# Later Age of Onset and Longer Duration of Untreated Psychosis are Associated with Poorer Outcome in Delusional Infestation

Peter LEPPING[1,2], Sara ABOALKAZ[2], Stephen Bertel SQUIRE[3], Dmitry V. ROMANOV[4], Anthony BEWLEY[5], Markus HUBER[6] and Eric O. NOORTHOORN[7]

*[1]Centre for Mental Health and Society, Wrexham Academic Unit, Bangor University, UK, Mysore Medical College and Research Institute, Mysuru, India, [2]Department of Psychiatry, BCUHB, LL13 7TD Wrexham, [3]Department of Tropical Medicine, Liverpool School of Tropical Medicine, Liverpool, UK, [4]Department of Psychiatry, Sechenov First Moscow State Medical University, Moscow, Russian Federation, [5]Department of Dermatology, University of London, London, UK, [6]Department of Psychiatry, Bruneck Hospital, Bruneck, Italy, and [7]Statistics, GGNet Community Mental Health Centre, Warnsveld, The Netherlands. E-mail: peter.lepping@wales.nhs.uk*

Accepted Aug 21, 2020; Epub ahead of print Aug 27, 2020

Delusional infestation is a mono-delusional psychotic disorder with a high disease burden and reduced social functioning (1). Patients have the delusional belief that they or their immediate environment is infested with living or non-living pathogens. Most commonly people believe that they are infested with insects, worms, parasites, or inanimate objects such as threads or fibres (1). Specialist clinics where psychiatrists see patients jointly with dermatologists or other physicians are rare. Patients tend to see multiple specialists without symptom improvement or engagement with meaningful treatment. Antipsychotics are highly efficacious but compliance is the main stumbling block to successful treatment (1, 2).

In the 1980's, two publications from a specialist clinic in Vienna suggested that later age of onset may be associated with poorer outcome in delusional infestation (3, 4). A study combining data from 4 specialist clinics in Europe, more recently suggested poorer outcome in patients with a long duration of untreated psychosis (5). We have updated the data from those 4 clinics (London and Liverpool in the UK, Bruneck in Italy, and Moscow in Russia) to include more patients and examined whether the association of older age of onset and the association of longer duration of untreated psychosis were confirmed as negatively associated with good outcome.

## METHOD

We used the patient data from the previous publication on duration of untreated psychosis (DUP) and added available data for patients seen since that publication (5). The data includes cases of primary and secondary DI, as these are not separated in the available data bases. Outcome was measured as change in the Clinical Global Impression – Severity score (CGI-S). The CGI-S score gives a comprehensive assessment of overall functioning. A decrease in CGI-S may be interpreted as improvement, where an increase may be seen as worsening.

We were able to include 236 cases at the first point of measurement. A second assessment was obtained in 189 (80%) of patients, which is a high value in clinical research regarding follow-up. In the findings of these 189, we used a simple linear regression analysis and transformed the beta-coefficient by calculating its exponent into an odds ratio (OR). This allows us to estimate proportional changes of variables such as age at presentation to the specialist clinic, age of illness onset, clinic location, and DUP, with the change in CGI-S scores between baseline and follow up scores. Because of the bimodal distribution of age at onset, this variable was categorised in 3 clinically relevant groups: age of onset below 55 years, between 56 and 75, and above 75.

## RESULTS

The distribution of completers by age and DUP was the same over all 4 locations, which discards the possibility of location selection bias and the possibility of confounding of age onset and DUP by location. Out of the 4 sites the Bruneck sample was significantly smaller but with a good response at second measurements. The mean difference of CGI score between baseline and follow up was –2.7, indicating that most patients significantly improved. When inspecting the main variables, age showed a normal distribution. Age at illness onset showed a bimodal distribution and DUP showed an extreme skewedness, with many short and some very long DUP patients.

The outcome variable, change in CGI scores showed a normal distribution. This allowed a simple linear regression analysis. **Table I** shows the linear regression analysis as well as the ORs. It is particularly interesting to look at the Ex(b) results, which represent an OR and is the most important finding to look at. Age at onset showed an OR of 2.344, implying that a higher age of onset category is

**Table I. Association between current age, duration of untreated psychosis (DUP), age at onset, clinic location and Clinical Global Impression decrease**

| | Unstandardized coefficients | | | | 95% CI for OR (EX (β)) | |
|---|---|---|---|---|---|---|
| | β | SE | Significance | OR (Ex (β) | Lower bound | Upper bound |
| (Constant) | 6.351 | 0.476 | <0.001 | | | |
| Current age | –0.055 | 0.020 | 0.009 | 0.946 | 0.928 | 0.966 |
| Duration of untreated psychosis | 0.110 | 0.029 | <0.001 | 1.116 | 1.084 | 1.149 |
| Age onset categories | 0.852 | 0.348 | 0.018 | 2.344 | 1.656 | 3.320 |
| Location | –0.618 | 0.086 | <0.001 | 0.539 | 0.495 | 0.587 |

SE: standard error; CI: confidence interval; OR: odds ratio.



doi: 10.2340/00015555-3625
Acta Derm Venereol 2020; 100: adv00261

related to worse outcome, in other words: the younger the patient at onset of illness the better the outcome. However, higher DUP and lower age at onset are inversely related to one another ($r=-0.294$, $p<0.001$). DUP shows an OR of 1.116, implying a rise of 0.116 in the CGI-S score per DUP year. As with the age of onset, the longer the DUP, the worse the outcome as shown in a smaller decrease of CGI. Because DUP has a range of 29 years this is a substantial association. Another way to look at the statistics is that a lower current age is associated with better outcome (OR=0.946, $p=0.009$).

These results strengthen our previous findings showing an association between longer duration of untreated psychosis and poorer outcome as well as confirming the Austrian results from the 1980's, suggesting that older age at illness onset is also negatively correlated with good outcome.

## DISCUSSION

Delusional infestation is a rare disorder and data is scarce. We managed to include 236 patients from a multicentre specialist clinic setting. The dataset is an update from a previous dataset and strengthens the association between long duration of untreated psychosis in delusional infestation and poor outcome. In addition, we show that suggestions from Austrian specialist clinics in the 1980, hypothesising an association between age at illness onset and negative outcome, are also correct (4, 5). This is important because it emphasises the need for early treatment to avoid long durations of untreated psychosis. Comparing DI with other delusional disorders, we find a number of similarities. Delusional disorders generally seem to have a relatively late onset, seem to be more severe in older age, show poor compliance with treatment, and poorer outcomes with longer duration of untreated illness (6). However, differences include a better response to antipsychotic medication in DI patients (6), and structurally different changes at grey matter level (7).

Early antipsychotic treatment is particularly pertinent in an illness like DI, where doctor hopping is commonplace, and patients are reluctant to take antipsychotic medication despite its proven efficacy. Unfortunately, no research and little practical experience is available to evaluate the efficacy of psychotherapeutic interventions in this patient group. Specialist clinics combining expertise from psychiatry and dermatology or tropical medicine appear to produce good outcomes overall. Clinicians treating DI should specifically focus on engagement with older patients in order to produce the best possible outcome. More research is needed to look at the specific characteristics of those people who drop out of treatment early and further research into various methods of engaging the patient may be useful to optimise our approaches. A small minority of DI patients appears to make a recovery without the use of antipsychotic medication (8). Our study naturally controls for that as it includes all consecutive patients from all participating centres. However, more research into spontaneous recoveries would be desirable.

The limited sample remains a shortcoming of studies into Delusional Infestation. For this reason coincidental differences between patient compilations over the samples cannot be ruled out.

## ACKNOWLEDGEMENTS

*Ethical declaration*. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

*The authors have no conflicts of interest to declare.*

## REFERENCES

1. Freudenmann RW, Lepping P. Delusional infestation. Clin Microbiol Rev 2009; 22: 690–732.
2. Lepping P, Russell I, Freudenmann RW. Antipsychotic treatment of delusional parasitosis – a systematic review. Br J Psychiatry 2007; 191: 198–205.
3. Musalek M, Kutzer E. Psychiatrische and parasitologische Aspekte des Dermatozoenwahns. Wien Klin Wochenschr 1989; 101: 153–160.
4. Musalek M, Bach M, Gerstberger K, Lesch OM, Passweg V, Wancata J, Walter H. Zur Pharmakotherapie des Dermatozoenwahns. Wien Med Wochenschr 1989; 139; 297–302.
5. Romanov DV, Lepping P, Bewley A, Huber M, Freudenmann RW, Lvov AN, et al. Duration of untreated illness and outcome in delusional infestation. Acta Derm Venereol 2018; 98: 848–854.
6. González-Rodríguez A, Guàrdia A, Palao DJ, Labad J, Seeman MV. Moderators and mediators of antipsychotic response in delusional disorder: Further steps are needed. World J Psychiatry 2020; 10: 34–45.
7. Huber M, Wolf RC, Lepping P, Kirchler E, Karner M, Sambataro F, et al. Regional gray matter volume and structural network strength in somatic vs. non-somatic delusional disorders. Prog Neuropsychopharmacol Biol Psychiatry 2018; 82: 115–122.
8. Wilson JW, Miller HE. Delusion of parasitosis (acarophobia). Arch Derm Syphilol 1946; 54: 39–56.