ORIGINAL PAPER

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Evidence for a relationship between the duration of untreated psychosis and the proportion of psychotic homicides prior to treatment

■ **Abstract** *Background* Recent studies of homicide during psychotic illness have shown that the risk of homicide is greatest during the first episode of psychosis. It is also possible that the proportion of patients who commit homicide before they receive effective treatment may be associated with the length of time they were unwell. We aimed to establish whether there was an association between the average duration of untreated psychosis and the proportion of homicides committed during the first episode of psychosis in the same countries. *Methods* Systematic searches of published studies of homicide in psychosis and the duration of untreated psychosis were conducted. The results were combined to examine the relationship between the reported delay in receiving treatment and the proportion of homicides committed before initial treatment. *Results* We found 16 studies that reported the proportion of psychotic patients who committed homicide prior to treatment. The proportion of first episode patients ranged from 13% to 76%. We were able to match 13 of those studies with DUP studies from the same country. Longer average DUP was associated with a higher proportion of patients who committed homicide prior to receiving treatment. *Conclusions* The possibility that the proportion of patients who commit homicide before receiving treatment may be related to the average treatment delay in the region that the homicide occurs needs to be examined using a case controlled design. If this finding were confirmed, then any measure that reduced the delay in treating emerging psychosis would save lives.

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Introduction

Four recently published studies of homicide by patients with psychotic illness from developed countries [4, 13, 51, 59] and one from Pakistan [27] reported that between 38% and 76% of those homicides were committed during the first episode of psychosis (FEP), prior to effective treatment. If the findings of these studies apply to other populations, the risk of homicide prior to effective treatment is about one in 500 new presentations whereas the annual risk of homicide after initial treatment is of the order of one in 10,000 patients per annum. In other words, the risk of homicide before effective treatment is about twenty times the subsequent annual risk [45].

Three of the four studies performed in developed countries reported that many of the FEP patients had been unwell for several years prior to the lethal assault [4, 51, 59]. Meehan et al. [51] found 25% had been psychotic for more than three years, Appleby and Shaw [4] found that 28% had been mentally ill for more than five years and Nielssen et al. [59] found that 41% had been unwell for more than two years and 15% had been unwell for more than 5 years, all without treatment. Although the three studies did not make a clear distinction between the prodromal phase of mental illness and the date of onset of definite psychotic symptoms such as hallucinations or delusions, the finding that a significant proportion of subjects had been unwell for as long as five years suggests that the interval between the onset of psychosis and effective treatment, known as the duration of untreated psychosis (DUP) may increase the risk of homicide.

In the published distributions of DUP, fewer than 5% of patients remain untreated for more than five years, and as the distributions of treated patients

reach an asymptote, it is unlikely that there are large numbers of patients who never receive treatment [8, 62, 67]. For example, a recent study of DUP conducted in the same region and at a similar time as Nielssen et al. [59] found that 86% of patients were treated within two years and fewer than 4% of patients had a DUP of more than 5 years [39].

There are four possible explanations for the apparent relationship between an increased risk of psychotic homicide and long treatment delay. The first is that the three population based studies [4, 51, 59] published within six months of each other were all subject to the same chance finding. A second is that some of patients who committed homicide during the FEP had not been unwell for as long as reported or had in fact been previously treated, and a third is that many more untreated people in the general community have psychotic symptoms that may cause them to become violent [57].

We believe a fourth explanation, that there is a relationship between the DUP and the risk of homicide in FEP, deserves investigation because it raises the possibility that homicides in psychotic illness can be significantly reduced by measures taken to reduce the DUP.

Ideally, to examine the relationship between the DUP and FEP homicide, the DUP of all the homicide and non-homicide FEP patients in the same population would be compared using the same methods. A more would be to case match the DUP of first episode patients who commit homicide with other first episode patients drawn from the same region. A prolonged DUP in the homicide group would then be direct evidence for an association between DUP and homicide and a large enough study might determine whether the risk increases the longer a patient has been unwell. However, either method would require the measurement of DUP in homicide patients in a country or region in a complex legal and custodial setting, using standardized measures over a long period of time. Moreover, most published studies of DUP have been performed within a single health area and there are as yet no national studies of DUP.

In the absence of national population based DUP data, we examined a possible association between the incidence of homicide in FEP and the DUP reported in published studies of samples of patients from the same countries. The hypothesis for this study was that the proportion of homicides that were committed during the FEP would be associated with the average figure for DUP from studies performed in the same country.

Methods

We searched for published studies of homicide by patients with psychotic illness that provided sufficient information for reasonable inferences to be made about the number of patients who had received adequate treatment prior to the homicide. We then searched for published studies of the DUP in patients with schizophrenia spectrum psychosis conducted in the same country.

■ **Homicide data**

The electronic data-bases [Medline], [Embase], [Psychlit] and [Pub Med] were searched from 1966 to December 2006 combining the terms psychosis OR schizophrenia OR major mental disorder OR first episode psychosis AND violence OR homicide and the references of relevant publications were hand searched. A list of population based studies held by another research group was used to confirm that we had found all the relevant studies.

We included studies from English language journals that reported groups of subjects with psychotic illness who were charged with homicide or attempted homicide and included sufficient information to determine whether the subjects had received treatment prior to the homicide. Evidence for previous treatment included whether there had been prior contact with mental health services, admissions to psychiatric hospitals or if the author stated whether the subjects had previously been treated for psychosis.

More than 300 abstracts were examined and 71 articles were read in full text. Of the 71 papers only 16 studies described the previous psychiatric treatment of patients with psychosis who were only charged with homicide offences. Many of the large and well conducted studies of abnormal homicide provided no information about treatment status [25, 28, 68]. We excluded case reports, small personal series, studies of homicide due to misidentification syndromes and studies of specific types of offences such as infanticide. A more complete set of data from one study was located on the internet after communication from one author [4] and the number of non-first episode psychotic homicide offenders and the duration and area in which the homicides occurred was provided by another author [13].

Three homicide studies that did report treatment status were excluded as we were unable to locate any samples of the DUP of schizophrenia spectrum disorders from those countries, leaving 13 studies from eight countries (Table 1). The excluded studies from Israel, France and New Zealand reported respectively that 39%, 40% and 40% of patients had never been admitted to hospital or were not known to mental health services prior to the homicide [10, 70, 76].

The studies defined previous treatment in several ways. The most accepted definition of DUP and therefore the total period of FEP is the period between the onset of definite psychotic symptoms and a period of adequate treatment with antipsychotic medication, usually judged to be about a month of treatment with a moderate dose of antipsychotic medication [61]. However, only two publications used a clinical definition of homicide in first episode psychosis [13, 59] while two more had enough clinical information to report both the number of patients who had had contact with mental health services and the smaller number of patients who had received treatment for psychosis [4, 51]. Previous treatment, previous contact with mental health services (MHS) or the history of an admission to a psychiatric hospital were accepted as indications that the patients were no longer in the first episode of psychosis (Table 1).

We accepted a hospital admission as a definition of previous treatment, as even in specialist early psychosis services as many as 80% of patients have an admission to a hospital early in their treatment [72, 78]. Although a minority of patients are successfully managed in the community without an admission to hospital, some other first episode patients do not receive adequate treatment despite contact with services or even during an admission to hospital [19].

Because the proportion of patients who had received treatment was the crucial independent variable, the accuracy of the estimation of the number of treated patients in each study was considered. In six studies [4, 13, 24, 33, 51, 59] the proportion of patients who had received treatment was a major focus of the paper or was specifically discussed. The first author of a further study [36] was quoted in a later report stating that the patients who had not been admitted were unlikely to have received treatment [24]. The authors of all but the smallest [53] of the remaining six studies were contacted by email. Four authors were able to confirm that the number of patients who had been in contact with mental health services, had some treatment or were admitted to hospital was an accurate assessment of the

Table 1 Thirteen studies of homicide ranked in order of the proportion of homicides in first episode psychosis

	Year of publication	Country (region)	Defined region	% of all homicides	Proportion of homicides solved	Recruitment and Inclusion criteria	Definition of FEP	First episode of psychosis/previously treated N	First episode of psychosis % (95% CI)
Farooq et al. [27]	2003	Pakistan (Peshawar)	No	Not reported		Referred for assessment Mental illness	Previous treatment	38/50§	76 (63–86)
Nielssen et al. [59]	2007	Australia (NSW)	Yes	8.80%	90%	Mental illness defences, psychosis	Clinical definition	54/88	61 (51–71)
Leong & Silva [46]	1995	United States (Los Angeles)	No	Not reported	65%	Forensic examination, psychosis	Previous admission	12/25	48 (30–67)
Bourget et al. [13]	2004	Canada (Ontario)	Yes	Not reported	84%	Forensic examination, psychosis	Clinical definition	22/51†	43 (30–57)
Meehan et al. [51]	2006	England & Wales	Yes	5%	90%	Schizophrenia	Previous treatment	36‡/85	42 (32–53)
Häfner and Böker* [36, 37]	1982	FDR-Germany	Yes	8.2%	92%	Schizophrenia	Previous admission	116/284	41 (35–47)
Appleby & Shaw [4]	2006	England & Wales	Yes	5.2%	90%	Schizophrenia	Previous treatment	53†/141	38 (30–46)
Millaud [49]	1989	Canada (Quebec)	No	Not reported	84%	Hospital disposition, psychosis	Previous admission	8/24	33 (18–54)
Grunberg et al. [33]	1978	United States (New York)	Yes	Not reported	70–80%	Mental illness defences	Previous admission	3/9	33 (11–67)
Erb et al.* [24]	2001	Germany (Hessen)	Yes	10.0%	92%	Hospital disposition, schizophrenia	Previous admission	9/29	31 (17–50)
Dolan and Parry [21]	1996	UK (Liverpool)	No	No	90%	Hospital disposition, psychosis	Previous contact with MHS	12/54	22 (13–35)
Nijman et al. [60]	2003	Netherlands/Germany (Pootugaal/Duren)	No	Not reported	78%/92%	Hospital disposition psychosis	Previous treatment	5/33	15 (7–32)
Laajasalo & Häkkänen [44]	2004	Finland	Yes	Not reported	95%	Schizophrenia	Previous contact with MHS	14/106	13 (8–21)

*Includes some cases of attempted homicide
†Denominator by personal communication
‡Includes patients who were not treated for psychosis during prior contact with MHS
§Includes two patients who may not have been psychotic

number of patients who had received adequate treatment for psychosis prior to the homicide [27, 44, 46, 60] and a fifth [21] confirmed that the reported proportion who had not been in contact with mental health services had never received treatment for psychosis. Thus we believe that the studies provided reasonably accurate accounts of the proportion of patients who had received treatment for psychosis prior to committing the homicides. It is possible that a small number of patients were wrongly classified as having received treatment for psychosis as a result of contact with mental health services and had only received treatment for conditions such as depression or substance abuse and had not received antipsychotics.

All the studies used legal findings to define whether a homicide offence had been committed and whether the person accused of homicide had a psychotic illness. These definitions included the availability of a mental illness defence, transfer to hospital after conviction with the diagnosis of schizophrenia and the findings of statutory authorities set up to investigate homicide and mental illness (Table 1). Reliance on the legal process to diagnose psychosis may miss some cases [28], which is likely to have resulted in fewer FEP cases, as the psychiatric status of defendants who do not have a known history of treatment for psychotic illness may be less likely to be come to the attention of the courts.

The subjects are likely to have been correctly diagnosed, as malingered mental illness rarely survives the close examination of suspects in legal proceedings for serious offences. Moreover, a legal finding of reduced criminal responsibility is more likely if there is evidence of pre-existing illness or a period of disability indicating the presence of a significant illness. Thus, although the reliance on legal findings may not be a sensitive way of detecting psychosis, it has the advantage of other tests with low sensitivity, that it is likely to be more specific.

Eight of the homicide samples were complete, in that they included all the known cases of psychotic homicide for a given country or region during the period of the study. Less complete samples did not differ from complete samples in the overall proportion of FEP homicide patients. The regions varied considerably in their rates of homicide but had an average homicide clearance rate of 86% [20, 25, 55, 56, 74, 79]. The use of the proportion of FEP patients, rather that the absolute rate of homicide in FEP allowed the inclusion of a larger number of studies and comparison between regions without having to control for the possible influence of the overall rate of homicide on the number of patients who commit homicide in the FEP.

Schizophrenia spectrum disorders defined as schizophrenia, delusional disorder or psychosis NOS were reported in 95% of patients in the studies. Affective psychosis, schizo-affective psychosis and a few patients with organic psychosis made up the remaining 5%. The average age was 34.7 years and 88% of the homicide patients were men.

■ DUP data

We searched the electronic data-bases [Medline], [Embase], [Psychlit] and [PsychINFO] from 1975 to Jan 2007 with the search terms 'duration of untreated psychosis' OR 'delay in treatment' OR 'treatment delay' OR 'initiation of treatment' AND 'psychosis', 'psychotic disorders' OR 'schizophrenia' OR 'schizoaffective' OR 'first-episode psychosis'. This method also yielded just over 300 publications.

We searched these publications for samples of patients with schizophrenia spectrum psychosis from the eleven countries for which we had relevant homicide data. We included articles that reported mean or median DUP or provided the mean age of onset of psychotic symptoms and the mean age of presentation to at least one decimal point, which allowed us to calculate mean DUP. We excluded studies of the duration of untreated illness and only accepted studies that dated the onset of DUP to the beginning of definite psychotic symptoms. Most studies used a period of adequate antipsychotic treatment to define the end point of DUP but about a third used initial hospitalisation.

We found a total of 99 published studies of DUP with non-overlapping samples of patients, of which 31 studies reported the DUP of 40 samples of patients with schizophrenia spectrum psychosis that could be matched with those studies reporting treatment status in psychotic homicide (Table 2).

Table 2 DUP and service indicators from eight countries, ranked in order of decreasing average Mean DUP

Country	Average year of publication	References	Number of samples with Mean DUP	Number of samples with Median DUP	Total number of subjects	Mean DUP (range)	Median DUP	Dangerousness required for involuntary admission	Psychiatristss per 100 000
Pakistan	2005	[58]	2	0	60	146 (118–175)	–	Yes	0.2
Canada	2001	[1, 7, 9, 12, 16]	7	5	631	83 (46–112)	29	Most jurisdictions	12
USA	1999	[15, 17, 18, 34, 35, 40, 50, 49, 63, 75]	12	7	1379	80 (39–166)	33	Yes	14
Germany	2001	[30, 38, 64]	3	1	497	56 (41–114)	8	Yes	12
Australia	2005	[39]	2	2	76	49† (45–53)	28	Yes	14
Netherlands	2004	[48, 80]	2	1	233	35 (23–46)	5	No	9
UK	2001	[8, 11, 22, 26, 65, 71, 73]	7	4	901	34 (18–59)	15	No	11
Finland	2005	[43, 69]	3	1	124	17 (14–18)	9	No	22

†Mean DUP by personal communication from Dr A. Harris

There was evidence for the assumption that DUP is reasonably constant within countries from the results of multiple studies performed in the same countries and the significant differences in the DUP measurements between countries (Kruskal–Wallis statistic = 26.5, $P < 0.001$). For example, both samples from Pakistan reported a longer DUP than all but one of the samples from the USA, all but one of the fourteen samples from the USA were longer than all but one of the seven samples from the UK, and the Mean DUP of all the samples from the UK were longer than any sample from Finland.

This suggests that national factors such as economic development, the quality of mental health services, the availability of some types of treatment, mental health law or cultural beliefs may all contribute to a degree of uniformity in the DUP within a country. By way of illustration, Pakistan may have a long DUP because it has only 2 psychiatrists per million people and has fewer than one psychiatric hospital bed per 40,000 people [5] whereas Finland, which has the shortest median DUP in this study, has more involuntary psychiatric admissions than any country in the European Union [23] and has more psychiatrists per head than the other countries in this study [5].

A final example of national factors that may influence DUP is that countries which have mental health acts that require a patient to be assessed to be dangerous before they can be admitted for involuntary treatment [2, 3, 23, 31, 32, 52, 66] had a much longer DUP than those countries that had other criteria for involuntary treatment.

A further assumption made in this study is that DUP data collected at one interval is relevant to homicide data collected over a different period. This applies particularly to the three homicide studies that were performed before the importance of DUP was recognized, as in the other studies there were DUP samples collected within similar periods (see Tables 1 and 2). We found that the Mean DUP was stable over the three decades in which DUP studies have been conducted ($R^2 = 0.03$, $F = 2.02$, $P = 0.16$). It was also stable over time in individual countries including the USA ($R^2 = 0.04$, $F = 1.5$, $P = 0.25$), UK ($R^2 = 0.07$, $F = 0.37$, $P = 0.57$) and Canada ($R^2 = 0.03$, $F = 0.14$, $P = 0.72$).

■ Data collection and statistical analysis

The authors independently extracted the data. A third examination comparing the electronic spread sheet data to the publications was also conducted. There were differences in two of 58 DUP data points after the initial examination, both of which were the result of errors in converting the DUP from other units of time to weeks. There was an initial disagreement about the numbers of FEP patients who had committed homicide in one publication and in a further study both authors initially made the same incorrect determination about the numbers of FEP patients. This error was detected in a further examination of the homicide data.

Average Mean and Median DUP in the studies from the respective countries were used as the independent variables and the proportion of FEP homicides was considered as the dependant variable. In those countries with more than one sample of psychotic homicide (The UK, USA and Canada) the average DUP values calculated for that country was assigned to each of the homicide samples. In the one study in which the homicide sample was drawn from two countries (The Netherlands and Germany), the average of the DUP samples from both countries was used.

Multiple linear regression was used to examine the relationship between the independent variable of DUP and the dependant variable of the proportion of psychotic homicides in FEP. For this analysis Mean DUP values were Log_{10} transformed because they were not normally distributed. The studies were weighted according to the total number of psychotic homicides, as smaller studies would necessarily report a less accurate mean proportion of homicides in FEP (see confidence intervals in Table 1). A definite history of prior treatment was included as an independent covariable as this group had a higher proportion of untreated patients than those who reported previous contact with mental health services or admission to a psychiatric hospital that may have been for reasons other than psychosis. An analysis using the median value for both Mean and Median DUP for each country was not reported, as the results were very similar to those using average Mean and average Median DUP.

The null hypothesis was that the proportion of cases of homicide in FEP would not be associated with DUP. Statistical analysis was performed using SPSS 15.0.

Results

A relationship was found between average Mean DUP and the proportion of homicides in FEP using unweighted and untransformed variables ($R = 0.694$, $R^2 = 0.484$, $t = 3.20$, $P = 0.008$), however a possible relationship between average Median DUP and the proportion of homicides in FEP just failed to reach significance ($R = 0.570$, $R^2 = 2.56$, $t = 2.195$, $P = 0.053$).

As (i) there were very considerable differences in the samples sizes between the studies and thus the confidence intervals of the proportion of homicides in FEP, (ii) average Mean DUP values were not normally distributed (skew 1.35, $P = 0.03$) and (iii) because of the different definitions of FEP were employed in the studies, a multiple linear regression, weighted for sample size and using Log_{10} transformed DUP values was performed. A relationship was found between both Log_{10} Mean DUP and the proportion psychotic homicides committed in FEP using previous treatment ver-

Table 3 The proportion FEP/Total psychotic homicides Vs Mean DUP

ANOVA					
	Sum of Squares	df	Mean square	F	P
Regression	152255	2	76127	10.43	0.004
Residual	72983	10	7298		
Coefficients					
	Un-standardized Coeff.		Standardized Coeff.	T	P
	B	Sts. error	Beta		
constant	−46.5	21.0		−2.22	0.051
Log_{10} Mean DUP	48.3	12.6	0.69	3.83	0.003
No previous admission or no contact with MHS	11.4	5.5	0.375	2.07	0.065

sus contact with services and hospitalization as a co-variable. This analysis confirmed a significant relationship between average Mean DUP and the proportion of homicides in FEP ($R = 0.822$, $R^2 = 0.676$, Table 3).

A further analysis excluding of the outlying sample from Pakistan also found a significant association between Log_{10} Mean DUP and the proportion of homicides in FEP (weighted for samples size, clinical definitions of FEP as co-variable ($R = 0.738$, $R^2 = 0.545$, Log_{10} Mean DUP: Beta = 0.632, $t = 2.81$, $P = 0.02$).

We did not find a significant association between Median DUP and the proportion of homicides in FEP using multiple linear regression weighted for sample size (Table 4).

Discussion

We were able to locate 16 studies that reported whether patients had received treatment of psychosis at the time of the homicide. Eleven of the 16 studies reported a proportion of FEP homicides of between 30 and 50% and seven studies reported a proportion of between 35 and 45%. As the incidence of new cases of schizophrenia is about 0.002% per year in most regions [6, 42] and the prevalence of chronic psychotic illness is at least 0.5% [42] we would expect to find 25 times as many patients committing homicide after treatment than prior to treatment if initial treatment did not reduce the rate of subsequent homicide. In fact most studies reported that about four in ten patients had not been treated prior to the homicide which indicates a greatly increased risk of homicide prior to treatment and that there is a dramatic decline in the risk of homicide after treatment for psychosis. Hence on theoretical grounds any delay in treatment is likely to result in a higher proportion of homicides in FEP. We found that the longer the Log_{10} Mean DUP, the higher the reported proportion of homicides during the FEP in the same region.

Although this study indicates there is a greater risk of homicide in FEP in regions with a long DUP, it is possible that the homicides themselves were not committed by subjects with longer DUP and both observations are a result of a third factor, such as worse mental health services. Studies like this that rely on the comparison of two or more data sets may be criticized because of the increased likelihood of finding non causative or coincidental associations. It

Table 4 The proportion FEP/Total psychotic homicides Vs Median DUP

ANOVA					
	Sum of Squares	Df†	Mean square	F	P
Regression	43782	2	21891	1.80	0.220
Residual	109326	9	12147		
Coefficients					
	Un-standardized		Standardized	T	P
	B	Sts. error	Beta		
Constant	25.20	7.43		3.39	0.008
Median DUP	0.660	0.497	0.42	1.329	0.217
No Previous admission or No contact with MHS	4.957	8.20	0.191	0.604	0.561

† reduced N as there was no median value for the study from Pakistan

can also be criticized for comparing data from different time frames and studies that use different definitions and have different sampling methods and inclusion criteria [14].

In response to this criticism of the type of study we argue that there is both a plausible mechanism and supportive clinical data with respect to DUP and the proportion of homicides in FEP. Recent studies have found a disproportionate number of subjects with very long delays in initial treatment [4, 51, 59] and this is also consistent with three studies of non-lethal violence that have suggested that risk of serious violence increases the longer a patient is untreated [41, 54, 77]. It should be noted that a fourth study found no relationship [29] and in the studies that did very few of the incidents of what was regarded as serious violence resulted in serious physical injury.

However, the relationship between DUP and homicide may also be quite different to the relationship between measurements of DUP and scales developed for measuring violence, as homicide (except when more than one person is killed) is a categorical event. Hence the risk of homicide may not rise the longer a person is untreated and the higher rates of FEP homicide may be simply because there is more time to kill someone.

The methodological limitations of this study include both the small sample size of some studies included and the number of regions considered, the use of proxy measures of FEP, and DUP data collected on patients who did not commit homicide all indicate a need for further research. Only a small number of psychotic homicide studies described treatment status and even if there had been more data to confirm the proportion of FEP patients, the correlation with measurements of DUP would not be conclusive. Studies that directly compared the DUP of homicide offenders and case matched controls, or a whole population of FEP patients are required to establish (i) if patients who have a significantly longer DUP are more likely to commit homicide (ii) if the risk of homicide escalates with the DUP or is simply due to the longer time available for an FEP patient to commit a homicide and (iii) if long DUP is causally related to homicide in FEP or if both are a result of a third factor such as the absence of negative symptoms or even the presence of particular symptoms such as threatening delusions that are known to cause violence and also deter some patients from accepting treatment [47].

Conclusion

The data, with its limitations, suggests an association between treatment delay and the likelihood of homicide in FEP. This finding should be tested using case controlled or population based methods.

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