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## **Social causes and outcomes of Acute Transient Psychotic Disorder: a review of recent evidence**

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### **Introduction**

There is evidence that presentations of acute psychosis to mental health services have increased since 2019. A recent report from England (NHS Digital 2021) suggests that referrals for suspected first episode psychosis (FEP) increased by 75% between 2019 and 2021. Published case reports, and information from local services in North Wales, similarly suggest that there has been an increase in presentations of acute psychosis since 2019. The increase during the earliest phase of the Covid-19 pandemic appears to have been even higher. In the last week of May 2020, there were 31 acute inpatient and Home Treatment Team (HTT) patients (16-64 years) in North Wales, of whom five had a diagnosis first episode psychosis (FEP). Psychosis is a high prevalence/low incidence disorder, and this is an unusually high proportion of FEP amongst a small cohort of acutely unwell patients. These changes were of concern and demanded further research. In order to assess social impacts and outcomes, we conducted a literature review, which we report below, and a pilot study of new Acute Transient Psychotic Disorder (APTD) cases in one NHS health board in Wales. The latter will be reported separately.

### **Background**

Brief psychotic reactions were prominent in the nosological systems in Scandinavia, Germany and France prior to the development of operationalised international diagnostic systems (Pull et al., 2003). Research interest in them has waned subsequently. Brief psychotic episodes are classified as “acute and transient psychotic disorders” (ATPDs) in ICD-10, and “brief psychotic disorder” (BPD) in DSM-5 (Castagnini and Fusar-Poli, 2017). The World Health Organization (WHO, 1992) defines ICD-10 ATPDs as psychotic episodes fully remitting within 1 to 3 months, with acute onset within 2 weeks, and the presence of associated acute stress, such as bereavement or loss of job. In DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, fifth edition: APA 2013) the American Psychiatric Association classifies Brief Psychotic Disorders (BPD) as psychotic conditions lasting 1 day or more but less than 1 month, with complete remission to the premorbid level of functioning.

Rutigliano et al. (2018, p127) state that there is “converging evidence that brief psychotic episodes are associated with a very high risk of developing persistent psychotic disorders, in particular schizophrenia spectrum psychoses”. They estimated that up to half of patients with ATPD developed another psychotic disorder over an average follow-up of 4.5 years, mostly schizophrenia-spectrum disorders (Fusar-Poli, Cappucciati, Rutigliano et al. 2016). **There is little evidence on long-term outcomes for brief psychotic episodes, and what evidence exists is mainly based on small samples.**

More recently, Malhotra, et al (2019) have argued that there is now sufficient evidence to support the possibility that ATPDs are a distinct entity and underscore the need for pursuing alternative causal hypotheses such as neuro-inflammatory or metabolic processes. They summarise the evidence that ATPD is more commonly seen in low-and-middle-income countries (LMICs); more often affects women; onset is usually in early to middle adulthood; and occurs in people with pre-morbid good functioning and well-adjusted personality. Reports from LMICs, and in migrant populations, suggest that the most common precipitating factors are social and cultural. Studies in two LMICs countries (Nigeria and India) on acute brief psychoses reported strong associations with similar psychosocial factors (departure from parental village in females and job distress in males).

“Social outcome” refers to the ability of the person to fully and freely conduct their life, whereas “clinical outcome” refers to the presence of signs and symptoms of mental illness. Social outcome comprises a number of component domains, including employment, accommodation, financial independence, leisure activity, family relationships and safety issues. Social inclusion and quality of life are social outcome constructs. The measurement of social outcome involves capturing changes in these domains over time using quantitative and qualitative measures. Whilst psychosocial factors are generally accepted to be relevant to onset, their role in relation to recovery and outcome has been relatively ignored. As indicated above, diagnostic systems include criteria related to rapid recovery, but this is based on clinical rather than social outcomes. Social parameters are rarely measured in the ATPD literature, and when they are, the measures used lack sophistication (Singh et al., 2004). This is odd, in the light of the evidence for social/environmental causation. Malhotra et al. (2019, p7) conclude that “there is an utmost need to enhance the research in the field of ATPD to investigate various neurobiological and social aspects and identify the bio-psycho-social underpinnings of this clinical entity”.

The societal impact of the pandemic will be long lasting, which may affect social recovery from psychosis (Huxley, et al, 2021). There is a significant risk that the CV19 may recur or other infections may cause new pandemics. The pandemic has created global circumstances that may lead to different clinical and social presentations with different short- and long-term outcomes. Tailored interventions may be necessary to address social stressors associated with ‘lockdowns’, such as job-loss, financial stress, family, and childcare needs to prevent relapse or deterioration in mental health

## **Methods**

### *Literature review:*

We undertook a rapid review of the literature on social outcomes of ATPD. A full description of the search terms is set out in the online supplementary material A. Four major databases (Medline, Embase, Psychinfo and Cochrane Covid19) were searched for ATPD, psychosis and social outcomes in adults 18-65. Duplicates were removed. There were no language limitations.

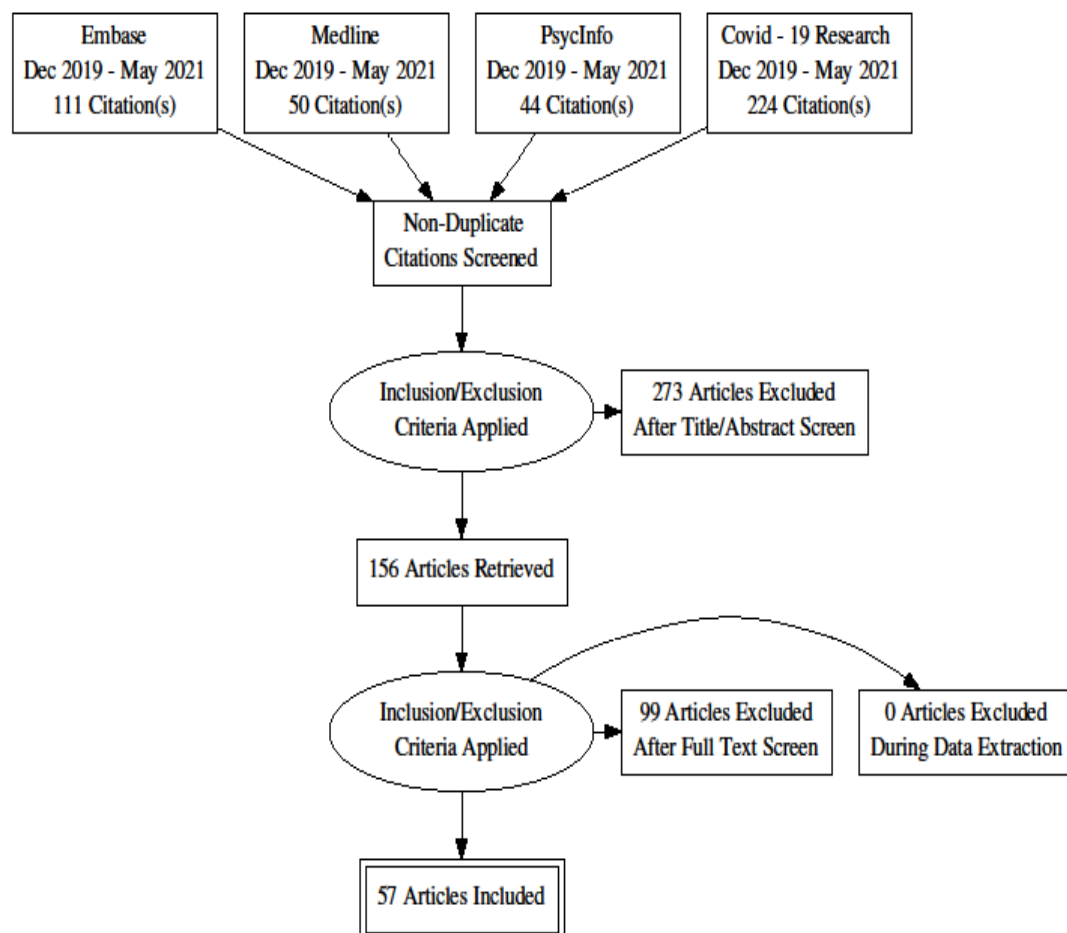
## **Results**

### *ATPD Literature*

A database search using Embase, Psychinfo, Medline and CV19 Research database was conducted in December 2020 and updated in May 2021 covering the period between 2018-2021. A total of 427 papers were identified. Following removal of duplicates and initial review of all papers, 156

publications were read by two of the authors (JC & PH), and a final total of 57 papers were used for this report. The full list of included studies is given in supplementary material B.

**Figure 1** Prisma Diagram (placed here)



The searches identified 18 original-data research papers and six reviews on the impact of CV19 on mental illness. The combined number of patients in the 18 studies is 112,597. Of the original data papers, one sample was of students, and two of health care workers. There were four samples of 'community residents', and five, first onset hospitalised cases and people with existing severe mental illness. Three studies took place in psychiatric emergency settings and there was one national cohort from South Korea.

It is important to begin with a comment on the quality of these papers. One review of 115 papers relating to health workers only (Salazar de Pablo et al 2020) concludes that many study designs are

sub-optimal and that there is little evidence concerning outcomes other than clinical measures. The study designs in our included empirical papers are also sub-optimal. 44% are on-line surveys and the rest are based upon routinely collected data. There are no cohort studies or epidemiological studies within the search period.

There is a universal acceptance that the clinical outcomes for ATPD is good in the short term, but very few papers made any mention of, or assessed, psychosocial stressors. So, with regard to the short and long term social outcome, this remains a notable gap in our understanding. The emergency data from New York (Ferrando et al 2021) showed that 11% of the sample suffered financial strain and 11% were unemployed. Another study in the USA (Szmulewicz et al 2021) found a reduction in emergency room visits year on year for patients of an early intervention service and unsurprisingly unemployment increased in the sample. Two studies used loneliness and social network measures (Lee et al 2020; , Tso et al. 2020) and one study (Van Rheenen 2020) reported that, compared to depressed patients and healthy controls, bipolar patients were more concerned about financial problems.

The study of loneliness and social networks in South Korea (Lee et al. 2020) found that in linear regressions, loneliness and low social network contacts predicted poor mental health status. The major effect was due to loneliness (more loneliness led to worse mental health). A similar finding was observed in Hong Kong (Tso et al. 2020) in 432 community residents. In a study of acute psychotic conditions in India, Malhotra et al (1998) reported that stress factors were present in 50% of female cases of but only 25.8% of males (Chi-squared = 8.43,  $p < 0.005$ ). The authors suggested that this might be due to a greater vulnerability amongst women, but did not consider whether male under-reporting of stress could be responsible for the finding.

An issue that has previously received little or no attention is whether the social stressors that contribute to first episode ATPD are the same as those that precipitate subsequent episodes of illness. As Minichino et al. (2019, p31) argue, this gap in the evidence may undermine preventive interventions. “The high long-term clinical needs of ATPDs contrasts with the relatively short clinical follow-up, high discharge rates and heterogeneous treatments observed in this group, confirming that these patients currently present with unmet needs that are not targeted by existing mental health services”. Rutigliano et al. (2018) followed up 3074 patients who had received a diagnosis of ATPD (first episode) for 8 years and reported that 61.26% retained a diagnosis of ATPDs (see also Komuravelli et al 2011). The cumulative risk of developing schizophrenia spectrum disorder over 8 years was 36.14%. In addition, Minichino et al (2019) report that over an eight-year follow-up period, 32.9% of their sample went on to be hospitalised and 28.5% were compulsorily admitted. It is very unlikely that these admissions had no social consequences, but these are not reported. **In the absence of reporting or longitudinal studies specifically examining these issues, it is therefore unknown how long social problems may persist after clinical recovery, or what factors are influential in future relapse.**

#### *ATPD and COVID-19 case reports*

A total of 33 papers / letters were reviewed, describing a total of 60 individual cases where new psychotic symptoms arose during the pandemic. (Table of extracted case study data is presented in **Table 1.**). The clinical features were heterogeneous. The majority of the papers described one and two cases, although a number of papers described small case series. Ferrando. et al (2020), Huarcaya-Victoria. et al (2020) and Jaworowski. et al (2020) all described three cases each. Valdes-Florida. et al (2020) described four cases, with D’Agostino. et al (2020) and Lazarri. et al (2020) both describing six cases. Booth and Chakraborty (2020) described eight cases of emerging psychosis, three of which presented to an Early Intervention in Psychosis service in the United Kingdom.

Almost all of the cases reported (n= 59) were assessed in an emergency department, and the majority of these cases were then admitted to a mental health unit. There were 24 individuals who were diagnosed with, and received treatment for, Covid-19, (15 Male / 9 Female) prior to transfer to a psychiatric unit. The gender mix was broadly equal (male n= 33). Mean age of males was 4 years older (44.6yrs) than females (40.6 yrs.). The age range was 20 – 73 yrs. of age. Females had a longer period of untreated symptoms before coming to the attention of services (mean 7.4 days) compared to males (mean 5 days). In nine cases there was a past history of mental health problems (3 male, 6 female). Four further participants described a family history of mental health problems.

**Table 1.** Case study extracted data (placed here)

Data extracted from 33 case study papers							
Cases				Male		Female	Total
				33 / 55%		27 / 45%	60
Age range				n = 30		n = 27	57 / 95%
				20 - 73 yrs		21 - 64 yrs	
	Mean Gender			44.6 yrs		40.6 yrs	
	Mean				42.7 yrs		
Covid DX				15 / 25%		9 / 15%	57 / 95%
Onset / DUP				n = 17		n = 16	33 / 55%
	Range			1-14 days		1-30 days	
	Mean Gender			5 days		7.4 days	
	Mean				6.2 days		
Time to remission				n = 23		n = 19	42 / 70%
	Range			1-42 days		2-34 days	
	Mean Gender			12.6 days		11 days	
	Mean				11.9 days		
Family History of MH				2		2	4 / 6.6%
Personal History of MH				3		6	9 / 15%
Married				Y = 14		Y = 5	19 / 32%
				N = 6		N = 9	15
				N/A = 13		N/A = 12	24
				Total			59
Employed				10		9	19 / 32%
Children				5		5	10 / 16.6%
Suicide attempt				6			6 / 10%

<b>Hallucinations</b>								26
<b>Delusional beliefs</b>								51
<b>Catatonia</b>								5
<b>Diagnoses n = 58</b>			Brief Psychosis / ATPD / New					30 /50%
			Acute Polymorphic Psychosis					10 / 19%
			Psychosis due to Covid					9 /15%
			Mania with Psychosis					2 /3.4%
			Exacerbation of SCZ					2
			Psychosis due medical reason					1
			Substance induced					2
			Delirium / Stress					1 / 1.7%
			Post Peurperal					1
<b>Medication</b>			Olanzapine					19 / 32%
			Risperidone					10 / 19%
			Haloperidol					10 / 19%
			Aripiprazole					6 / 10%
			Quetiapine					6 / 10%
			Depot medication					3 / 5%
			Lorazepam					12 / 20%
			Clonazepam					7 / 11.65%
			Diazepam					2 / 3.4%
			Fluoxetine					2
			Sertraline					2
			Valproic Acid					2

Clinical outcome data was reported, for example, time to remission of psychotic symptoms, where this occurred whilst in hospital. Females recovered slightly more quickly (mean 11 days) than males (mean 12.6 days). Where clinical follow up information was presented, this reported either compliance with or discontinuation of medication and whether psychotic symptoms remained following discharge. Social outcome data reported was limited and where reported was vague, for example: “a return to employment had taken place quickly”; “a return to baseline functioning had occurred”; “a return to employment had not materialised”.

A number of case descriptions (n=9) commented that the emergence of psychotic symptoms was consistent with a neuropsychiatric manifestation of Covid -19 infection, or that psychotic features might be an early indicator of viral infection (Lanier et al 2020, Lim, 2020, Mawhinney et al, 2020, Noone et al, 2020, Ferrando et al 2020, Lorenzo-Villalba, et al 2020, Majadas, et al 2020 and Kozato et al, 2021). Majadas (2020) concludes that whilst triggering of psychosis by Covid-19 infection is speculative, inflammatory and auto-immune process are implicated in a proportion of cases of acute psychosis. These same process can occur in viral infection.

The predominant symptoms of psychosis highlighted in the case studies were delusional beliefs (n=51) frequently with themes concerning Covid-19 infection, such as being responsible for spreading the virus. Auditory hallucinations (n=26), and catatonic type presentations (n= 5) were also present. Six male patients made suicide attempts; there were none reported amongst women.

Pharmacological treatment for presenting psychotic symptoms was mainly antipsychotic medication (n=54). Olanzapine (n=19), Risperidone (n=10) and Haloperidol (n=10) were most frequently prescribed. Quetiapine and Aripiprazole were each prescribed in six cases. In 21 cases, antipsychotics were given in combination with an anxiolytic, usually Lorazepam or Clonazepam. Antidepressant medication was used in six cases, in combination with an antipsychotic.

Of the 60 cases reviewed, 58 cases (96.6%) received a formal diagnosis which included: Acute and transient psychosis / brief reactive psychosis accounted for 40 cases (69%); there were 9 cases (15%) where the diagnosis was considered to be consistent with neuropsychiatric manifestation. The remaining nine cases (15%) diagnoses were as follows: mania with psychosis, exacerbation of previously diagnosed schizophrenia and substance induced psychosis each accounted for two cases. Diagnoses of post-puerperal psychosis, psychosis due to medical reason and delirium / stress, accounted for the remaining three cases.

Within the cases reviewed, the stressors associated with the pandemic were considered influential in the development of a psychotic episode. However, in most papers, social precipitants were not reported, and outcome was predominantly focussed on symptomatic remission. It was possible to identify 23 cases (38%) where social, health and familial factors were stress inducing events, potentially implicated in the development of the episode.

## Discussion

Despite the limitations, the literature and case study series all point to similar social factors as precipitants of ATPD. Some of these are related to the pandemic and to the impact of lockdown, whereas others have a more everyday character. With regard to the latter, prominent factors are bereavement, homelessness, unemployment, financial strain, and lack social support and contacts, including loneliness. The focus on 'life-events' in the earlier literature may have taken attention away from more chronic social difficulties faced by these individuals, such as long-term unemployment status or debt. In a local historical precedent, the Welsh religious revival of 1904–1905 was reportedly associated with a marked increase in admissions for short-lived psychoses. It was suggested that these episodes (which are probably similar to the modern diagnostic terms of Acute and Transient Psychotic Disorder-ATPD, or Brief Psychotic Disorder, BPD) were caused, at least in part, by environmental factors, such as attendance at religious revival meetings (Linden et al. 2009).

The quality of the literature leaves a great deal to be desired, as noted by Salazar de Pablo and colleagues (2020). There is therefore a case for better organised and more rigorous cohort and epidemiological studies in future. There is a clear need to describe and assess social stressors, making use of the many standardised measures that are available, with more attention to qualitative research on the lived experience of patients. ATPD is believed to be intrinsically linked to social stress. The almost complete lack of examination of social assessment, interventions and outcomes is not only a sorry state of affairs, but, as some have argued (Minichino et al., 2019), is bound to place severe limits on primary and secondary prevention efforts. This lack of attention to social factors is reflected within



the case study papers, where, overwhelmingly, emergence of the psychotic presentation and outcome was only viewed through the lense of a clinical presentation. As some individuals go on to develop other acute or chronic psychoses (Rutigliano et al, 2018) with probable difficulties with functional activities, this is a matter of concern that warrants attention within clinical practice.

Fusar-Poli et al (2022) argue, that whilst International guidelines (Australia and UK) for Early Intervention in Psychosis Services recommend the full range of treatment interventions for individuals with a new psychosis, usually for up to 3 years, there may be a reluctance amongst clinicians to continue prescribing antipsychotic medication upon symptom remission. With reference to the case studies discussed in this review, remission was achieved on average within 11 days for females and 12.6 days for males. Given this rapid pace of remission, it seems likely that longer term input is perceived to be superfluous, even where such services exist, and that remission is followed by discharge from services. However, symptom remission and social recovery are not necessarily closely linked, and it is possible that problems in social domains may persist. However, without rigorous, longitudinal studies, that look beyond clinical recovery, and focus on these social outcome domains, we do not have a full understanding of this area. Rapid discharge may lead to missed opportunities for stage specific interventions.

### Limitations

As highlighted, the literature that we have reviewed has a number of limitations. The studies have methodological flaws, including weak designs and sub-optimal or absent social assessments. Amongst the case studies, there were a number of limitations. It is in the nature of case studies that there are no standard criteria that can be applied to ensure rigour. Whilst some presented a wide range of information about cases, most offered limited data and most were limited to a narrative about the development of symptoms. Consequently, there were major inconsistencies in the presentation of case study data.

### Conclusion

Within the case studies, clinical remission was the primary outcome reported in most cases, with only occasional reference to social precipitants and outcomes. Improving the care for ATPDs patients demands more efficient detection by specialized services and appropriate longitudinal follow-up and care. Such services need to be aware of psychosocial stressors and social risk factors, focussing on social assessments and interventions, and on measuring social as well as clinical outcomes. This is important if services are to take action to prevent transition to further episodes of psychotic illness and longer term mental ill health.

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