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Prevention

Schizophrenia and related psychoses CHAPTER 1 Omega-3 fatty acid (fish oils) in schizophrenia Fish oils contain the omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA) – also known as polyunsaturated fatty acids or PUFAs. These compounds are thought to be involved in maintaining neuronal membrane structure, in the modulation of membrane proteins and in the production of prostaglandins and leuko trienes.1 Imaging studies suggest that the ratio between omega-6 and omega-3 may be relevant in the development of psychotic disorders.2 One genetic study has suggested that people with schizophrenia may have difficulty converting short-chain fatty acids to long-chain polyunsaturated fatty acids.3 High dietary intake of PUFAs may protect against psychosis4 and antipsychotic treatment seems to normalise PUFA deficits.5 Animal models suggest a protective effect for PUFAs.6 They have been suggested as treatments for a variety of psychiatric illnesses.7,8 In schizophrenia, case reports,9–12 case series13 and prospective trials originally suggested useful efficacy.14–18 Treatment A 2012 meta-analysis of these RCTs19 concluded that EPA had ‘no beneficial effect in established schizophrenia’. Since then, an RCT comprising 71 patients with first-episode schizophrenia given 2.2g EPA + DHA daily for 6 months showed a reduction in symptom severity for patients in the active arm, finding a number needed to treat (NNT) of 4 to produce a 50% reduction in symptoms measured by PANSS.20 However, a further RCT of 97 patients in acute psychosis showed no advantage for EPA 2g daily21 and a relapse prevention study of EPA 2g + DHA 1g/day failed to demonstrate any value for PUFAs over placebo (relapse rate was 90% with PUFAs, 75% with placebo).22 The limitations affecting the published data in this area (small sample sizes, heterogeneity of diagnosis and stage of illness, differences in intervention combinations and doses) mean that overall findings remain at best inconclusive.23,24 A 2019 meta-review of published meta-analyses found no evidence for the use of PUFAs in the treatment of schizophrenia.25 On balance, evidence now suggests that EPA (2–3g daily) is unlikely to be a worthwhile option in schizophrenia when added to standard treatment. Omega-3 fatty acids are not recommended by the World Federation of Societies of Biological Psychiatry for use in schizophrenia.26 Set against doubts over efficacy are the facts that fish oils are relatively cheap, well tolerated27 (mild gastrointestinal [GI] symptoms may occur) and benefit physical health.1,28–32 A few small RCTs suggest some benefit to neurocognition (social cognition),33 verbal fluency and working memory34 in recent-onset psychosis or young people at ultra-high risk of psychosis. Other studies have failed to show any benefit on aggressive behaviour.35 Prevention The Vienna High Risk study (VHR) gave 700mg EPA + 480mg DHA to adolescents and young adults at high risk of psychosis, and showed that such treatment greatly reduced emergence of psychotic symptoms compared with placebo36 (although a review described this study as ‘very low quality evidence’).37 Since publication of this single-site study, the large, multi-site NEURAPRO trial38 gave adult patients at high risk of psychosis 840mg EPA +

560mg DHA for 6 months and failed to find any evidence of efficacy either for

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