Title:

Effectiveness of psychoeducational interventions for family carers of people with psychosis: A systematic review and meta-analysis

Short title: Psychoeducation for psychosis family carers

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Abstract:
Psychoeducational interventions for family carers of people with psychosis are effective for improving compliance and preventing relapse. Whether carers benefit from these interventions has been little explored. This systematic review investigated the effectiveness of psychoeducation for improving carers' outcomes, and potential treatment moderators. We searched for randomised controlled trials (RCTs) published in English or Chinese in eight databases. Carers' outcomes included wellbeing, quality of life, global morbidities, burden, and expressed emotion. Thirty-two RCTs were included, examining 2,858 carers. Intervention duration ranged from 4 to 52 weeks, and contact times ranged from 6 to 42 hours. At post intervention, findings were equivocal for carers' wellbeing (SMD 0.103, 95% CI -0.186 to 0.392). Conversely, psychoeducation was superior in reducing carers' global morbidities (SMD -0.230, 95% CI -0.386 to -0.075), perceived burden (SMD -0.434, 95% CI -0.567 to -0.31), negative caregiving experiences (SMD -0.210, 95% CI -0.396 to -0.025) and expressed emotion (SMD -0.161, 95% CI -0.367 o -0.045). The lack of available data precluded meta-analysis of outcomes beyond short-term follow-up. Meta-regression revealed no significant associations between intervention modality, duration, or contact time and outcomes. Further research should focus on improving carers' outcomes in the longer-term and identifying factors to optimise intervention design.

Keywords: Psychoeducation – family – carers – informal caring/caregiving – psychosis – systematic review

Introduction

Psychoeducational interventions, generally defined as information provided about a condition and its management, are proven to be effective for improving compliance in psychosis, and in reducing relapse (National Institute for Clinical Excellence (NICE), 2014; Xia, Merinder, & Belgamwar, 2011). Psychoeducation is commonly delivered via individual or group programmes, and involves clinicians taking on the role of information-provider, and patients and family carers as participants (Sin, Jordan, Barley, Henderson, & Norman, 2015; Sin & Norman, 2013; Xia et al., 2011). More recently, interventions delivered via eHealth (internet-based) or mHealth (using mobile apps) have also garnered increasing interest and usage, perhaps augmenting conventional face-to-face formats (Alvarez-Jimenez et al., 2014; Cavanagh et al., 2006; Chi & Demiris, 2015; Glynn, Randolph, Garrick, & Lui, 2010; Proudfoot et al., 2004; Sin, Henderson, & Norman, 2014; Sin, Moone, Harris, Scully, & Wellman, 2012). Multi-component programmes, which comprise peer support and discussion with others in a similar position, information about coping strategies and problem solving techniques for common illness-management or care-related issues, have become increasingly popular (Gillard, Gibson, Holley, & Lucock, 2015; Lobban, Postlethwaite, et al., 2013; Sin, Moone, & Newell, 2007; Sin, Moone, & Wellman, 2005; Sin & Norman, 2013; Xia et al., 2011). Involvement of family carers in psychoeducational interventions, with or without patients, has been identified as a pivotal mechanism for promoting patients' outcomes (NICE, 2010; Xia et al., 2011; Yesufu-Udechuku et al., 2015). In general, it is hypothesised that the effectiveness of psychoeducation is contingent on carers' knowledge about psychosis, their cognitive appraisal about the caring situation, and subsequently, their perceived burden and (self-efficacy in) coping with caring (Bandura, 1977a, 1977b, 1988; Birchwood, Smith, & Cochrane, 1992; Lazarus & Folkman, 1984).

Carers' perceived burden and appraisal about their ability to manage the caring for a loved one with psychosis, are well established as being highly correlated with their wellbeing and global morbidities (Guerriero Austrom et al., 2015; Kuipers, 2010; Kuipers & Raune, 2000; Smith et al., 2014). That is, the burden of caring can incur clinically significant levels of stress and distress in carers themselves, increasing vulnerabilities to both physical and mental health morbidities. Furthermore, studies have identified that carers' wellbeing is associated with their caregiving capacity; that is, poorer wellbeing affects propensity to provide adequate support, which in turn is believed to be influential in shaping patients' prognosis and relapse rates (Johnson et al., 2000; Kuipers, Onwumere, & Bebbington, 2010; Smith et al., 2014). Based on the stress-appraisal-coping theory as applied in family caregiving (Lazarus & Folkman, 1984; Lazarus, 1966; Szmukler, 1996; Szmukler et al., 1996), it has long been hypothesised that psychoeducation, with education as its core features and prime aim, works directly in

improving carers' knowledge about psychosis and related caregiving issues. Improved knowledge about coping strategies and resources can lead to a more positive appraisal of their caregiving experiences as well as carers' own self-efficacy in coping with the demands. These, in turn, can translate into decreases in perceived burden and global morbidities (Joyce et al., 2003; Joyce, Leese, & Szmukler, 2000; Szmukler, 1996). It is possible that these caregiving-related outcomes would mediate into better carers' wellbeing and quality of life (Joyce et al., 2003; Kuipers et al., 2010; Martens & Addington, 2001; Szmukler, 1996). However, little is known about the specific impact of such interventions on family carers' outcomes, potentially because: (1) carers' outcomes are often reported as secondary to those of patients in trials, despite carers often being the sole participants (Sin et al., 2015; Sin & Norman, 2013; Xia et al., 2011); (2) most carers are not recipient of health and/or social care services, and hence their needs are not considered to take priority (Kuipers, 2010); and (3) the significant heterogeneity of interventions tested and broad-ranging carer-outcome measures used, rendering pooling of data for meta-analysis difficult (Lobban, Postlethwaite, et al., 2013; Miyar & Adams, 2013; Sin & Norman, 2013).

While previous systematic reviews on psychoeducation have been undertaken, none of these have solely included randomised controlled trials (RCTs), nor sought to undertake meta-analyses on carers' outcomes (Lobban, Postlethwaite, et al., 2013; Sin et al., 2015; Sin & Norman, 2013). The current systematic review had two aims:

(1) to assess the effectiveness of psychoeducation on family carers' wellbeing, health morbidities, and caregiving-related outcomes; and
(2) to identify intervention-factors (such as intervention duration, contact time, and different modes of delivery), which may moderate intervention effectiveness. Understanding these factors further is likely to enhance the development of more targeted interventions.

Method

We published the review protocol in PROSPERO (International Prospective Register of Systematic Reviews) (Sin et al., 2016). The review process followed PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman, & Group, 2009).

Search Strategy

We followed the search strategy originally developed for our earlier review (Sin & Norman, 2013). Key search terms were devised using the Cochrane Schizophrenia Group and Central Register of Controlled Trials (CENTRAL), synonyms for "schizophrenia", "psychosis" and "psychoeducation* intervention*", in combination with free text to maximise the

sensitivity of the search. We searched for RCTs published from the date of inception to 31st May 2016 in eight databases: MEDLINE (via Ovid); PsycINFO; CINAHL; EMBASE; Cochrane Reviews Library; CENTRAL; Web of Science and ASSIA. In addition, the reference lists of all included studies and of relevant existing systematic reviews were checked for further possible studies. Authors of studies screened were contacted for information regarding unpublished data and ongoing trials.

Inclusion and exclusion criteria

In order to extract data for meta-analyses and meta-regression, only RCTs (including cluster and crossover trials) were eligible. We included studies which investigated psychoeducational interventions which primarily aimed to provide information about illness and symptom management, involved interaction between information providers and participants, and were delivered via any modalities or a combination of modalities (Sin et al., 2016; Sin & Norman, 2013). We included interventions which were professionally-led, although those which involved co-facilitation from a family carer or other lay-person were not excluded. Pure bibliotherapy, and treatment programmes that solely relied on educational materials (such as booklets or non-interactive websites), but which comprised no actual interaction, were excluded. Considering that psychoeducational interventions commonly aim to change complex behaviours and attitudes, we excluded interventions that had a duration shorter than 4 weeks, but imposed no upper limit on intervention duration.

The population studied was informal or family carers of any age (excluding paid, professional or formal carers), of individuals affected by psychosis however defined and treated in any setting. Family carers could be either biologically (e.g. parents, siblings) or non-biologically (e.g. spouses, close friends) related to the patients. Carers could attend the interventions with or without the patients.

Comparators reported in the control arms were categorised into two types:
(1) inactive controls which included waitlist, standard, usual care and/or 'attention-control'; and;
(2) active controls which comprised alternative active interventions targeting family carers, other than psychoeducational in principle, whose content, mode of delivery and design were clearly described. Examples of active controls included cognitive behavioural therapy, counselling, or family intervention.

Study selection, data extraction and risk of bias assessment

Initial screening of study titles, abstracts and full text articles was undertaken by two authors (JS and DS) independently and in parallel. Data extraction from included papers was also undertaken by JS and DS independently, and reviewed by VC and TC as required. The Cochrane Collaboration risk of bias tools for RCTs (Higgins & Green, 2011) were used to assess quality of studies and evidence, again by JS and DS independently. At each stage, the whole review team reviewed the searches, abstract and full-text screening, and data extraction results. We resolved uncertainties through: (1) seeking additional data or clarification from trialists when possible; and (2) review team discussion and consensus.

Outcomes and measures

The primary outcome measures were the standardised mean difference (SMD) in three carers' outcome domains: wellbeing; quality of care; and their proxy measures such as stress, global morbidities (including poor physical and/or psychological health), and depression. Secondary outcomes focused on common caregiving-related outcomes such as: positive and negative appraisals of caregiving experiences; perceived burden; 'expressed emotion' (commonly measured as hostility and criticism towards the patient) (Bebbington & Kuipers, 1994; Brown, Monck, Carstairs, & Wing, 1962; Kuipers & Raune, 2000; Raune, Kuipers, & Bebbington, 2004); family functioning, perceived social support, and knowledge. Only data from validated outcome measures were included in the meta-analysis and meta-regression. Outcome data were grouped according to the following time points: end of intervention; up to 6-month follow up; longer than 6-month but up to 12-month follow up; and over 12-month follow up. For outcomes measured at several time points within these intervals, we reported the analyses separately.

Analysis strategy

The analysis began with an overview of study characteristics followed by tabulation of extracted data, in STATA version 13 [StataCorp. 2013. *Stata Statistical Software: Release 13*]. In addition to conducting overall analyses comparing psychoeducational interventions with all comparators pooled together, we also conducted separate comparisons on psychoeducational interventions with all inactive controls pooled together, then proceeded to compare psychoeducational interventions against active controls grouped together according to their shared modalities whenever there were sufficient data extracted from the included studies. Considering the outcomes were measured with different validated scales, we therefore calculated standardised mean difference (SMD) and 95% confidence interval (CI) for continuous outcomes; and, risk ratio (RR) and its 95% CI for dichotomous data (Egger, Smith, & Altman, 2001; Higgins & Green, 2011); using the random effects model (Higgins & Green, 2011). Statistical heterogeneity was quantified using the I-squared (I^2)

statistic (Higgins, Thompson, Deeks, & Altman, 2003). We interpreted I^2 values around 50% or above as evidence of substantial levels of heterogeneity. When heterogeneity was identified, we explored reasons for the inconstancy through pre-specified subgroup analysis. In general, the magnitude of SMD is interpreted as follow: small = 0.2; medium = 0.5; large ≥ 0.8 (Egger et al., 2001; Higgins & Green 2011). Moreover, the effect size should be interpreted within the context of overall quantity (such as number of studies and participants) and quality (such as methodological quality of studies and heterogeneity across studies) of the data included in the meta-analysis.

We also undertook meta-regression to investigate intervention-factors, namely: treatment contact time (in terms of hours as continuous measures); treatment duration (in terms of weeks as continuous measures); and the modes of delivery using group or individual format (as categorical measures), when data from at least eight studies were available (Higgins & Thompson, 2004). Such intervention-level factors were identified from published systematic reviews about psychoeducational interventions (Lobban, Postlethwaite, et al., 2013; NICE, 2010; Sin et al., 2015; Sin & Norman, 2013; Xia et al., 2011), and were derived from theories or conceptual frameworks underpinning these interventions.

Results

The database search resulted in 8141 records; of these 46 papers of 32 studies met all inclusion criteria and were included in this review (See Figure 1 for the PRISMA flowchart and Table 1 for a summary of included studies). In reporting the results below, studies are referred to according to the numbering in Table 1. Twenty-one RCTs (studies 1-5, 10-12, 14-19, 23, 26, 27, 29-32) published between 1987 and 2011, were identified in our earlier review where results were synthesised using a narrative approach without meta-analysis (Sin & Norman, 2013). This update added 11 studies (reported in 13 papers) published since 2012 (studies 6-9, 13, 20-22, 24, 25, 28). Altogether, the 32 studies included 2,858 family carers and 1,305 patients from 15 (out of 32, 47%) studies where patients also participated in (part of) the interventions. These studies were undertaken in the following countries: China [k=10, eight published in English (studies 2-7, 18, 31); two in Chinese (studies 17, 19)]; North America [k=4 (studies 11, 26, 27, 30)]; Europe [k=4 (studies 1, 10, 21, 23)]; U.K. [k=4 (studies 16, 20, 30, 32)]; Middle East [k=6 (studies 9, 13, 14, 24, 25, 28)]; South America [k=1 (study 12)]; Australia [k=2 (studies 8, 22)]; and India [k=1 (study 15)].

Insert Figure 1: PRISMA flowchart

Insert Table 1: Characteristics of included studies.

Overview of interventions, settings and family carer-participants

Most studies included carers of patients living in the community, excluding four trials which recruited carers of patients while they were receiving treatment in hospital (studies 9, 11, 18, 25). Five studies recruited carers of patients who experienced psychosis for the first time, and were under the care of Early Intervention in Psychosis Service (EIPS) (studies 7, 16, 20, 22, 31). The remainder targeted carers of individuals with a long term psychotic disorder, most commonly schizophrenia. In 75% of studies (k=24), and where the relationships between the carers and patients were reported, parents, especially mothers, made up the majority of participants in 21 studies, and indeed were the only kind of family carers in three studies (studies 14, 29, 31).

In terms of delivery formats, most interventions used the conventional face-to-face medium: three studies evaluated individual (carer or family as units) programmes (studies 11, 16, 25); 19 used groups where carers from different families undertook the programmes together (studies 1-6, 9, 10, 12, 14, 15, 21, 23, 24, 26, 28-31); and four used a combination of individual and group sessions (studies 17-19, 32). Several studies included telephone- (studies 8, 13, 22) and/or email-support (study 20) to supplement text-based psychoeducational interventions; one also included face-to-face group sessions, in addition to telephone-supported bibliotherapy-based intervention (study 7). One RCT evaluated a web-based psychoeducation programme which was provided to both patients and their carers (study 27).

All studies were randomised at the level of the individual, bar one (study 18) which was a cluster trial based on wards. Most trials compared psychoeducation with treatment as usual/standard care, or an attention-control comparator. Two studies employed a three-arm RCT design, comparing a psychoeducation group with a mutual support group and standard care (studies 4, 6). One study compared a psychoeducation group with individual counselling for carers (study 29), and another compared psychoeducation group with postal information (study 30).

Table 1: Characteristics of included studies

Study No.	Study first author** and year published	Country	Sample size of carers (Patient if included)	Psychoeducation • Format • Contact time (hours) / Duration (weeks)	Comparator	Gender of carer (Female - %)	Mean age of carer (years)	Follow up
1	Carra, 2007	Italy	101	Groups 42 hours / 22 weeks	TAU	65	NR	12, 24 months
2	Chan, 2009	Hong Kong	73 (73)	Groups 20 hours /12 weeks	Waitlist	Majority female	NR	6, 12 months
3	Cheng, 2005	Hong Kong	64	Groups 20 hours / 12 weeks	TAU	63%	NR	No FU
4	Chien, 2006*: Chien 2004; Chien 2005	Hong Kong	96 (96)	Groups 24 hours / 26 weeks	TAU Mutual support group	31%	42	6, 12, 18 months
5	Chien, 2007	Hong Kong	84 (84)	Groups 36 hours / 36 weeks	TAU	67%	41	12 months
6	Chien, Thompson, 2013*; Chien, Chan, 2013	Hong Kong	135 (135)	Groups 28 hours / 40 weeks	TAU Mutual support group	38%	42	12, 24 months
7	Chien, Yip, 2016*; Chien, Thompson, 2016	Hong Kong	116	Text-based with telephone support and group sessions 16 hours / 20 weeks	TAU	65%	50	6, 12 months
8	Deane, 2015	Australia	80	Text-based with telephone support 24 hours / 52 weeks	Information booklet	88%	54	No FU
9	Fallahi Khoshknab, 2014	Iran	71	Groups 8 hours / 5 weeks	TAU	93%	54	1 month
10	Fiorillo, 2011	Italy	230 (212)	Groups 21 hours / 26 weeks	TAU	65%	59	No FU
11	Glick, 1990*; Glick, 1991; Clarkin, 1991; Haas, 1990 & 1988; Spencer, 1988	USA	92 (92)	Individual family sessions 6 hours / 10 weeks	TAU	NR	NR	6, 18 months

Study No.	Study first author** and year published	Country	Sample size of carers (Patient if included)	Psychoeducation • Format • Contact time (hours) / Duration (weeks)	Comparator	Gender of carer (Female - %)	Mean age of carer (years)	Follow up
12	Gutierrez-Maldonado, 2009*; Gutierrez-Maldonado, 2007	Chile	45	Groups 27 hours / 18 weeks	TAU	76%	54	No FU
13	Hasan, 2015	Jordan	121 (121)	Text-based with telephone support 146 hours / 12 weeks	TAU	76%	48	3 months
14	Koolaee, 2010	Iran	62	Groups 24 hours / 14 weeks	TAU Behavioural family management	100% mothers	55	3, 6 months
15	Kulhara, 2009	India	76 (76)	Individual family sessions 9 hours / 40 weeks	TAU	25%	47	No FU
16	Leavey, 2004	UK	106	Individual carer sessions 7 hours / 18 weeks	TAU	NR	NR	5 months
17	Li, Xu, 2003	China	139 (120)	Individual family sessions 6 hours / 26 weeks	TAU	NR	NR	No FU
18	Li. Arthur, 2005	China	101 (101)	Individual family sessions 42 hours / 18 weeks	TAU	NR	NR	6 months
19	Liu, 2004	China	118 (118)	Individual family sessions and groups 13 hours / 52 weeks	TAU	NR	NR	No FU
20	Lobban, 2013	UK	103	Text-based with telephone/email support unspecified[b] / 26 weeks	TAU	82%	NR	No FU
21	Martin-Carrasco, 2016	Spain & Portugal	223	Groups 21 hours / 12 weeks	TAU	76%	60	4 months
22	McCann, 2013	Australia	124	Text-based with telephone support 10 hours / 5 weeks	TAU	82%	47	2 months
23	Merinder, 1999*; Merinder, 1998a & b, Merinder, 2000	Denmark	46 (46)	Groups 16 hours / 9 weeks	TAU	NR	NR	12 months
24	Navidian, 2012	Iran	50[a]	Groups 8 hours / 5 weeks	TAU	NR[a]	NR[a]	3 months

Study No.	Study first author** and year published	Country	Sample size of carers (Patient if included)	Psychoeducation • Format • Contact time (hours) / Duration (weeks)	Comparator	Gender of carer (Female - %)	Mean age of carer (years)	Follow up
25	Ozkan, 2013	Turkey	62	Individual sessions with telephone support 6 hours / 30 weeks	Waitlist	53%	NR	6 months
26	Posner, 1992	Canada	55	Groups 12 hours / 9 weeks	Waitlist	NR	NR	6 months
27	Rotondi, 2005*; Rotondi, 2010	USA	21 (31)	Web-based multi-component programme Unspecified[b] / 14 weeks	TAU	NR	NR	6, 12 months
28	Sharif, 2012	Iran	70	Groups 15 hours / 5 weeks	TAU	Majority were mothers	51	1 month
29	Shin, 2004	USA	48	Groups 15 hours / 12 weeks	Individual carer counselling	65%	66	No FU
30	Smith, 1987	UK	40	Groups 6 hours / 4 weeks	Information booklet	NR	NR	6 months
31	So, 2006	Hong Kong	45	Groups 9 hours / 6 weeks	Waitlist	78%	49	6 months
32	Szmukler, 2003	UK	61	Mixed individual and group carer sessions 24 hours / 40 weeks	1 hour individual carer session	82%	54	6 months

** Additional author names are cited to differentiate publications if necessary, *denotes the major publication for the study, TAU = Treatment as usual, NR = not reported, [a]only data on 50 carers of patients diagnosed with schizophrenia out of the total 100 carers were extracted for the review, [b]no contact hours specified as carers were encouraged to use the resource as much as they wish.

Quality of included studies

Our overall evaluation of the risk of bias of included RCTs is presented in Supplementary Figures 1 and 2. Sequence generation was adequately described in 12 studies, unclear in 18, and regarded as high risk in two given somewhat contradictory accounts of randomisation process. Thirteen studies were rated as low risk in terms of allocation concealment, 19 as unclear. Masking of participants and trial therapists was not possible in all studies; a common challenge in psychological intervention research. Therefore we rated all studies as moderate risk as such. For masking of outcome assessment, we rated 14 studies as low risk, 17 unclear, and one high risk. Regarding incomplete outcome data due to attrition or missing data, 15 studies were at low risk of bias, 10 unclear, and seven high. Approximately one-third of studies had published protocols or trial registration forms, and so we were able to confirm that outcomes were reported in 12 studies as planned. However, 11 studies were rated as unclear risk and nine high risk of selective outcome reporting. Overall, carers' outcomes were often not reported as primary outcomes even in those trials in which only carers participated; patients' outcomes, such as and mental state and relapse rates, took primacy. Carers' outcomes were measured in a variety of ways using different scales and follow up data beyond the end of the intervention were sparse. We considered that these factors incurred other biases which were subsequently rated as either unclear or high risk in 20 studies.

Primary outcomes: carers' wellbeing, quality of life and proxy measures

Two studies (8, 20), including 184 carers, examined the effectiveness of psychoeducational interventions, delivered via booklets and augmented with weekly telephone and/or email support, for carers. Results were equivocal when comparing these interventions with inactive controls, at post-intervention respectively (2 RCTs, n=184, SMD 0.103, 95% CI -0.186 to 0.392, I^2=0%). Only one study (13) measured carers' quality of life as an outcome when comparing psychoeducation with usual care. Study findings indicated no significant differences between groups (1 RCT, n=121, SMD 0.145, 95% CI -0.205 to 0.495). See Figure 2 for meta-analysis on the primary outcomes.

Insert Figure 2: Meta-analysis on carers' wellbeing and quality of life

In terms of proxy measures of carers' wellbeing, we examined carers' stress, global morbidities, and depression. The analysis of stress included four studies. Three studies compared telephone-supported bibliotherapy-based psychoeducation (studies 8, 22), or web-based multi-component psychoeducation (study 27) with inactive controls; results

showed no significant differences between groups (3 RCTs, n=226, SMD -0.133, 95% CI -0.394 to 0.128, I^2=0%). One study (30) compared psychoeducational groups with postal booklets as an active control (1 RCT, n=40). When combined, the overall analysis indicated no significant differences in stress levels across psychoeducation and comparator groups (4 RCTs, n=266, SMD -0.169, 95% CI -0.410 to 0.072, I^2=0%). Regarding global morbidities, seven studies provided data about a range of physiological and emotional morbidity outcomes. Psychoeducation yielded a small but significant effect when compared to inactive controls (6 RCTs, n=616, SMD -0.22, 95% CI -0.386 to -0.065, I^2=37.5%) (studies 12, 17, 20-22, 26). Only one study (30) compared psychoeducation to postal booklets (1 RCT, n=40). The meta-analysis including these seven studies showed an overall significant effect of psychoeducation compared to controls in reducing global morbidities (7 RCTs, n=656, SMD -0.230, 95% CI -0.386 to -0.075, I^2=25.6%). Two studies (21, 25) examined the impact of psychoeducation on depression; and psychoeducation showed a significant positive effect over inactive controls (2 RCTs, n=245, SMD -0.70, 95% CI -0.97 to -0.44, I^2=97.2%). Of note, heterogeneity of these two studies was high: one was a European study examining psychoeducation groups for carers (study 21); and one investigated psychoeducation delivered to carers individually in the Middle East (study 25). See Figure 3 for meta-analysis on proxy measures of carers' wellbeing.

Insert Figure 3: Meta-analysis on proxy measures of carers' wellbeing

Secondary outcomes: caregiving-related outcomes

Five studies (7, 8, 20, 22, 31) examined positive and negative aspects of caregiving in carers. While psychoeducation did not yield significantly different results for enhancing carers' positive caregiving experiences, compared with inactive controls (5 RCTs, n=452, SMD 0.032, 05% CI -0.151 to 0.216, I^2=0%), there was some suggestion that negative appraisals were improved (5 RCTs, n=446, SMD -0.21, 95% CI -0.396 to -0.025, I^2=0%).

Considering caregiving-related burden, the meta-analysis, including 10 studies with 878 participants (studies 2, 3, 5, 7, 9, 13, 21, 24, 25, 28) showed a significantly superior effect of psychoeducation to inactive controls in reducing carers' perceived burden (10 RCTs, n=878, SMD -0.434, 95% CI -0.567 to -0.301, I^2=0%).

Analysis of carers' expressed emotion (5 RCTs, n=337, SMD -0.161, 95% CI -0.367 to 0.045, I^2=0%) (studies 1, 22, 23, 25, 31), family functioning (3 RCTs, n=238, SMD 0.135, 95% CI -0.120 to 0.391, I^2=0%) (studies 4-6), and perceived social support (4 RCTs, n=303, SMD 0.133, 95% CI -0.093 to 0.360, I^2=0%) (studies 2, 4, 6, 15), revealed no significant

differences between psychoeducational interventions and inactive controls. Nonetheless, psychoeducation showed a significantly improved effect compared to inactive controls, in improving carers' knowledge in psychosis (4 RCTs, n=310, SMD 0.361, 95% CI 0.136 to 0.586, I^2=49.8%) (studies 8, 13, 18, 26). The heterogeneity of these studies was bordering on high. The four studies concerned were undertaken in Australia (study 8), the Middle East (study 13), China (study 18), and Canada (study 26), and each investigated a different modality of psychoeducation, in which the duration ranged from 9 to 52 weeks. See Table 2 for meta-analyses on all a priori outlined secondary outcomes.

Insert Table 2: Overview of meta-analyses on secondary outcomes

Table 2 – Overview of meta-analyses on secondary outcome measures

Outcome measures	Studies (k)	Sample (N (n/n))[a]	SMD	95% CI	P value	I^2 (%)
Positive caregiving experience	5	452 (224/228)	0.032	-0.151 to 0.216	0.729	0
Negative caregiving experience	5	446 (220/226)	**-0.210**	**-0.396 to -0.025**	**0.026**	**0**
Perceived burden	10	878 (445/433)	**-0.434**	**-0.567 to -0.301**	**<0.001**	**0**
Coping	2	151 (75/76)	-0.178	-0.500 to 0.144	0.278	82.6
Self-efficacy	2	137 (68/69)	0.187	-0.148 to 0.522	0.274	0
Expressed emotion	5	337 (155/182)	-0.171	-0.377 to 0.035	0.104	0
Family functioning	3	238 (120/118)	0.135	-0.120 to 0.391	0.299	0
Perceived social support	5	393 (197/196)	0.103	-0.096 to 0.301	0.310	0
Knowledge	4	300 (154/156)	**0.361**	**0.136 to 0.586**	**0.002**	**49.8**
Hope	2	184 (92/92)	0.032	-0.257 to 0.321	0.826	0
Satisfaction with support	4	264 (131/133)	0.238	-0.004 to 0.480	0.054	0

[a]Total number of carer-participants included in the analysis (number of carer-participants in psychoeducation groups/number of carer-participants in comparator groups), bold print denotes significant effect.

Follow up outcome data

Follow up data beyond the post-intervention period were sparse, limiting the meta-analysis to largely secondary outcomes, all of which compared psychoeducation with inactive controls. At 6-month post-intervention, no data were available on carers' wellbeing or quality of life; and only one study provided data on proxy measures such as global morbidities (study 26) or depression (study 25). Indeed, meta-analysis was only feasible on one secondary outcome, that is, carers' perceived burden, which had data available from 10 studies (10 RCTs, n=821, SMD -1.628, 95% CI -2.307 to -0.948, I^2=94.5%) (studies 2, 4, 7, 9, 13, 14, 21, 24, 25, 28). The analysis suggested that the superior effects of psychoeducation on reducing carers' burden seem to sustain up to 6-month post-intervention. At 12-month post-intervention, no data were available for any of our primary outcomes. Three studies reported carers' perceived burden (studies 2, 5, 7); the analysis identified no significant differences between psychoeducation and inactive controls at one year follow up (3 RCTs, n=269, SMD -0.024, 95% CI -0.279 to 0.230, I^2=96.7%). Analysis on family functioning (2 RCTs, n=174, SMD 0.663, 95% CI -0.382 to 1.707, I^2=0%) and on carers' perceived social support (2 RCTs, n=163, SMD 0.255, 95% CI -0.053 to 0.563, I^2=0%) showed no significant differences between psychoeducation and inactive control groups (studies 2, 6). Data for over 12-month follow up were limited and precluded any meta-analysis on both primary and secondary outcomes.

Meta-regression on intervention factors and treatment effect

Intervention duration ranged from four to 52 weeks, mean duration across 32 trials was 20 weeks (median=16 weeks). Intervention contact times ranged from six to 42 hours, with a mean of 17.4 hours (median=15.5 hours). Meta-regression investigating the differential effects, if any, of the intervention contact times (in terms of hours), intervention duration (in terms of weeks), and modes of delivery (group or individual) could only be conducted for the outcome of carers' perceived burden. All other analyses on outcomes included data from less than eight studies. There was no association between intervention contact time and effect size of carers' perceived burden (regression coefficient 0.006, 95% CI -0.038 to 0.051, p=0.732). A similar lack of relationship between intervention duration and intervention effects on carers' perceived burden was also observed (regression coefficient 0.020, 95% CI -0.021 to 0.061, p=0.266). Meta-regression on interventions delivered using group formats or otherwise was highly imbalanced, as group programmes significantly outnumbered other modalities. For instance, for the 10 studies that provided usable data for the meta-analysis on carers' perceived burden, eight reported group programmes which included multiple carers in face-to-face sessions (studies 2, 3, 5, 7, 9, 21, 24, 28); and two used an individual format with the patient-carer pairs as a family unit (studies 13, 25). Nevertheless, the

analysis showed no significant relationships between outcome effect and mode of delivery using either format (regression coefficient 0.095, 95% CI -0.293 to 0.483, p=0.588).

Discussion

The aim of this review was to quantitatively synthesise data obtained from RCTs about the effectiveness of psychoeducation for improving psychosis carers' wellbeing, quality of life and caregiving-related outcomes. Thirty-two RCTs, providing data on 2,858 carers, were included in the review. Importantly although carers participated in all interventions, not all of them reported carers' outcomes (6 studies (19%) provided no usable carer outcome data which could be included in the meta-analysis), let alone carers' wellbeing, quality of life or proxy measures as an individual. At post-intervention, only two studies provided data on carers' wellbeing and one on carers' quality of life. Psychoeducation showed a significant albeit small effect, compared with usual care or inactive comparators in ameliorating carers' global morbidities, as a proxy measure of carers' wellbeing. Relatively more data were available on caregiving-related outcomes. Results showed an overall significant small effect of psychoeducation on carers' negative appraisal of caregiving experiences, perceived burden, and knowledge about psychosis and illness-related management. The available data limited our planned meta-regression on intervention factors and carers' outcomes. Nonetheless, it is worth noting that the majority of interventions included a group-element which enabled carers to exchange experiences and support with their peers, and intervention duration and contact times varied between studies. Follow-up data were lacking, limiting the extent of meta-analysis on any carers' longer term outcomes.

There is currently no evidence existing from the few studies indicating any associations between the pre-specified intervention factors (duration, contact time and using a group format or otherwise) and effect on carers' outcomes. It is possible, however that the analyses lacked power to detect significant differences. Interventions solely delivered via face-to-face group meetings were most commonly used (k=19, 59%), and when calculating the number of interventions that incorporated a group element, a further 6 studies were included (78% of all included studies). It may be that the opportunity to share personal experiences with peers, and learn from others' experiences, serves to reduce isolation, normalising the experiences and enhance self-efficacy (Gillard et al., 2015; Sin & Norman, 2013).

Despite the growing popularity of eHealth and mHealth interventions (Chi & Demiris, 2015; Cucciare & Weingardt, 2010; Powell & Clarke, 2006), only one study (Rotondi et al., 2005; Rotondi et al., 2010) included here (and one protocol of a study yet to be published by Sin, Henderson, Pinfold, & Norman, 2013) described a fully web-based intervention delivered to both the carers and the cared-for persons. Web-based interventions are advantageous because participants can decide which components or strategies resonate with them, how much to spend accessing the site, and when to do so (Chi & Demiris, 2015; Sin, 2013; Sin et al., 2014). The early indications are that recruitment and retention rates are comparable between face-to-face and online interventions. However, compared to interventions for carers of individuals with dementia (Chi & Demiris, 2015; Powell, Chiu, & Eysenbach, 2008) or eating disorders (Grover et al., 2011; Hoyle, Slater, Williams, Schmidt, & Wade, 2013), we have some way to go to ensure that e and mHealth interventions for carers of people with psychosis incorporate and integrate evolving technologies to enhance accessibility and flexibility (Powell et al., 2013; Sin et al., 2014; Webb, Joseph, Yardley, & Michie, 2010).

Strengths, Limitations and Recommendations

Building upon previous reviews (Sin et al., 2015; Sin & Norman, 2013), we have been able to synthesise data from 32 RCTs and produce meta-analyses focusing on carers' outcomes. Furthermore, this review has yielded new data about mixed-modality interventions, and facilitated comparisons of the effectiveness of these interventions compared with active and inactive controls. While the wide range of interventions, undertaken across geographical regions may have contributed to heterogeneity in the planned analyses, this may also have enhanced generalisability of the review findings. Fewer than half of the included studies (k=14) were undertaken in English-speaking or western cultures, while one-third were conducted in China (k=10) and the rest in the Middle East, South America and South-East Asia (k=8). This evidence may suggest that psychoeducational interventions are popular and widely adaptable in different clinical settings world-wide, and that psychoeducation for carers could be beneficial for those caring for a loved one across the diverse range of psychotic disorders, from first episode psychosis to long-term schizophrenia.

As culture has a significant role in how mental (ill) health is understood and treated, the process and meaning of family caregiving for a loved one with psychosis is also likely to be interpreted differently across ethnic-cultural context (Earl, 2007; Sin et al., 2012). For instance, it is much more common for the patients to live under the same roof with their family carers in the Chinese culture. In fact, all the Chinese studies (e.g. Chien et al., 2005; Chan et al., 2009; Li & Arthur, 2005) stipulated that carers and patients had to live together, as one of the eligibility criteria. These ethnic-cultural factors are likely to influence the

caregiving roles, activities, and the carer's outcomes. With the growing interest for research and clinical development in family psychoeducation globally, we expect to see further studies coming out from both Western and non-Western cultures in the near future. Richer study data should allow further exploration into intervention effectiveness and any moderating mechanisms considering the ethnic-cultural factors.

We acknowledge several limitations to this review. First, the available data underpinning our primary and secondary outcomes were limited. Similarly, follow-up data were sparse, limiting analyses on outcomes beyond post-intervention time point to nearly non-existent. Results of meta-analyses should be interpreted with caution due to a high risk of inadequate power when data were only available from a small number of studies. While the published literature was comprehensively searched and carer outcome data meticulously extracted for this review, there remains a possibility of publication bias in that studies with null results for patients and/or carers are in the "file drawer" and never published (Miyar & Adams, 2013; Higgins et al., 2011). If such publication bias, in fact, exists, it may imply that the results presented in this review may have overstated the direct benefits of family psychoeducational interventions to carers. Second, we took the approach to report all secondary outcomes which were outlined a priori (Sin et al., 2016). In the event, the secondary outcomes related to caregiving experiences were more frequently reported by included studies. However, some of the meta-analyses of the secondary outcomes also reflected significant heterogeneity (likely both clinical and methodological) and a lack of precision. Third, although carers were (sometimes the only) recipients of the psychoeducational interventions, their outcomes and characteristics were often poorly or not reported by the studies. This not only limited the data on carers' outcomes, but also impeded our understanding of the carers' demographic characteristics, and hence any possible differential response to the intervention based on carers' characteristics. Fourth, our meta-analyses focused on carer's outcomes solely without exploring any possible associations between carer's and patient's outcomes. Hence it is possible that patient's improved clinical status might have contributed, in part, to carer's improved outcomes (such as perceived burden). Fifth and lastly, it is worth-noting that the quality of some of the included studies, in particular their reporting of randomisation sequence generation, allocation concealment, blinding, and reporting bias, were considered as high risk of bias. The quality of the evidence of some of the results should be interpreted in light of the risk of bias assessment of the data source.

We suggest several key priorities for future research. It is evident that although carers have been offered psychoeducational interventions, outcomes are often not reported for this group of participants, a situation which should not be repeated in future studies. With the

increasing recognition of carers' right and contribution to their loved one's care, we expect studies targeting carers (with or without the patients) to gain significance in funded research priorities (NICE, 2010; Kuipers, 2010). We propose that carers' outcomes could constitute primary study outcomes (i.e. acknowledging carers in their own right), or it may be that studies are designed to measure dual primary outcomes (i.e. for patients *and* for carers). Further systematic reviews could then take advantage of such data to explore any correlation between patient's and carer's outcomes. More evidence is needed to establish which modalities are associated with improved outcomes, and whether there is an optimal duration and contact time. Additionally, we suggest that outcomes are measured at distinct time points, at medium and long-term follow-up periods as it may take participants some time to be able to implement strategies consistently. We also recommend that carers' wellbeing and proxy measures are evaluated using standardised questionnaires and scales (Miyar & Adams, 2013). This will help facilitate understanding of the relational process between carers' wellbeing and their caregiving capacity. Essentially, and, in turn, how these carers' outcomes correlate to patients' outcomes like decreased relapse and better compliance, and to family-wide outcomes like family relationship and communication, and vice versa, needs to be better explored. Lastly as is good practice we would encourage study authors to report data according to CONSORT guidelines (Schulz, Altman, Moher, & The CONSORT Group, 2010).

Conclusion

The review findings indicate that psychoeducation is beneficial for enhancing carers' knowledge about mental health, appraisal about caregiving, perception of burden, and emotional support. Better understanding of treatment mediators and moderators may inform optimal design of psychoeducational interventions, targeting both patients' and carers' outcomes. Additionally, while improving caregiving capacity is of pivotal importance for patients' outcomes, carers' needs in terms of their own health and wellbeing should be better understood, and subsequently, addressed.

Highlights

- Wellbeing and other outcomes of carers of individual with psychosis lack research.
- Psychoeducation improves carers' global morbidity, as a proxy measure to wellbeing.
- Psychoeducation ameliorates caregiving-related outcomes, in particular burden.
- 78% studies used group format, mean duration 20 weeks, mean contact time 17 hours.
- No significant associations identified between intervention factors and outcomes.

References

Alvarez-Jimenez, M., Alcazar-Corcoles, M.A., Gonzalez-Blanch, C., Bendall, S., McGorry, P., & Gleeson, J.F. (2014). Online, social media and mobile technologies for psychosis treatment: A systematic review on novel user-led interventions. *Schizophrenia Research, 156*, 96-106.

Bandura, A. (1977a). Self-efficacy: Towards a unifying theory of behaviour change. *Psychological Review, 84*, 199-215.

Bandura, A. (1977b). *Social Learning Theory*. New Jersey: Prentice-Hall.

Bandura, A. (1988). Perceived self-efficacy: exercise of control through self belief. *Annual Series of European Research in Behavioural Therapy, Volume 2*, 27-59.

Bebbington, P.E., & Kuipers, E. (1994). The predictive utility of expressed emotion in schizophrenia. *Psychological Medicine, 24*, 707-718.

Birchwood, M., Smith, J., & Cochrane, R. (1992). Specific and non-specific effects of educational intervention for families living with schizophrenia. A comparison of three methods. *British Journal of Psychiatry, 160*, 806-814.

Brown, G.W., Monck, E.M., Carstairs, G.M., & Wing, J.K. (1962). Influence of family life on the course of schizophrenic illness. *British Journal of Preventive and Social Medicine, 16*, 55-68.

Carra, G., Montomoli, C., Clerici, M., & Cazzullo, C. L. (2007). Family interventions for schizophrenia in Italy: Randomized controlled trial. *European Archives of Psychiatry and Clinical Neuroscience, 257 (1)*, 23-30.

Cavanagh, K., Shapiro, D., Van den Berg, S., Swain, S., Barkham, M. , & Proudfoot, J. (2006). The effectiveness of computerised cognitive-behavioural therapy in routine primary care. *British Journal of Clinical Psychology, 45*(4), 499-514.

Chan, S. W., Yip, B., Tso, S., Cheng, B. S., & Tam, W. (2009). Evaluation of a psychoeducation program for Chinese clients with schizophrenia and their family caregivers. *Patient Education & Counseling, 75*(1), 67-76.

Cheng, Lai Yu, & Chan, S. (2005). Psychoeducation program for Chinese family carers of members with schizophrenia. *Western Journal of Nursing Research, 27*(5), 583-599.

Chi, N-C., & Demiris, G. (2015). A systematic review of telehealth tools and interventions to support family caregivers. *Journal of Telemedicine and Telecare, 21*(1), 37-44.

Chien, W. T., & Chan, S. W. (2013). The effectiveness of mutual support group intervention for Chinese families of people with schizophrenia: a randomised controlled trial with 24-month follow-up. *International Journal of Nursing Studies, 50*(10), 1326-1340.

Chien, W. T., & Thompson, D. R. (2013). An RCT with three-year follow-up of peer support groups for Chinese families of persons with schizophrenia. *Psychiatric Services, 64*(10), 997-1005.

Chien, W. T., Thompson, D.R., Lubman, D.I., & McCann, T.V. (2016). A randomised controlled trial of clinician-supported problem-solving bibliotherapy for family caregivers of people with first-episode psychosis. *Schizophrenia Bulletin*. doi:10.1093/schbul/sbw054.

Chien, W. T., Yip, A.L.K., Liu, J.Y.W., & McMaster, T. (2016). The effectiveness of manual-guided, problem-solving-based self-learning programme for family caregivers of people with recent-onset psychosis: A randomised controlled trial with 6-month follow up. *International Journal of Nursing Studies, 59*, 141-155.

Chien, W.T., & Chan, S.W. (2004). One-year follow-up of a multiple-family-group intervention for Chinese families of patients with schizophrenia. *Psychiatric Services, 55*(11), 1276-1284.

Chien, W.T., Chan, S.W., Morrissey, Jean, & Thompson, D. (2005). Effectiveness of a mutual support group for families of patients with schizophrenia. *Journal of Advanced Nursing, 51*(6), 595-608.

Chien, W.T., Chan, S.W., & Thompson, D. R. (2006). Effects of a mutual support group for families of Chinese people with schizophrenia: 18-month follow-up. *British Journal of Psychiatry, 189*(1), 41-49.

Chien, W.T., & Wong, K.F. (2007). A family psychoeducation group program for Chinese people with schizophrenia in Hong Kong. *Psychiatric Services, 58*(7), 1003-1006.

Clarkin, J. F., Glick, I. D., Haas, G. L., & Spencer, J. H. (Eds.). (1991). *The effects of inpatient family intervention on treatment outcome*. New York: American Psychiatric Press, Inc.

Cucciare, M.A., & Weingardt, K.R. (Eds.). (2010). *Using Technologies to Support Evidence-Based Behavioural Health Practices - A Clinician's Guide*. New York: Routledge.

Deane, F.P., Marshall, S., Crowe, T., White, A., & Kavanagh, D. (2015). A randomized controlled trial of a correspondence-based intervention for carers of relatives with psychosis. *Clinical Psychology & Psychotherapy, 22*(2), 142-152.

Earl, T.R. (2007). Chapter 3. Mental health care policy. *Journal of Human Behaviour in the Social Environment*, 14(1/2), 51-72.

Egger, M., Smith, C.D., & Altman, D.G. (Eds.). (2001). *Systematic Reviews in Health Care: Meta-Analysis in Context*. London: BMJ Books.

Fallahi Khoshknab, M., Sheikhona, M., Rahgouy, A., Rahgozar, M., & Sodagari, F. (2014). The effects of group psychoeducational programme on family burden in caregivers of Iranian patients with schizophrenia. *Journal of Psychiatric and Mental Health Nursing, 21*(5), 438-446.

Fiorillo, A., Bassi, M., de Girolamo, G., Catapano, F., & Romeo, F. (2011). The impact of a psychoeducational intervention on family members' views about schizophrenia: Results from the OASIS Italian multi-centre study. *International Journal of Social Psychiatry, 57*(6), 596-603.

Gillard, S., Gibson, S., Holley, J., & Lucock, M. (2015). Developing a change model for peer worker interventions in mental health services: a qualitative research study. *Epidemiological & Psychiatric Sciences, 24*(5), 435-445.

Glick, I. D., Clarkin, J. F., Haas, G. L., Spencer, J. H., & Chen, C.L. (1991). A randomised clinical trial of inpatient fmaily intervention: VI. Medicating variables and outcome. *Family Process, 30*, 85-99.

Glick, I. D., Clarkin, J. F., Haas, G. L., & Spencer, J. H., Jr. (1993). Clinical significance of inpatient family intervention: conclusions from a clinical trial. *Hospital & Community Psychiatry, 44*(9), 869-873.

Glick, I. D., Clarkin, J. F., Spencer, J. H., Haas, G. L., Lewis, A. B., Peyser, J., . . . Lestelle, V. (1990). A controlled evaluation of inpatient family intervention: preliminary results of the six-month follow-up. *Archives of General Psychiatry, 42*(9), 882-886.

Glick, I. D., Spencer, J. H., Jr., Clarkin, J. F., Haas, G. L., Lewis, A. B., Peyser, J., . . . Lestelle, V. (1990). A randomized clinical trial of inpatient family intervention. IV. Follow up results for subjects with schizophrenia. *Schizophrenia Research, 3*(3), 187-200.

Glynn, S.M., Randolph, E.T., Garrick, T., & Lui, A. (2010). A proof of concept trial of an online psychoeducational program for relatives of both veterans and civilians living with schizophrenia. *Psychiatric Rehabilitation Journal, 33*(4), 278-287.

Grover, M., Naumann, U., Mohammad-Dar, L., Glennon, D., Ringwood, S., Eisler, I., . . . Schmidt, U. (2011). A randomised controlled trial of an Internet-based cognitive-behavioural skills package for carers of people with anorexia nervosa. *Psychological Medicine, 41*(12), 2581-2591.

Guerriero Austrom, M., Geros, K.N., Hemmerlein, K., McGuire, S.M., Gao, S., Brown, S.A., . . . Clark, D.O. (2015). Use of a multiparty web based videoconference support groupfor family caregivers: Innovative practice. *Dementia, 14*(5), 682-690.

Gutierrez-Maldonado, J., Caqueo-Urizar, A., & Ferrer-Garcia, M. (2009). Effects of a psychoeducational intervention program on the attitudes and health perceptions of relatives of patients with schizophrenia. *Social Psychiatry and Psychiatric Epidemiology, 44 (5)*, 343-348.

Gutierrez-Maldonado, J., & Caqueo-Urizar, A. (2007). Effectiveness of a psycho-educational intervention for reducing burden in Latin American families of patients with schizophrenia. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation, 16*(5), 739-747.

Haas, G.L., Glick, I.D., Clarkin, J.F., Spencer, J.H., & Lewis, A.B. (1990). Gender and schizophrenia outcome: a clinical trial of an inpatient family intervention. *Schizophrenia Bulletin, 16*(2), 277-292.

Haas, G.L., Glick, I.D., Clarkin, J.F., Spencer, J.H., & et al. (1988). Inpatient family intervention: A randomized clinical trial: II. Results at hospital discharge. *Archives of General Psychiatry, 45*(3), 217-224.

Hasan, A., Callaghan, P., & Lymn, J.S. (2015). Evaluation of the impact of a psycho-educational intervention for people diagnosed with schizophrenia and their primary caregivers in Jordan: a randomized controlled trial. *BMC Psychiatry, 15*. doi:10.1186/s12888-015-0444-7.

Higgins, J.P.T., & Green, S. (Eds.). (2011). *Cochrane Handbook for Systematic Reviews of Interventions v.5.1.0 (updated March 2011)*. Oxford: The Cochrane Collaboration.

Higgins, J.P.T., & Thompson, S.G. (2004). Controlling the risk of spurious findings from meta-regression. *Statistics in Medicine, 23*, 1663-1682.

Higgins, J.P.T., Thompson, S.G., Deeks, J.J., & Altman, D.G. (2003). Measuring inconsistency in meta-analysis. *BMJ, 327*, 557-560.

Hoyle, D., Slater, J., Williams, C., Schmidt, U., & Wade, T.D. (2013). Evaluation of a web-based skills interventon for carers of people with anorexia nervosa: A randomised controlled trial. *International Journal of Eating Disorders, 46*(6), 634-638.

Johnson, S., Ramsay, R., Thornicroft, G., Brooks, E., Lelliott, P., Peck, E., . . . Goldberg, C. (2000). *London's mental health: the report for the King's Fund Commission*. Retrieved from London:

Joyce, J., Leese, M., Kuipers, E., Szmukler, G., Harris, T., & Staples, E. (2003). Evaluating a model of caregiving for people with psychosis. *Social Psychiatry & Psychiatric Epidemiology, 38*, 189-195.

Joyce, J., Leese, M., & Szmukler, G. (2000). The Experience of Carefiving Inventory: further evidence. *Social Psychiatry & Psychiatric Epidemiology, 35*, 185-189.

Koolaee, A.K., & Etemadi, A. (2010). The outcome of family interventions for the mothers of schizophrenia patients in Iran. *International Journal of Social Psychiatry, 56*(6), 634-646.

Kuipers, E. (2010). Time for a separate psychosis caregiver service? *Journal of Mental Health, 19*, 401-404.

Kuipers, E., Onwumere, J., & Bebbington, P. (2010). Cognitive model of caregiving in psychosis. *The British Journal of Psychiatry, 196*, 259-265.

Kuipers, E., & Raune, D. (2000). The early development of EE and burden in the families of first onset psychosis. In M. Birchwood & D. Fowler (Eds.), *Early Intervention in Psychosis: A Guide to Concepts, Evidence and Interventions* (pp. 128-140). Chichester: John Wiley and Sons.

Kulhara, P., Chakrabarti, S., Avasthi, A., Sharma, A., & Sharma, S. (2009). Psychoeducational intervention for caregivers of Indian patients with schizophrenia: A randomised-controlled trial. *Acta Psychiatrica Scandinavica, 119 (6)*, 472-483.

Lazarus, P., & Folkman, S. (1984). *Stress, Appraisal and Coping*. New York: Springer Publishing Company.

Lazarus, R.S. (1966). *Psychological Stress and the Coping Process*. New York: McGraw-Hill Book Co.

Leavey, G., Gulamhussein, S., Papadopoulos, C., Johnson-Sabine, E., Blizard, B., & King, M. (2004). A randomized controlled trial of a brief intervention for families of patients with a first episode of psychosis. *Psychological Medicine, 34*(3), 423-431.

Li, F.M., & Xu, J.H. (2003). Comparative study on the effect of family intervetnion on schizophrenia patients in convalence and their family member. *Health Psychology Journal, 11*(2), 129-130.

Li, Z., & Arthur, D. (2005). Family education for people with schizophrenia in Beijing, China - Randomised controlled trial. *British Journal of Psychiatry, 187*, 339-345.

Liu, L, Gao, C.F., Yue, S.Y., Zhan, L.Y., & Liu, W.G. (2004). Effect of family intervention on rehabilitation of schizophrenic patients in community. *Journal of Nursing Science, 3*(19), 3-6.

Lobban, F., Glentworth, D., Chapman, L., Wainwright, L., Postlethwaite, A., Dunn, G., . . . Haddock, G. (2013). Feasibility of a supported self-management intervention for relatives of people with recent-onset psychosis: REACT study. *The British Journal of Psychiatry, 203*, 366-372.

Lobban, F., Postlethwaite, A., Glentworth, D., Pinfold, V., Wainwright, L., Dunn, G., . . . Haddock, G. (2013). A systematic review of randomised controlled trials of interventions reporting outcomes for relatives of people with psychosis. *Clinical Psychology Review, 33*, 372-382.

Martens, L., & Addington, J. (2001). The psycholgocial well-being of family members of individuals with schizophrenia. *Social Psychiatry & Psychiatric Epidemiology, 36*, 128-133.

Martin-Carrasco, M., Fernandez-Catalina, P., Dominguez-Panchon, A.I., Goncalves-Pereira, M., Gonzalez-Fraile, E., Munoz-Hermoso, P., . . . the EDUCA-III group. (2016). A randomised trial to assess the efficacy of a psychoeducational intervention on caregiver burden in schizophrenia. *European Psychiatry, 33*, 9-17.

McCann, T. V., Lubman, D. I., Cotton, S. M., Murphy, B., Crisp, K., Catania, L., . . . Gleeson, J. F. M. (2013). A randomized controlled trial of bibliotherapy for carers of young people with first-episode psychosis. *Schizophrenia Bulletin, 39*(6), 1307-1317.

Merinder, L.B. (2000). *Impact of patient and relative education on knowledge, satisfaction with services and clinical outcome in schizophrenia.* Retrieved from Aarhus.

Merinder, L.B., Viuff, A.G., Laugesen, H., Clemmensen, K., Misfelt, S., & Espensen, B. (1998a). Effects of psychoeducative methods: a randomised controlled study. *Nordic Journal of Psychiatry, 41*(Supplement), 144.

Merinder, L.B., Viuff, A.G., Laugesen, H.D., Clemmensen, K., Misfelt, S., & Espensen, B. (1998b, 20-24 September 1998). *Patient and relative education in community psychiatry: a randomised trial regarding its usefulness.* Paper presented at the Proceedings of the 9th Congress of the Association of European Psychiatrists, Denmark, Copenhagen.

Merinder, L., Viuff, A., Laugesen, H., Clemmensen, K., Misfelt, S., & Espensen, B. (1999). Patient and relative education in community psychiatry: A randomized controlled trial regarding its effectiveness. *Social Psychiatry and Psychiatric Epidemiology, 34*(6), 287-294.

Miyar, J., & Adams, C.E. (2013). Content and quality of 10000 controlled trials in schizophrenia over 60 years. *Schizophrneia Bulletin, 39*(1), 226-229.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., & Group, The PRISMA. (2009). Preferred reporting items for systematic reviews and meta-analyses. *PLoS Med, 6*(6), e1000097. doi:10.1371/journal.pmed1000097.

National Institute for Clinical Excellence (NICE). (2014). *Psychosis and Schizophrenia in Adults: Treatment and Management (National Clinical Guideline No. 178)*. London: National Collaborating Cebtre for Mental Health.

Navidian, A., Kermansaravi, F., & Rigi, S.N. (2012). The effectiveness of a group psycho-educational program on family caregiver burden of patients with mental disorders. *BMC Research Notes, 5*, 399.

NICE. (2010). *Schizophrenia - The NICE Guideline on Core Interventions in the Treatment and Management of Schizophrenia in Adults in Primary and Secondary Care (Updated Edition).* London: The British Psychological Society & The Royal College of Psychiatrists.

Ozkan, B., Erdem, E., Ozsoy, S.D., & Zararsiz, G. (2013). Effect of psychoeducation and telepsychiatric follow up given to the caregiver of the schizophrenic patient on family burden, depression and expression of emotion. *Pakistan Journal of Medical Sciences, 29*(5).

Posner, C.M., Wilson, K.G., Kral, M.J., Lander, S., & McIlwraith, R.D. (1992). Family psychoeducational support groups in schizophrenia. *American Journal of Orthopsychiatry, 62*(2), 206-218.

Powell, J., Chiu, T., & Eysenbach, G. (2008). A systematic review of networked technologies supporting carers of people with dementia. *Journal of Telemedicine and Telecare, 14*, 154-156.

Powell, J., & Clarke, A. (2006). Internet informaiton-seeking in mental health - population survey. *British Journal of Psychiatry, 189*, 273-277.

Powell, J., Hamborg, T., Stallard, N., Burls, A., McSorley, J., Bennett, K., . . . Christensen, H. (2013). Effectiveness of a web-based cognitive-behavioural tool to improve mental well-being in the general population: Randomised controlled trial. *Journal of Medical Internet Research, 15*(1), e2.

Proudfoot, J., Tryden, C., Everitt, B., Shapiro, D.A., Goldberg, D., Mann, A., . . . Gray, J. (2004). Clinical efficacy of computerised cognitive behavioural therapy for anxiety and depression in primary care: randomised controlled trial. *British Journal of Psychiatry, 185*, 46-54.

Raune, D., Kuipers, E., & Bebbington, P. (2004). Expressed emotion at first-episode psychosis: investigating a carer appraisal model. *British Journal of Psychiatry, 184*, 321-326.

Rotondi, A.J., Anderson, C.M., Haas, G.L., Eack, S. M., Spring, M.B., Ganguli, R., . . . Rosenstock, J. (2010). Web-based psychoeducational intervention for persons with schizophrenia and their supporters: One-year outcomes. *Psychiatric Services, 61 (11)*, 1099-1105.

Rotondi, A.J., Haas, G.L., Anderson, C.M., Newhill, C.E., Spring, M.B., Ganguli, R., . . . Rosenstock, J.B. (2005). A clinical trial to test the feasibility of a telehealth psychoeducational intervention for persons with schizophrenia and their families: intervention and 3-month findings. *Rehabilitation Psychology, 50*(4), 325-336.

Schulz, K.F., Altman, D.G., Moher, D., & The CONSORT Group. (2010). CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *British Medical Journal, 340*, c332.

Sharif, F., Shaygan, M., & Mani, A. (2012). Effect of a psycho-educational intervention for family members on caregiver burdens and psychiatric symptoms in patients with schizophrenia in Shiraz, Iran. *BMC Psychiatry, 12*, 48.

Shin, S-K. (2004). Effects of culturally relevant psychoeducation for Korean American families of persons with chronic mental illness. *Research on Social Work Practice, 14*(4), 231-239.

Sin, J. (2013). Focus group study of siblings of individuals with psychosis: views on designing an online psychoeducational resource. *Journal of Psychosocial nursing and Mental Health Services, 51*(6), 28-36.

Sin, J., Gillard, S., Spain, D., Cornelius, V., Chen, T., & Henderson, C. (2016). Effectiveness of psychoeducational interventions for family carers of people with psychosis. Retrieved from http://www.crd.york.ac.uk/PROSPERO_REBRANDING/display_record.asp?ID=CRD42016033176

Sin, J., Henderson, C., & Norman, I. (2014). Usability of online psychoeducation for siblings of people with psychosis. *International Journal of Technology Assessment in Health Care, 30*(4), 374-380.

Sin, J., Henderson, C., Pinfold, V., & Norman, I. (2013). *The E Sibling Project* - Development and exploratory randomised controlled trial of an online multi-component psychoeducational intervention for siblings of individuals with first episode psychosis. *BMC Psychiatry, 13*, 123. doi:10.1186/1471-244X-13-123.

Sin, J., Jordan, C., Barley, E., Henderson, C., & Norman, I. (2015). Psychoeducation for siblings of individuals with severe mental illness. Cochrane Database of Systematic Reviews (Publication no. 10.1002/14651858.). (Art. No.: CD010540.Pub.2).

Sin, J., Moone, N., Harris, P., Scully, E., & Wellman, N. (2012). Understanding the experiences and service needs of siblings of individuals with first episode psychosis: A phenomenological study. *Early Intervention in Psychiatry, 6*, 53-59.

Sin, J., Moone, N., & Newell, J. (2007). Developing services for the carers of young adults with early-onset psychosis - implementing evidence-based practice on psychoeducaitonal family intervention. *Journal of Psychiatric and Mental Health Nursing, 14*, 282-290.

Sin, J., Moone, N., & Wellman, N. (2005). Developing services for the carers of young adults with early onset psychosis: listening to their experiences and needs. *Journal of Psychiatric and Mental Health Nursing, 12*, 589-597.

Sin, J., & Norman, I. (2013). Psychoeducational interventions for families of individuals with schizophrenia: A mixed method systematic review. *Journal of Clinical Psychiatry, 74*(12), e1145-e1162.

Smith, J.V., & Birchwood, M.J. (1987). Specific and non-specific effects of educational intervention with families living with a schizophrenic relative. *British Journal of Psychiatry, 150*, 645-652.

Smith, L., Onwumere, J., Craig, T., McManus, S., Bebbington, P., & Kuipers, E. (2014). Mental and physical illness in caregivers: results from an English national survey sample. *British Journal of Psychiatry, 205*, 197-203.

So, H., Chen, E., Wong, C., Hung, S., Chung, D., Ng, S., & Chan, C. (2006). Efficacy of brief intervention for carers of people with first-episode psychosis: A waiting list controlled study. *Hong Kong Journal of Psychiatry, 16*(3), 92-100.

Spencer, J. H., Glick, I. D., Haas, G. L., Clarkin, J. F., Lewis, A. B., Peyser, J., . . . Lestelle, V. (1988). A randomised controlled trial of inpatient family intervention: III. Effects at 6-month and 18-month follow-ups. *American Journal of Psychiatry, 145*(9), 1115-1121.

Szmukler, G. (1996). From family 'burden' to caregiving. *Psychiatric Bulletin, 20*, 449-451.

Szmukler, G., Burgess, P., Herrman, H., Benson, A., Colusa, S., & Bloch, S. (1996). Caring for relatives with serious mental illness; the development of the experience of caregiving inventory. *Social Psychiatry & Psychiatric Epidemiology, 31*, 137-148.

Szmukler, G., Kuipers, E., Joyce, J., Harris, T., Leese, M., Maphosa, W., & Staples, E. (2003). An exploratory randomised controlled trial of a support programme for carers of patients with a psychosis. *Social Psychiatry & Psychiatric Epidemiology, 38*, 411-418.

Webb, T.L., Joseph, J., Yardley, L., & Michie, S. (2010). Using the internet to promote health behaviour change: A systematic review and meta-analysis of the impact of theoretical basis, use of behaviour change techniques, and mode of delivery on efficacy. *Journal of Medical Internet Research, 12*(1), e4.

Xia, J., Merinder, L.B., & Belgamwar, M.R. (2011). Psychoeducation for schizophrenia. Cochrane Database of Systematic Reviews 2011 (Publication no. Issue 6. Art No.: CD002831. DOI: 10.1002/14651858.CD002831.pub2.).

Yesufu-Udechuku, A., Harrison, B., Mayo-Wilson, E., Young, N., Woodhams, P., Shiers, D., . . . Kendall, T. (2015). Interventions to improve the experience of caring for people with severe mental illness: systematic review and meta-analysis. *British Journal of Psychiatry, 206*, 268-274.