

# Best Evidence Summaries of Topics in Mental Healthcare

**BEST in MH** *clinical question-answering service*

## Question

“In adults with psychosis and comorbid substance misuse, how effective is family/carer work, in improving patient outcomes?”

## Clarification of question using PICO structure

*Patients:* In adults with psychosis and comorbid substance misuse  
*Intervention:* Family/carer work  
*Comparator:* Treatment as usual/any other intervention  
*Outcome:* Improving patient outcomes

## **Clinical and research implications**

Evidence from one small, high quality randomised controlled trial indicated that family interventions may benefit both patients with psychosis and co-morbid substance misuse and their family members. However, there were problems in establishing initial engagement and maintaining continued participation. Further research is needed to confirm these findings, and to explore the relative effectiveness of different types of family intervention.

### **What does the evidence say?**

#### ***Number of included studies/reviews (number of participants)***

We identified one randomised controlled trial (RCT), reported in two publications,<sup>2,3</sup> which provided data relevant to this evidence summary. This trial assessed the effects, on both patients and family members, of a long-term (9 to 18 month) program that combined education with teaching communication and problem-solving skills, Family Intervention for Dual Disorders (FIDD), compared to a brief (2 to 3 month) Family Education (ED) program.<sup>3</sup>

#### ***Main Findings***

Both the FIDD and the ED were associated with significant improvements over time for patients (substance abuse (Substance Abuse Treatment Scale (SATS), Alcohol Use Scale (AUS), Drug Use Scale (DUS)), psychiatric symptoms (Brief Psychiatric Rating Scale (BPRS) total, BPRS depression sub-scale, BPRS retardation subscale), functioning (percent stable days in the community, Global Assessment Scale (GAS)), and knowledge of co-occurring disorders) and for family members (knowledge of co-occurring disorders, quality of life (SF-12 mental component, and worry, stigma and financial expenditure components of the Family Experiences Interview Schedule (FEIS)).<sup>3</sup> There were significant treatment effects, in favour of FIDD, for patient symptoms (BPRS total and BPRS psychosis sub-scale).<sup>3</sup> There were also significant treatment effects, in favour of FIDD, for family member knowledge of co-occurring conditions and family member SF-12 mental component.<sup>3</sup> However, initial engagement and continued participation of families was problematic in both FIDD and ED groups.<sup>3</sup>

#### ***Authors Conclusions***

The authors concluded that their findings support the utility of family interventions for co-occurring disorders, and the added benefits of communication and problem-solving training over education alone. They also noted the need to modify these interventions to improve retention in treatment.

#### ***Reliability of conclusions/Strength of evidence***

One small, but good quality RCT provided evidence to indicate that family interventions may be beneficial to both patients with psychosis and co-morbid substance misuse and their family members.<sup>3</sup> There was some evidence to indicate that a longer-term intervention, combining education with teaching communication and problem-solving skills, may offer greater benefits than a short term educational intervention alone.<sup>3</sup> The results of this study are likely to be reliable, but further research is needed to confirm these findings.

## What do guidelines say?

NICE guidelines regarding psychosis and coexisting substance misuse (CG120, 2011) makes the following recommendations for family/carer work;

“When families, carers or significant others live or are in close contact with the person with psychosis and coexisting substance misuse, offer family intervention as recommended in Schizophrenia: core interventions in the treatment and management of schizophrenia in adults in primary and secondary care (NICE clinical guideline 82).” (pp.11, see below)

“When families, carers or significant others are involved in supporting the person with psychosis and coexisting substance misuse, discuss with them any concerns about the impact of these conditions on them and on other family members... a carer's assessment of their caring, physical, social, and mental health needs... Offer written and verbal information to families, carers or significant others appropriate to their level of understanding about the nature and treatment of psychosis and substance misuse... Offer information to families, carers or significant others about local family or carer support groups and voluntary organisations.”  
(CG120 pp. 12)

NICE guidelines for schizophrenia (CG82) as mentioned above has been updated (now CG178, 2014). This guideline makes the following recommendations regarding carer/family work;

“Offer family intervention to all families of people with psychosis or schizophrenia who live with or are in close contact with the service user.” (pp.9)

“Offer carers of people with psychosis or schizophrenia an assessment (provided by mental health services) of their own needs and discuss with them their strengths and views. Develop a care plan to address any identified needs, give a copy to the carer and their GP and ensure it is reviewed annually.” (pp.12)

“Give carers written and verbal information in an accessible format about:

- diagnosis and management of psychosis and schizophrenia
- positive outcomes and recovery
- types of support for carers
- role of teams and services
- getting help in a crisis.”

“Offer a carer-focused education and support programme, which may be part of a family intervention for psychosis and schizophrenia, as early as possible to all carers. The intervention should:

- be available as needed
- have a positive message about recovery.” (all pp.13)

The evidence included in this summary is consistent with current guidelines.

**Date question received:** 25/02/2014

**Date searches conducted:** 04/03/2014

**Date answer completed:** 24/03/2014

## References

### ***Randomised controlled trials***

1. Mueser, K.T., Glynn, S.M., Cather, C., Xie, H., Zarate, R., Smith, L.F., Clark, R.E., Gottlieb, J.D., Wolfe, R. and Feldman, J. (2013) A Randomized Controlled Trial of Family Intervention for Co-occurring Substance Use and Severe Psychotic Disorders. *Schizophrenia Bulletin* 39 (3) pp.658-672.
2. Meuser, K.T., Glynn, S.M., Cather, C., Zarate, R., Fox, L., Feldman, J., Wolfe, R. and Clark, R.E. (2009) Family intervention for co-occurring substance use and severe psychiatric disorders: Participant characteristics and correlates of initial engagement and more extended exposure in a randomised controlled trial. *Addictive Behaviours* 34 pp.867-877.

### ***Guidelines***

National Institute for Health and Care Excellence (2011) Psychosis with coexisting substance misuse. Assessment and management in adults and young people. CG120. London: National Institute for Health and Care Excellence. <http://www.nice.org.uk/nicemedia/live/13414/53729/53729.pdf>

National Institute for Health and Care Excellence (2014) Psychosis and schizophrenia in adults: treatment and management. CG178. London: National Institute for Health and Care Excellence. <http://www.nice.org.uk/nicemedia/live/14382/66534/66534.pdf>

## Results

### *Randomised controlled trials*

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
<p>Mueser et al. (2009); this article reports only participant characteristics and correlates of initial and ongoing engagement.</p> <p>AND</p> <p>Mueser et al. (2013); this article looks at the three year outcomes of the study. *</p>	<p><i>Participants:</i> Inclusion criteria: age ≥18 years; psychiatric diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder DSM-IV (SCID); diagnosis of active substance abuse or dependence within the past 6 months, based on the SCID; at least 4 hours per week contact between the study client and index relative, close friend, or other person with a caring but non-professional relationship; client currently receiving services at 1 of the 3 agencies participating in the study; willingness of the client and a family member to provide written informed consent for the study.</p> <p><i>Intervention:</i> Family Intervention for Dual Disorders (FIDD). This intervention involved teaching the client and family members information about co-occurring disorders in order to facilitate their ability to make informed treatment</p>	<p>n=108 (ED n=56, FIDD n=52)</p>	<p>The aim of the study aimed to assess the effects, on patients and families, of a long-term (9 to 18 month) program that combined education with teaching communication and problem-solving skills, Family Intervention for Dual Disorders (FIDD), compared to a brief (2 to 3 month) Family Education (ED) program.</p> <p>There were no significant baseline differences between patients and families in the ED and FIDD groups.</p> <p>Forty-six of 52 families (88%) were engaged in the FIDD program and received a mean of 20 ± 11 sessions, compared with 47/56 (84%) of families in the ED group who received an average of 7 ± 2 sessions. Of the 52 families in FIDD, 32 (66%) had extended exposure to the program, compared with 31/56 (55%) of families in the ED group. Multivariate logistic regression analysis indicated three consistent predictors of engagement and exposure to ED or FIDD were study site (Boston higher than Los Angeles), absence of patient amphetamine use disorder, and key relative in full-time employment. Predictors of engagement only: Key relative having a lower perception of benefit from their relationship with the patient.</p>	<p>Randomisation was undertaken by an off-site project co-ordinator, using a computer program. No one was aware of the randomisation sequence in advance.</p> <p>The nature of the intervention precludes blinding of participants and practitioners.</p>

	<p>decisions and access desired services, using the same curriculum and teaching techniques in single family sessions as the family education condition. In addition, FIDD sought to reduce family tension and stress that could exacerbate psychiatric symptoms and facilitate the ability of the family to address substance abuse problems by teaching communication and problem solving skills using social learning methods such as role plays and home assignments to practice the skills. Family sessions were provided on a declining contact basis, starting with weekly sessions for approximately 3 months, followed by biweekly sessions for 6 months, and monthly sessions thereafter for a total duration of 9–18 months.</p> <p><i>Comparator:</i> Family psychoeducation (ED); focused on teaching family members, including the client information about co-occurring disorders and their treatment in order to help them make informed treatment decisions and to access desired services within their mental health agency or their broader community. Education was provided in single-family sessions over 6–8 weekly 1-hour sessions, with all involved family members at a location convenient for the family.</p>		<p>Predictors of exposure only: male patient; fewer days of patient drug use over preceding six months.</p> <p>Forty-eight participants completed the three year assessment (25 in the ED group and 23 in the FIDD group). Patients who completed the three year assessment were less likely to have baseline opiate use disorder, had less severe baseline DUS drug abuse ratings, and had used drugs on fewer days during the six months preceding the study.</p> <p><i>Patient outcomes:</i> Outcomes showing significant improvement in mean (SD) score, from baseline to 36 months, in both ED and FIDD groups were: Substance Abuse Treatment Scale (SATS), ED 2.89 (1.37) to 4.20 (2.24), FIDD 3.21 (1.24) to 4.21 (2.59); Alcohol Use Scale (AUS), ED 3.88 (0.63) to 2.13 (1.41), FIDD 3.78 (0.54) to 1.92 (1.38); Drug Use Scale (DUS), ED 4.06 (0.57) to 2.38 (1.26), FIDD 3.98 (0.56) to 2.50 (1.52); Brief Psychiatric Rating Scale (BPRS) total, ED 2.04 (0.50) to 1.87 (0.53), FIDD 2.02 (0.59) to 1.86 (0.51); BPRS depression, ED 2.65 (0.95) to 2.18 (0.89), FIDD 2.78 (1.10) to 2.42 (1.07); BPRS retardation, ED 1.68 (0.60) to 1.64 (0.61), FIDD 1.55 (0.56) to 1.51 (0.51); percent stable days in the community, ED 0.87 (0.25) to 0.93 (0.18), FIDD 0.84 (0.29) to 0.92 (0.19); Global Assessment Scale (GAS), ED 42.68 (8.21) to 47.54 (9.07), FIDD 43.38 (10.06) to 48.27 (12.01); patient knowledge, ED 24.09 (13.77) to 30.90 (14.77), FIDD 27.04 (13.96) to 34.77 (16.61). Number of</p>	<p>Assessments were conducted by trained interviewers who were blind to treatment assignment at baseline.</p> <p>Intention-to-treat (ITT) analyses were conducted.</p> <p>Results were reported for all specified outcome measures.</p>
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	<p><i>Outcomes:</i></p> <p>Psychiatric symptoms, medication adherence and overall functioning (BPRS, GAS); knowledge and social problem solving (test adapted from McGill et al., The Social Problem-Solving Inventory), key relative mental and physical functioning (SF-12), family caregiving (FEIS); substance abuse (SATS, AUS, DUS, days drinking/using drugs).</p>		<p>days using drugs, the psychosis sub-scale of the BPRS, and number of days of medication non-adherence showed borderline significant improvements in both ED and FIDD groups.</p> <p>There were significant treatment group differences, favouring FIDD, in BPRS total score, <math>F = 3.79</math>, <math>df = 1.86</math>, <math>P = 0.05</math>, and the psychosis sub-scale, <math>F = 7.10</math>, <math>df = 1.86</math>, <math>P = 0.009</math>. There were significant treatment effects (based on comparisons of baseline score with mean follow-up score), favouring FIDD over ED, for BPRS total score (effect size 0.17) and BPRS psychosis sub-scale (effect size 0.32). There was a borderline significant treatment effect, favouring FIDD, for GAS.</p> <p><i>Family member outcomes:</i></p> <p>Outcomes showing significant improvement in mean (SD) score, from baseline to 36 months, in both ED and FIDD groups were: family member knowledge, ED 29.34 (17.46) to 35.55 (19.99), FIDD 31.51 (20.09) to 41.19 (21.88); SF-12 mental component, ED 47.66 (10.73) to 52.16 (8.20), FIDD 43.35 (12.51) to 49.91 (10.61); Family Experiences Interview Schedule (FEIS) worry sub-scale, ED 2.37 (0.89) to 2.15 (1.01), FIDD 2.53 (0.83) to 2.06 (0.81); FEIS stigma sub-scale, ED 0.19 (0.25) to 0.03 (0.08), FIDD 0.24 (0.27) to 0.13 (0.26); FEIS financial expenditure sub-scale, ED 3.07 (2.50) to 2.09 (2.05), FIDD 3.36 (2.59) to 2.52 (2.73); FEIS dollars spent in previous 30 days, ED 279.80 (332.49) to 212.55 (416.11), FIDD 309.12 (366.92) to 200.90</p>	
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			(318.65).  There were significant treatment group differences, favouring FIDD, in knowledge of co-occurring disorders, $F = 11.55$ , $df = 1.75$ , $P = 0.001$ , and the mental component of the SF-12, $F = 4.48$ , $df = 1.78$ , $P = 0.04$ .	
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**\* Two publications relating to the same trial**




## Risk of Bias


### *Randomised controlled trials*

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Mueser et al. (2009) and Mueser et al. (2013)*						

\* Two reports of the same trial

 Low Risk

 High Risk

 Unclear Risk

## Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
<i>SRs and Guidelines</i>			
NICE			
DARE	<p>1 ((Schizo* OR psycho* OR psychosis, substance-induced)) IN DARE 4268 Delete</p> <p>2 MeSH DESCRIPTOR Psychotic Disorders EXPLODE ALL TREES 143 Delete</p> <p>3 MeSH DESCRIPTOR Schizophrenia EXPLODE ALL TREES 472 Delete</p> <p>4 MeSH DESCRIPTOR Schizophrenia and Disorders with Psychotic Features EXPLODE ALL TREES 564 Delete</p> <p>5 MeSH DESCRIPTOR Schizophrenia, Paranoid EXPLODE ALL TREES 1 Delete</p> <p>6 ((alcohol* OR drinker* OR drinking*)) IN DARE 694 Delete</p> <p>7 ((substance abus* OR drug abus* OR alcohol* OR cannabis*)) IN DARE 827 Delete</p> <p>8 ((drug* OR substanc* OR alcoh* OR opioid* OR amphetamine* OR opiate* OR cocaine* OR marijuana* OR cannabis OR phencyclidine OR benzodiaz OR polydrug* or tranquiliz* or narcot* or (street adj1 drug*) or solvent* or inhalan* or intoxi*) adj3 (misuse OR abuse* OR addict* OR depend* OR disorder*)) IN DARE 697 Delete</p> <p>9 MeSH DESCRIPTOR Substance-Related Disorders EXPLODE ALL TREES 720 Delete</p> <p>10 MeSH DESCRIPTOR Alcohol-Related Disorders EXPLODE ALL TREES 241 Delete</p> <p>11 MeSH DESCRIPTOR Alcoholism EXPLODE ALL TREES 169 Delete</p> <p>12 MeSH DESCRIPTOR Alcoholics EXPLODE ALL TREES 0 Delete</p> <p>13 MeSH DESCRIPTOR Drug Users EXPLODE ALL TREES 9 Delete</p> <p>14 MeSH DESCRIPTOR Heroin Dependence EXPLODE ALL TREES 29 Delete</p> <p>15 MeSH DESCRIPTOR Alcohol Drinking EXPLODE ALL TREES 126 Delete</p> <p>16 ((carer* OR caregiv* OR care-giver OR spouse-caregiver* OR family support OR family intervention*)) IN DARE 634 Delete</p> <p>17 MeSH DESCRIPTOR Caregivers EXPLODE ALL TREES 179 Delete</p> <p>18 MeSH DESCRIPTOR Family Therapy EXPLODE ALL TREES 72 Delete</p>	30	1

	19 MeSH DESCRIPTOR Family Relations EXPLODE ALL TREES 138 Delete 20 #1 OR #2 OR #3 OR #4 OR #5 4528 Delete 21 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 1519 Delete 22 #16 OR #17 OR #18 OR #19 875 Delete 23 #20 AND #21 AND #22 30 Delete		
<b>Primary studies</b>			
CENTRAL	#1 MeSH descriptor: [Psychotic Disorders] explode all trees 1464 #2 psychosis or psychoticpsychosis or psychotic 5077 #3 #1 or #2#1 or #2 5077 #4 MeSH descriptor: [Substance-Related Disorders] explode all trees 8993 #5 substance or drug* or alcohol*:ti (Word variations have been searched) 21879 #6 "substance misuse""substance misuse" 264 #7 "substance abuse""substance abuse" 3290 #8 "dual diagnosis""dual diagnosis" 121 #9 co-occurringco-occurring 379 #10 co-morbidco-morbid 730 #11 #8 or #9 or #10#8 or #9 or #10 1191 #12 substance or drug or alcoholsubstance or drug or alcohol 341949 #13 #11 and #12#11 and #12 860 #14 #4 or #5 or #6 or #7 or #13#4 or #5 or #6 or #7 or #13 28480 #15 family or familiesfamily or families 19509 #16 carers or caregiverscarers or caregivers 4356 #17 MeSH descriptor: [Family Therapy] explode all trees 650 #18 MeSH descriptor: [Caregivers] explode all trees 1071 #19 MeSH descriptor: [Family] explode all trees 5077 #20 #17 or #18 or #196250 #21 #3 and #14 and #20 = 20 (7 in Central)	7	
PsycINFO	1. PsycINFO; PSYCHOSIS/; 19212 results. 2. PsycINFO; psychosis.ti,ab; 27032 results. 3. PsycINFO; psychotic.ti,ab; 31154 results. 4. PsycINFO; DRUG ABUSE/; 35446 results.	33	

<p>5. PsycINFO; (substance adj3 abuse*).ti,ab; 26242 results.</p> <p>6. PsycINFO; (substance adj3 misuse).ti,ab; 1996 results.</p> <p>7. PsycINFO; (drug* OR alcohol* OR substance*).ti; 98666 results.</p> <p>8. PsycINFO; addict*.ti; 11779 results.</p> <p>9. PsycINFO; "dual diagnosis".ti,ab; 1761 results.</p> <p>10. PsycINFO; co-occurring.ti,ab; 3772 results.</p> <p>11. PsycINFO; comorbidity.ti,ab; 14924 results.</p> <p>12. PsycINFO; 9 OR 10 OR 11; 19739 results.</p> <p>13. PsycINFO; (drug* OR alcohol* OR substance*).ti,ab; 259423 results.</p> <p>14. PsycINFO; 12 AND 13; 7241 results.</p> <p>15. PsycINFO; 5 OR 6 OR 7 OR 8 OR 14; 123660 results.</p> <p>16. PsycINFO; 1 OR 2 OR 3; 51898 results.</p> <p>17. PsycINFO; 15 AND 16; 3345 results.</p> <p>18. PsycINFO; "family intervention".ti,ab; 1150 results.</p> <p>19. PsycINFO; "family work".ti,ab; 961 results.</p> <p>20. PsycINFO; "family therapy".ti,ab; 12468 results.</p> <p>21. PsycINFO; family.ti; 58244 results.</p> <p>22. PsycINFO; families.ti; 19475 results.</p> <p>23. PsycINFO; FAMILY INTERVENTION/; 1875 results.</p> <p>24. PsycINFO; FAMILY THERAPY/; 18373 results.</p> <p>25. PsycINFO; FAMILY MEMBERS/ OR FAMILY [+NT]/; 46500 results.</p> <p>26. PsycINFO; carer*.ti,ab; 6146 results.</p> <p>27. PsycINFO; caregiver*.ti,ab; 28390 results.</p> <p>28. PsycINFO; CAREGIVERS/; 18286 results.</p> <p>29. PsycINFO; 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28; 135225 results.</p> <p>30. PsycINFO; 17 AND 29; 94 results.</p> <p>31. PsycINFO; CLINICAL TRIALS/; 7349 results.</p> <p>32. PsycINFO; random*.ti,ab; 126950 results.</p> <p>33. PsycINFO; groups*.ti,ab; 361055 results.</p>		
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	<p>34. PsycINFO; (doubl* adj3 blind*).ti,ab; 18078 results.</p> <p>35. PsycINFO; (singl* adj3 blind*).ti,ab; 1600 results.</p> <p>36. PsycINFO; EXPERIMENTAL DESIGN/; 8959 results.</p> <p>37. PsycINFO; controlled.ti,ab; 79049 results.</p> <p>38. PsycINFO; (clinical adj3 study).ti,ab; 7768 results.</p> <p>39. PsycINFO; trial.ti,ab; 66889 results.</p> <p>40. PsycINFO; "treatment outcome clinical trial".md; 26186 results.</p> <p>41. PsycINFO; RCT.ti,ab; 1796 results.</p> <p>42. PsycINFO; 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41; 558615 results.</p> <p>43. PsycINFO; 30 AND 42; 33 results.</p>		
Embase	<p>44. EMBASE; PSYCHOSIS/; 61058 results.</p> <p>45. EMBASE; psychosis.ti,ab; 31646 results.</p> <p>46. EMBASE; psychotic.ti,ab; 31378 results.</p> <p>47. EMBASE; 44 OR 45 OR 46; 81264 results.</p> <p>48. EMBASE; (substance adj3 abuse*).ti,ab; 23836 results.</p> <p>49. EMBASE; (substance adj3 misuse).ti,ab; 2039 results.</p> <p>50. EMBASE; (drug* OR alcohol* OR substance*).ti; 531973 results.</p> <p>51. EMBASE; addict*.ti; 19689 results.</p> <p>52. EMBASE; DRUG ABUSE/; 41134 results.</p> <p>53. EMBASE; SUBSTANCE ABUSE/; 38534 results.</p> <p>54. EMBASE; DRUG DEPENDENCE/; 32254 results.</p> <p>55. EMBASE; 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54; 609611 results.</p> <p>56. EMBASE; "dual diagnosis".ti,ab; 1495 results.</p> <p>57. EMBASE; co-occurring.ti,ab; 4499 results.</p> <p>58. EMBASE; comorbidity.ti,ab; 39784 results.</p> <p>59. EMBASE; 56 OR 57 OR 58; 45104 results.</p> <p>60. EMBASE; (drug* OR alcohol* OR substance*).ti,ab; 1778703 results.</p> <p>61. EMBASE; 59 AND 60; 11227 results.</p> <p>62. EMBASE; 55 OR 61; 614548 results.</p>	36	

	<p>63. EMBASE; "family intervention".ti,ab; 788 results.</p> <p>64. EMBASE; "family work".ti,ab; 343 results.</p> <p>65. EMBASE; "family therapy".ti,ab; 3605 results.</p> <p>66. EMBASE; family.ti; 119155 results.</p> <p>67. EMBASE; families.ti; 26962 results.</p> <p>68. EMBASE; carer*.ti,ab; 11093 results.</p> <p>69. EMBASE; caregiver*.ti,ab; 39978 results.</p> <p>70. EMBASE; FAMILY THERAPY/; 10268 results.</p> <p>71. EMBASE; FAMILY/; 71867 results.</p> <p>72. EMBASE; CAREGIVER/; 37918 results.</p> <p>73. EMBASE; 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72; 250907 results.</p> <p>74. EMBASE; 47 AND 62 AND 73; 297 results.</p> <p>75. EMBASE; random*.tw; 848204 results.</p> <p>76. EMBASE; factorial*.tw; 22143 results.</p> <p>77. EMBASE; placebo*.tw; 192053 results.</p> <p>78. EMBASE; (crossover* OR cross-over*).tw; 66790 results.</p> <p>79. EMBASE; (doubl* adj3 blind*).tw; 137409 results.</p> <p>80. EMBASE; (singl* adj3 blind*).tw; 16051 results.</p> <p>81. EMBASE; assign*.tw; 230037 results.</p> <p>82. EMBASE; allocat*.tw; 80028 results.</p> <p>83. EMBASE; volunteer*.tw; 170847 results.</p> <p>84. EMBASE; CROSSOVER PROCEDURE/; 38055 results.</p> <p>85. EMBASE; DOUBLE-BLIND PROCEDURE/; 111871 results.</p> <p>86. EMBASE; SINGLE-BLIND PROCEDURE/; 17910 results.</p> <p>87. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 336876 results.</p> <p>88. EMBASE; 75 OR 76 OR 77 OR 78 OR 79 OR 80 OR 81 OR 82 OR 83 OR 84 OR 85 OR 86 OR 87; 1359756 results.</p> <p>89. EMBASE; 74 AND 88; 36 results.</p>		
Medline	90. MEDLINE; PSYCHOSIS/; 31471 results.	58	

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| <p>91. MEDLINE; psychotic.ti,ab; 23052 results.</p> <p>92. MEDLINE; 44 OR 45 OR 91; 57119 results.</p> <p>93. MEDLINE; (substance adj3 abuse*).ti,ab; 18918 results.</p> <p>94. MEDLINE; (substance adj3 misuse).ti,ab; 1386 results.</p> <p>95. MEDLINE; (drug* OR alcohol* OR substance*).ti; 441621 results.</p> <p>96. MEDLINE; addict*.ti; 15851 results.</p> <p>97. MEDLINE; DRUG ABUSE/; 76529 results.</p> <p>98. MEDLINE; ALCOHOLISM/; 65786 results.</p> <p>99. MEDLINE; 93 OR 94 OR 95 OR 96 OR 97 OR 98; 513630 results.</p> <p>100. MEDLINE; "dual diagnosis".ti,ab; 980 results.</p> <p>101. MEDLINE; co-occurring.ti,ab; 3947 results.</p> <p>102. MEDLINE; comorbidity.ti,ab; 27136 results.</p> <p>103. MEDLINE; 100 OR 101 OR 102; 31574 results.</p> <p>104. MEDLINE; (drug* OR alcohol* OR substance*).ti,ab; 1455017 results.</p> <p>105. MEDLINE; 103 AND 104; 7569 results.</p> <p>106. MEDLINE; 99 OR 105; 516836 results.</p> <p>107. MEDLINE; "family intervention".ti,ab; 587 results.</p> <p>108. MEDLINE; "family work".ti,ab; 245 results.</p> <p>109. MEDLINE; "family therapy".ti,ab; 2608 results.</p> <p>110. MEDLINE; family.ti; 110832 results.</p> <p>111. MEDLINE; families.ti; 24678 results.</p> <p>112. MEDLINE; carer*.ti,ab; 7838 results.</p> <p>113. MEDLINE; caregiver*.ti,ab; 30667 results.</p> <p>114. MEDLINE; FAMILY THERAPY/; 7531 results.</p> <p>115. MEDLINE; FAMILY/; 60108 results.</p> <p>116. MEDLINE; CAREGIVER/; 20693 results.</p> <p>117. MEDLINE; 107 OR 108 OR 109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115 OR 116; 214044 results.</p> <p>118. MEDLINE; psychosis.ti,ab; 23651 results.</p> <p>119. MEDLINE; psychotic.ti,ab; 23052 results.</p> <p>120. MEDLINE; PSYCHOTIC DISORDERS/; 31471 results.</p> <p>121. MEDLINE; 118 OR 119 OR 120; 57119 results.</p> |  |  |
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	<p>122. MEDLINE; 106 AND 117 AND 121; 183 results.</p> <p>123. MEDLINE; "randomized controlled trial".pt; 367276 results.</p> <p>124. MEDLINE; "controlled clinical trial".pt; 87861 results.</p> <p>125. MEDLINE; randomi?ed.ab; 343341 results.</p> <p>127. MEDLINE; "drug therapy".fs; 1675625 results.</p> <p>128. MEDLINE; randomly.ab; 208230 results.</p> <p>129. MEDLINE; trial.ab; 297224 results.</p> <p>130. MEDLINE; groups.ab; 1329140 results.</p> <p>131. MEDLINE; RCT.ti,ab; 8350 results.</p> <p>132. MEDLINE; 123 OR 124 OR 125 OR 127 OR 128 OR 129 OR 130 OR 131; 3280213 results.</p> <p>133. MEDLINE; 122 AND 132; 58 results.</p>		
<b>Summary</b>	<b>NA</b>	<b>NA</b>	



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