather reclassification of diagnosis. Aaltonen and colleagues (21) report incidence data based on the re-categorisation of service users' diagnoses from progress notes. It is not clear why the authors present data which were re-categorised post-hoc rather than original diagnosis rates (see Table 5). The authors state these outcomes suggest that the introduction of OD has not only had an impact on changing the pattern of diagnosis rates in the region but also the populations relationship with psychiatric services. However, the conclusions drawn from this analysis are not supported by the data. Furthermore, it highlights that across each treatment cohort in the original Western Lapland sites, API, ODAP1 and ODAP2, incidence rates indicate clear differences in the duration and severity of the patient presentations across the samples (see Table. 5). The authors do not address potential issues around the incomparability of the participants within each cohort.

Online Supplement 3. Summary of findings from the Quantitative Studies on OD in Finland

Table 3. Results for antipsychotic medication use, relapse, occupational status and individual therapy as published across original Open Dialogue studies.

	Seikkula et al. (1)				Seikkula et al. (5)						Seikkula et al. (6)								Seikkula et al. (18)					
	Outcome				2-year follow-up						2-year follow-up				5-year follow-up				2-year follow-up					
	Poor		Good		Comparison		API		ODAP1		API		ODAP1		API		ODAP1		API		ODAP1		ODAP2	
	N=17		N=61		N=14		N=22		N=23		N=33		N=23		N=33		N=42		N=33		N=42		N=18	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Antipsychotic medication started	8.9*	53	12*	20	14*	100	8*	36	8*	34	9	26	12a	26	10	30	8	19	9	26	12	26	9	50
Antipsychotic medication ongoing	--	--	--	--	10	71	5	18	4	17	5	15	5a	11	8	24	7	17	5	15	5	11	5	28
No. of Relapse Cases	--	--	--	--	10	71	8	36	6	26	9	27	8	17	11	32	8	19	15	26	8	17	5	28
Studying or working	9*	52	52*	85	3	21	13	59	65	65	21a	62	35a	78	23	70	32	76	21	62	35	78	13	72
Unemployed	2	12	6	10	3	21	1	4	6	26	4a	12	6a	13	1	3	4	10	4	12	6	13	2	12
Disability Allowance	6	35	3	5	8	57	8	36	2	9	9a	26	4a	9	10	27	6	14	9	26	4	9	4	16
Individual Psychotherapy	--	--	--	--	8	57	11	54	11	47	12a	33	21a	46	14	42	14	33	12	33	21	46	12	67

Number of participants (N), API includes cases 1 April 1992 -31 December 1993; ODAP incudes cases 1 January 1994 to 31 March 1997; ODAP2 includes cases 1 February 2003 to 31 December 2005; a= different sample size included in analysis (API n=34; ODAP1 n=46), * indicates that differences between groups on the measure were reported as statistically significant. – indicates that results on this variable could not be found in published literature; Brief Psychiatric Ratings Scale (BPRS); Global Assessment of Function Scale (GAF)

Table 4. Results for hospitalisation, number of meetings, symptom and function as published across original trial OD project in Western Lapland.

	Seikkula et al. (29)				Seikkula et al. (5)						Seikkula et al. (6)								Seikkula et al. (18)					
	Outcome				2-year follow-up						2-year follow-up				5-year follow-up				2-year follow-up					
	Poor		Good		Comparison		API		ODAP1		API		ODAP1		API		ODAP1		API		ODAP1		ODAP2	
	N=17		N=61		N=14		N=22		N=23		N=33		N=23		N=33		N=42		N=33		N=42		N=18	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Hospitalisation Days	47.5*	56	9	19.2	116.9	102.2	35.9*	44.0	14.3*	25.0	25.7*	44.2	9.3*	18.3	16.7	40.4	7.4	35.5	25.7*	44.2	9.3*	18.3	13.6*	27.8
No. of Family Meetings	--	--	--	--	8.9*	6.2	26.1*	14.1	20.1*	20.6	26.1	14.1	20.7	20.6	10.6*	16.3	3.8*	7.9	26.1	14.1	20.7	20.6	23.3	19.2
BPRS (lower = better)	49.1	11.9	43.5	15.5	--	--	--	--	--	--	47.2	12.8	46.1	9.4	47.2	12.8	46.4	9.4	47.4	12.5	48.8	12.2	52.1	9.8
BPRS Follow-up	--	--	--	--	26.5	7.1*	32.3	13.7*	24.9	5.2*	30.2	12.9*	23.7	4.5*	23.1	5.4	24.6	8.8	30.2	12.9	23.7	4.5	28.5	8.8
Residual Base-line	--	--	--	--	3.2	1.9	3.5	0.51	3.3	0.69	3.21	0.64	2.98	.80)	3.21	0.64	2.98	0.8	3.21	0.64	2.98	0.8	1.56	0.64
Residual 2-years	--	--	--	--	1.9	1.5	0.9	1.1	0.6	0.99	0.5	0.9	0.3	.70)	0.39	0.79	0.35	0.86	0.5	0.9	0.3	0.7	0.17	0.38
GAF (higher = better)	35.5	10.7	35.6	12.3	4.2	0.89	3.2	0.8	2.8	0.64	--	--	--	--	--	--	--	--	--	--	--	--	--	--
GAF 2-years	--	--	--	--	4.9	1.6	5.8	1.6	5.7	1.3	--	--	--	--	--	--	--	--	--	--	--	--	--	--

Number of participants (N), API includes cases 1 April 1992 -31 December 1993; ODAP incudes cases 1 January 1994 to 31 March 1997; ODAP2 includes cases 1 February 2003 to 31 December 2005; a= different sample size included in analysis (API N=34; ODAP1 N=46), * indicates that differences between groups on the measure were reported as statistically significant. – indicates that results on this variable could not be found in published literature; Brief Psychiatric Ratings Scale (BPRS); Global Assessment of Function Scale (GAF), M mean; SD +/- standard deviation

Table 5. Diagnosis rates across original treatment groups for the OD project in Western Lapland.

	Seikkula et al. (1)				Seikkula et al. (9)						Seikkula et al. (30)				Seikkula et al. (31)						Aaltonen et al. (21)				Bergström et al. (19)			
	Outcome				2-year follow-up						2 & 5-yearr follow up				2-year follow up						No of new cases							
	Poor		Good		Comparison		API		ODAP1		API		ODAP1		API		ODAP1		ODAP2		1985-1989		1990-1994		Included		Excluded	
	N=17		N=61		N=14		N=22		N=23		N=33		N=42		N=33		N=42		N=18		N=139		N=111		N=65		N=33	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Non-Specified Psychosis	0	0	16	26	--	--	--	--	--	--	7 a	12	10a	22	7	12	10	22	4	22	59	42	10	9	--	--	--	--
Brief Psychotic Episodes	0	0	17	28	--	--	--	--	--	--	5	15	11	24	5	15	11	24	7	39	3	2	14	14	15	23	5	15

Schizophrenia	15	88	17	28	8	57	13	59	19	83	13	38	19	41	13	38	19	41	4	22	59	42	22	22	10	15	16	49
Schizophreniform	2	11	11	18	6	43	9	41	4	17	9	26	6	13	9	26	6	13	3	17	14	10	14	14	13	20	5	15
Prodromal	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	51	37	39	40	27	42	7	21

Number of participants (N), API includes cases 1 April 1992 -31 December 1993; ODAP incudes cases 1 January 1994 to 31 March 1997; ODAP2 includes cases 1 February 2003 to 31 December 2005; a= different sample size included in analysis (API N=34; ODAP1 N=46), Bergström et al. (16) sample size for each group included API N=39, ODAP1 N=50, ODAP2 N=27

Online Supplement 4. References

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