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Variation in Duration of Untreated Psychosis in an 18-year perspective

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Abstract

Background—The Scandinavian TIPS project engineered an early detection of psychosis program that sought to reduce the duration of untreated psychosis (DUP) through early detection teams and extensive information campaigns since 1997. In 1997–2000, DUP was reduced from 26 to 4.5 weeks median. The program was continued beyond the initial project in modified forms for over 13 years.

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Objective—To track the vicissitudes of DUP over a 18 year period (1993–2010) with differing early detection efforts in a defined catchment area.

Method—The DUP of all patients meeting criteria for first episode psychosis was measured 1993–1994 and from 1997 through 2010 in a naturalistic long-term study. DUP values of all patients were included, irrespective of patients' participation in a clinical follow-up study, yielding a highly representative sample.

Results—DUP varied across studies with differing information campaign intensity and content. These variations will be described and explored.

Conclusions—Early detection campaigns should have a stable focus and high intensity level. Future research should further elucidate pathways to care in order to establish principal targets for information campaigns.

Keywords

First Episode Psychosis; Duration of Untreated Psychosis; Early Detection

Introduction

The Duration of Untreated Psychosis (DUP) has emerged as an important malleable factor in the prognosis of psychotic illness ^{1, 2}. Several mental health care programmes around the world have been designed to detect and treat first episode psychosis earlier. Recently reviewed by Lloyd-Evans et.al ³, eight programmes fit the defined criteria of being “designed to enhance the identification and prompt treatment of people with first-episode psychosis”. Information campaigns about psychosis were a central part of all these programmes. Three programmes were targeted to general practitioners (GPs), one to service providers, and four were multifocal, targeting GPs, service providers and the general public. However, only two of the eight programmes succeeded in significantly reducing DUP. These were the EPIP programme in Singapore, and the TIPS-project in Scandinavia, both of which engineered high intensity and volume of applied information campaigns. They provided the greatest quantity of information to the general public, combining mass media, such as radio, television, cinema, and newspapers, and were the only programmes to combine information campaigns with specialized clinical detection and processing services for all referrals.

The TIPS programme was the longest, with the initial information campaign lasting four years. It achieved the shortest DUP of all the programmes evaluated, with a median of 4.5 weeks compared to 26 weeks pre-intervention and 16 weeks in the parallel control areas ⁴. This is shorter than what is found in other studies which typically report median DUPs from seven to eight weeks at the short ^{5–7}, to 48 weeks at the long end ⁸. One programme even saw an increase of DUP length, possibly reflecting success in accessing long DUP patients who otherwise may not have presented to care at all ⁵.

According to the literature DUP appears to vary with content, focus and intensity of early detection programmes ³. In the TIPS programme, early detection moved through different phases. After the initial four-year programme there was a pause in early detection activities

due to practical and financial constraints. This period was studied as a no-information campaign period, and showed a significant increase in DUP⁹. Following this no-information campaign period, the full early detection programme was re-implemented, and in its latest phase was expanded in focus to include substance abuse with psychosis.

In this paper, we present lengths of DUP for complete first episode of psychosis samples across the different phases of the TIPS programme. The total time span of the study is 18 years, which to our knowledge represents DUP data for the longest period published so far. We wanted to examine whether variations in periods of active early detection information campaigns in the TIPS programme were associated with variations in shortening of DUP.

Method

Design

The study employs a naturalistic follow-along design. DUP-data were collected in FEP treated incidence samples from 1993–1994 and 1997 – 2010 (with a pause between January 2001 and June 2002). The setting was a Scandinavian mental health care region (south sector of Rogaland County, Norway; population 267 000¹ in 2010, mainly urban and sub-urban). Information campaigns were introduced (TIPS1), terminated (TIPS2²) and re-introduced (TIPS3 and TIPS4) during the study period. Except for 1993–1994 (pilot phase), detection teams were operational throughout the whole study. To rule out differences in recruitment of patients we estimated treated incidence of FEP across time periods.

Table 1 outlines study periods, samples sizes, and estimates of treated incidence per 10 000. To facilitate comparability, all study phases were divided into equal two-year periods, except TIPS2, which started in 2002 and stretched into the first six months of 2004, adding up to 2,5 years. To estimate treated incidence, we used the mean population of the catchment area for each of the periods studied, except for the pilot phase. During this phase, there were no early detection efforts and no reliable count of new cases admitted to mental health care, therefore, estimating incidence could not be done reliably and hence was omitted. Because one study site participated in the first but not the subsequent early detection periods, it was excluded. Therefore, population bases and treated incidence figures differ from figures reported previously ⁹. Population bases were calculated employing figures reported per year by the Central Bureau for Statistics in Norway (www.ssb.no).

Eligibility criteria from pilot phase through TIPS4 were as follows:

- Age: 16 through 65 years,
- Meeting the DSM-IV criteria for schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychotic episode, delusional disorder, affective psychosis with mood-incongruent psychotic features or psychotic disorder not otherwise specified;

¹In a previous publication, the population has been reported to be 290 000 for 2002–2004 [9]. Some municipalities included there have been excluded from this study because they were not involved in the phase where the information campaigns were re-implemented.

²Not to be confused with TIPSII, which stretches from 2002 and ongoing and contains TIPS2 through TIPS4.

- Being actively psychotic, as measured by a Positive and Negative Syndrome Scale (PANSS) ¹⁰ score of 4 or more on at least one of positive subscale items P1 (delusions), P3 (hallucinations), P5 (grandiosity), P6 (suspiciousness), or G9 (unusual thought content) for at least 7 days;
- Not having received previous adequate treatment for psychosis (defined as antipsychotic medication of > 3,5 haloperidol equivalents for > 12 weeks or until remission of the psychotic symptoms);
- Having no neurological or endocrine disorders with relationship to the psychosis;
- Understanding and speaking a Scandinavian language;
- Having an IQ score > 70;
- No diagnosis of primary substance abuse / substance induced psychosis

Patients were included based on the same criteria in all time periods. The sample studied here (total N= 602) is larger than that included in the previous papers because it also includes patients who did not give informed consent to participate in the add-on study concerning treatment and follow-up. The Regional Committee for Research Ethics for Health Region West approved of this study (registration number S-08010b).

Information campaigns 1997–2000 and 2005–2010—Information Campaigns were designed for multiple targets (general population, schools- both teachers and pupils, health professionals in primary, secondary and tertiary health care). They were aimed at reducing DUP through:

- Raising awareness about signs of psychosis
- Improving health-seeking behaviour of the population and referral practices of GPs.
- Simplifying the pathways to care through easy access to and knowledge about detection teams

Information campaign strategies varied somewhat over time from TIPS1 through TIPS4. TIPS4 marks a transition from excluding to including substance-induced psychosis. This implied a slight expansion of focus in the information campaigns. However, the patients with a diagnosis of substance-induced psychosis are not included in the data presented here, in order to secure comparability across time periods.

In the pilot phase, 1993 to 1994, there were no information campaigns efforts or detection teams. Also, only inpatients were included as opposed to the other study periods including patients from all of mental health care in the catchment area.

Detection team 1997–2010—The detection team consisted of psychiatric nurses with additional training in screening for and assessment of psychosis, and was operational throughout the study. The team was available by telephone every workday between 8am and 3pm, and the phone was receptive to all sources, including health professionals, social services, teachers, and the general public. Outside office hours there was a voicemail service ensuring that callers would be contacted on the following workday.

The team performed a telephone screening for psychosis for the person in question. In case of a positive screen, appointments were made and assessment by the PANSS carried out within 24 hours, or the next workday in case of weekend or holiday.

The team's phone number was assertively advertised in the information campaign. If the assessment concluded with the presence of psychosis, a psychologist or psychiatrist within the TIPS team conducted a clinical interview for diagnostic purposes.

Assessments

All available sources of information were used to estimate the length of DUP. Careful clinical interviews focused on when the patient first started to experience psychotic symptoms (estimated as a PANSS score of four -moderate- or more on Positive scale items P1 delusions, P3 hallucinatory behaviour, P5 grandiosity or P6 suspiciousness, or General scale item G9 unusual thought content), as well as if and when the patient started to experience problems in social and daily functioning. The evaluation included patient files in the case that the patient had presented to mental health care before. DUP was defined as time in weeks from onset of psychosis until start of adequate treatment.

The Structured Clinical Interview for the DSM-IV Axis I Disorders ¹¹ was used for establishing diagnosis.

Reliability

When TIPS1 baseline data collection was finished, we drew a stratified random sample of 30 cases. The site coordinators produced vignettes for cases from their own site, describing symptoms, symptom emergence and development of the illness. Two experts, who were blind to the site ratings, scored the vignettes. The first eight vignettes were used for calibration and training. The following 22 vignettes were used for reliability testing. In TIPS1, reliability of measures was fair to good (intra class correlations 0.99 for DUP; Kappa 0.76 for diagnosis) ¹². The high ICC for DUP can partly be explained by an extreme variation in DUP (0 weeks to 40 years). In TIPS2 new inter-rater reliability scores were obtained for central measures from 17 randomly selected clinical vignettes from the baseline data. Reliability of measurements ranged from moderate to very good (DUP: intra class correlation 0.99; diagnosis: K = 0.58) ⁹. During TIPS3 and TIPS4, three reliability trainings using video vignettes were conducted to avoid drift, and cases discussed at a weekly meeting to establish consensus.

Statistical Analyses

All statistical analyses were conducted using the PASW 18.0 software ¹³. Pearson Chi Square tests were used for analysis of categorical data, and Kruskal Wallis Chi Square for multiple, and Mann Whitney U-test for pairwise tests for differences between median values. Effect sizes were reported.

As DUP had a very skewed distribution, we report median values in descriptive statistics. DUP was also recoded into categories of length for the comparison of frequency distributions by the Pearson Chi² goodness-of-fit test statistic. For parametrical statistical

analyses, DUP was log-transformed. ANOVA was used to compare means over multiple groups, and Bonferroni post-hoc tests were carried out for multiple comparisons. We also tested for trends by using contrasts. DUP over time and the association with the presence of information campaigns were further examined using linear regression analyses with DUP as the dependent variable. Absence or presence of information campaigns was coded in a dummy variable and entered into the regression model as a predictor. Covariates entered were age, diagnostic category and gender. Diagnostic categories were recoded into dummy variables, one for each category. Variables were entered in a stepwise procedure yielding R square change, indicating effect size and amount of explained variance.

Results

Table 3 outlines sample characteristics. The pilot phase had significantly more patients with schizophrenia or schizophreniform disorder and less with schizoaffective disorder. The diagnostic category psychosis NOS was used for significantly more patients in TIPS 3 and 4 compared to TIPS1 and the pilot phase. There were no differences in age or gender distribution.

One-way ANOVA showed a significant association between TIPS phase and DUP (between groups effect $F: 3.6$; $df: 4$; $p < .007$); however Bonferroni post-hoc tests showed that this was due to a significant difference between the pilot phase and TIPS1 only. Contrast testing showed a significant association between the presence and absence of information campaigns, and DUP ($t: 3.4$; $df: 549$; $p < .001$), but not between the different phases of TIPS ($t: 1.3$; $df: 549$; $p < .18$) and DUP. However, a non-parametrical test (Mann Whitney U test) indicated a small but statistically significant increase in median DUP from TIPS1 to TIPS2 ($Z: -2.5$; $p < .014$; $r = 0.15$; small effect size).

Figure 1. details DUP median values and range per two-year period. The years 2007–2008, in which persons with substance-induced psychosis were first targeted, show an increase from the years 2005–2006 to 2007–2008, however statistically not significant ($Z: -1.7$; $p < .093$; $r = -0.12$), alongside a highly significant decrease from the pilot phase to the years 1997–1998 ($Z: -3.4$; $p < .001$; $r = -0.3$; medium effect size). Figure 2. details the distribution of patients across DUP length categories. The chi-square goodness of fit test statistic for the association between probability distributions and TIPS 2-year periods was 48.9; $df: 36$; ($p < .009$). In other words, the distributions differed significantly between periods; the pilot phase and TIPS4 including larger numbers of patients with a very long DUP (> 2 years) than the other phases.

Table 4 shows the regression model of DUP. Having affective or brief psychosis was associated with shorter DUP. Furthermore, the association between the presence of information campaigns and DUP was confirmed by this analysis.

Discussion

This is the first study to present long-term DUP values for complete samples of patients presented to treatment in a defined catchment area. This has been possible given the organisation of the Norwegian health care system, which is state owned and run. The

catchment area has no private facilities within mental health care. Hence, these data may be viewed as uniquely representative.

The data show a substantial variation over time in DUP length. This variation appears to be associated with the presence of information campaigns. Furthermore, the distribution of DUP differed across TIPS phases. TIPS4 showed an increase in patients with a DUP longer than two years. This phase was characterized by an expansion of the information campaigns' focus to including substance-induced psychosis. A part of the explanation may be that expanding the focus of the information campaigns alerted a slightly broader population, with a higher proportion of long DUP patients. This might be a population characterised by social marginalisation and insidious onsets, compatible both with negative symptoms and substance abuse. There may have been doubt over time as to what was drug use behaviour and what could be psychosis, and to a "wait-and see" attitude and hence, to longer DUP. Addressing substance induced psychosis may have prompted help-seeking in some of these cases, after prolonged periods of doubt. The fact that the yearly treated incidence was at its highest in 2007–2008 may point in the direction of a broader population. However, during 2009–2010 the percentage of patients with a DUP > 2 years was even higher, in spite of a drop in treated incidence. An alternative possibility is that an expanded focus may have meant a diluted one. We have previously shown that in TIPS1, the long DUP patients had low symptom levels, with deteriorating premorbid social function¹⁴. Perhaps a focus on drug-induced psychosis may have replaced some information about negative symptoms as a warning sign, and this may have contributed to delayed help seeking. Variations in DUP may also reflect a delay in effect of information campaigns. Twenty-five per cent of the patients in TIPS4 with DUP more than two years had their onset of psychosis during TIPS2 (No-information campaign), and 25% during TIPS3 (re-implementation of information campaigns), and remained undetected at those times. These patients began presenting to treatment after the re-implemented information campaigns had been running for at least two years. We were not able to control for possible independence of measurements across the different phases of the information campaigns, that is, the possibility that effects of the information campaigns in one phase carried over to the next. An argument against this line of reasoning is that no such delay was observed in TIPS1. However, with the information campaigns in TIPS4 focusing more on symptoms compatible with substance abuse and social marginalisation, one may have been able to help detect patients with more "quiet" symptomatology; withdrawal, social drop-out, and self neglect, overlapping with the insidious onsets and negative symptomatology associated with long DUP^{15, 16}.

The lack of a quick reduction in DUP following the re-implementation of information campaigns suggests there may have been a saturation point in the market of psychological and psychiatric awareness and information. In 1997, when TIPS started, there was very little information readily available through general media. Fifteen years later, however, such information is readily available, and perhaps denied. More information about psychological and psychiatric illness leads to habituation on the part of the public, rendering TIPS advertisements less salient. This could have had an impact on information response and help seeking behaviour. As a consequence, a certain amount of desensitisation and habituation may also have affected mental health workers within a treatment system that had known TIPS for almost two decades. Experienced clinicians supervising novices may have lost

some of the initial enthusiasm and hence, the early detection of psychosis and TIPS might have become less emphasised. These mechanisms may have increased the part of DUP stemming from within mental health care, or “post-help seeking DUP”, a component of DUP that has emerged in research as an important factor in treatment delay¹⁷, consisting of the time period from seeking help in mental health care to adequate diagnosis and anti-psychotic treatment. Help-seeking and post-help seeking delays have been shown to add evenly to total treatment delays¹⁸. Along these lines, it could prove useful to investigate in more detail the specific obstacles that may lead to a long DUP. For instance, according to some data, youth receiving treatment from child- and adolescent mental health care have a longer DUP than other patients, providing a possible direction for future research (Max Marshall, personal communication, October 2nd, 2012).

In sum, the findings of this study have several implications for further research and clinical practice. First, to be successful in reducing DUP via early detection programmes, information campaigns should probably have a clear and persistent focus with no major changes. Second, they must last long enough to enable an investigation of an effect beyond the influence of previously undetected, “quiet”, long DUP patients, perhaps in doubt or in denial of any problems, inducing an initial increase after implementation. Third there might be a critical DUP beyond which prognosis worsens¹⁹, a threshold phenomenon which would not be captured by a linear DUP variable. In future research, outcome should perhaps be investigated in relation to such a critical value.

Study limitations

One limitation of the study is the lack of a standardised measure of DUP. Furthermore, calculating reliability, DUP estimation based on direct clinical judgement instead of via vignettes would have been a preferable method. Unfortunately, we were unable to organize this. Another limitation concerns the fact that we could not study clinical variables other than initial diagnosis, because of patients who declined participation in the add-on clinical follow-up study. However, no other study has published data on a full epidemiological first episode of psychosis sample and hence, this study presents uniquely representative data.

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¹Median: 26 weeks; range 0-936 weeks

²Median: 6 weeks; range 0-416 weeks

³Median: 8 weeks; range 0-364 weeks

⁴Median: 15 weeks; range 0-2080 weeks

⁵Median: 14 weeks; range 0-520 weeks

⁶Median: 25 weeks; range 0-1530 weeks

⁷Median: 8 weeks; range 0-1300 weeks

Figure 1.

Median DUP values per year across early detection phases

Figure 2.
Percentage of patients per DUP length category for each TIPS phase

Table 1

study periods, samples sizes, and estimates of treated incidence per 10 000

Phase	Years	N	Yearly treated incidence, mean pr 10 000	Early detection effort
Pilot phase	1993–1994	44	-	None
TIPS1	1997–1998	86	1.9	Information campaigns plus detection team
TIPS1	1999–2000	60	1.3	Information campaigns plus detection team
TIPS2	2002– june2004	115	1.9	Detection team only
TIPS3	2005–2006	95	1.9	Information campaigns plus detection team
TIPS4	2007–2008	108	2.1	Information campaigns plus detection team; now including substance induced psychosis in campaigns
TIPS4	2009–2010	94	1.8	Information campaigns plus detection team

Table 2

Content of information campaign across TIPS1 through TIPS

	TIPS1	TIPS2	TIPS3	TIPS4
Educational programme for GPs about psychosis, early warning signs, and detection team	x		x	x
Distribution to GPs of a checklist for symptoms based on the DSM-III-R prodromal symptoms and a rating manual for core PANSS symptoms			x	x
Twice yearly news letter to GPs	x	x	x	x
Full-page advertisements in the largest newspapers in Norway (December 1996 and January 1997).	x			
6–7 yearly full-page local newspaper advertisements	x			
Four yearly full-page local newspaper advertisements			x	x
Two 12-page brochures about psychosis, early warning signs, and the TIPS project distributed to all households	x			
Frequent (approximately weekly) smaller newspaper advertisements	x	x	x	x
Active use of website (tips-info.com); Facebook page, youtube (film), Twitter			x	x
Flash-advertisements on the local newspapers' internet editions			x	x
Educational programmes for high school teachers and students (courses, lectures including a CD with 300 slides on the subject to choose from, and a textbook, information material)	x		x	x
Two local buses carrying large advertisements covering the back of the bus				x
Free postcards and small brochures with information, distributed at meeting places for young people, such as schools, university, cafés, restaurants, bus stations, etc.	x		x	x
Films and audio recorded advertisements for local cinemas, radio and television (some in collaboration with one of the country's most popular comedians)	x		x	x
Flyers, car-stickers, coffee mugs, pens and post-its distributed to all relevant parties	x	x	x	x
Brochures, newspaper ads, and education about substance abuse and psychosis				x

Table 3

Sample characteristics.

	Pilot (N=44)	TIPS (N=146)	TIPS2 (N=115)	TIPS3 (N=95)	TIPS4 (N=202)	Analysis
						Chi ² p
<i>Gender/ Diagnosis N(%)</i>						
Female	16(36.4)	59(40.4)	45(39.1)	41 (43.2)	90 (44.6)	1.6 .65
Schizophrenia/ schizophreniform disorder	37 (84.1)	76(52.1)	48(41.7)	24(25.3)	65(32.2)	57.1 .000 [*]
Delusional disorder	4(9.1)	6 (4.1)	10 (10.4)	12(12.6)	21(10.4)	6.5 .17
Brief psychotic disorder	1(2.3)	14(9.6)	13(11.3)	14(14.7)	18(8.9)	5.8 .21
Schizoaffective disorder	2(4.5)	22(15.1)	15(13.0)	9(9.5)	13(6.4)	9.6 .048 ^{**}
Mood incongruent affective psychosis	0(0)	14(9.6)	15(13.0)	15(15.8)	24(11.9)	8.4 .08
Psychosis NOS	0(0)	14(9.6)	12(10.4)	21(22.1)	61(30.2)	42.7 .000 [†]
ANOVA						
Age	28.4(8.3)	25.0(7.8)	26.7 (11.6)	28.2(10.8)	27.2(11.3)	F 1.8 p .12

^{*} Pilot phase > TIPS, TIPS2, TIPS3, TIPS4^{**} Pilot phase < TIPS, TIPS2, TIPS3, TIPS4[†] Pilot phase < TIPS < TIPS2, TIPS3 < TIPS4

Table 4

Regression model of DU

Measure	Standardized coefficients	t	Sig.
Age	-.07	1.7	.09
Gender	-.06	-1.6	.10
Schizoaffective disorder	-.03	-.8	.44
Delusional disorder	.06	1.4	.15
Brief psychotic disorder	-.4	-9.5	.000
Psychosis NOS	.1	-1.3	.20
Affective psychosis	-.2	-5.0	.000
Information Campaigns	-.1	-2.2	.025

Adjusted R²: 0.21 (large effect size)