DUAG

Who are we?
Danish University Antidepressant Group (DUAG) was established in 1983 as an organization that could carry out high quality, investigator-driven trials in the setting of a permanent multicenter group. This could create a basis for a better understanding of the basic elements of antidepressant therapy and conduct of clinical trials with antidepressants and thereby to contribute to the long-term strategies and development in the treatment of affective disorders.

DUAG has completed seven clinical studies. These seven studies have involved a total of 15 clinical psychiatry centers and one clinical pharmacology center in Denmark.

History, goals and activities
The Danish University Antidepressant Group (DUAG) was formally founded in 1983 in the course of a Danish multicenter trial involving the three university psychiatry clinics as well as other psychiatry departments and a department of clinical pharmacology in Denmark. The founders, Per Bech, Lars F. Gram, Per Kragh-Sørensen, Ole J. Rafaelsen, Niels Reisby and Per Vestergaard, represented these departments. The aim of DUAG was to establish an organization that could carry out high quality, investigator-driven trials in a setting of a permanent multicenter group. This, in turn, would create a better basis for understanding the basic elements of antidepressant therapy and trial conduct and thereby contribute to the long-term strategies and development in the field.

The DUAG studies have been initiated and planned by the DUAG-steering committees. Financial support has been obtained from interested drug companies. The DUAG steering committees have had the principal responsibility for data analyses and publications. The supporting drug companies have, to a varying extent, contributed to monitoring, data handling and data analyses. In the last four studies (DUAG-4,-5,-6,-7), these functions have entirely been undertaken by the DUAG Coordination Center and the steering groups. The individual members of DUAG have been encouraged to carry out more specific studies based on the DUAG material and this has resulted in publications on pharmacokinetics, clinical symptom profiles, adverse drug reactions and long-term prognosis (suicide); see publication list.

The DUAG-studies
DUAG has carried out four short-term trials, and two prophylaxis studies have recently been completed. In 2009 a post-ECT treatment study was started, this study was finalized in 2013.

The first two DUAG-studies (DUAG-1, DUAG-2) published 1986 and 1990 respectively, have received considerable international attention, each of them being cited 25 -30 times per year during the first 15 – 20 years following there publication. They showed a clearly weaker antidepressant effect of the two SSRIs citalopram and paroxetine in comparison with the tricyclic antidepressant clomipramine.

In a subsequent study, moclobemide was also found to be less effective than clomipramine (DUAG-3, 1993).
The dose-effect study on clomipramine (DUAG-4, 1999) showed flat and overlapping dose-effect curves for therapeutic effect and tolerability. High doses (125–200 mg/d) in comparison with the lower doses (25–50 mg/d), yielded better and/or faster antidepressant response, but with a higher rate of tolerability problems.

A prophylaxis study aimed at comparing the effect of citalopram versus clomipramine versus placebo in unipolar depression (DUAG-5). Final reports have dealt with the 6-month outcome in the pre-phase (published) and the prophylaxis part and the unsurmountable methodological issues in the severely ill patients enrolled for this study (published).

A prophylaxis study in bipolar depression, comparing lithium and lamotrigine (DUAG-6) indicating that lithium might perform better after episodes of mania and that lamotrigine might perform better after episodes of depression or mixed mania, was published in 2010.

A randomised controlled 6-month double-blind study on relapse prevention with escitalopram or nortriptyline following Electro-Convulsive Treatment (DUAG-7) was started in 2009 and finalized in 2013.

Derived studies, based on material from several of the DUAG-studies have dealt with pharmacokinetics, adverse events, baseline variables (age, gender, symptomatology) and long-term morbidity, suicidality etc.

A common database for the first four DUAG-studies with about 10.000 patient-years is presently being prepared for future register-based studies on psychiatric and somatic morbidity and mortality.

Earlier and present heads of Centers (DUAG-study no.)
Ole J. Rafaelsen (1,2), Søren Bøjholm (1,2), Niels Reisby (1,2,3,4), Per Kragh-Sørensen (1,2,3,4,5), Per Vestergaard (1,2,3,4,5,6), Lars F. Gram (principal coordinator: 1,2,3,4,5), Per Bech (1,2,3,4,5,6,7), Jens-Knud Larsen (2,3,4,5,6,7), Tom G. Bolwig (3,4), Jens Schmidt (3,4), John Andersen (4,5), Ib Scheel-Thomsen (4,5,6), Ellen Margrethe Christensen (4,5,6,7), John-Erik Andersson (5), Annette Gjerris (5), Niels-Anton Rasmussen (5), Kurt B. Stage (5), Rasmus W. Licht (5, principal coordinator:6), Birgitte Bjerg Bendsen (5,6,7), Klaus Martiny (5,6, principal coordinator:7), Connie Thurøe Nielsen (7), Dariusz Juchnowics (7), Erik Roj Larsen (7), Henrik Kirsmeier (7), Henrik Lublin (7), Inger Brødsgaard (7), Jens Kristoffersen (7)

Organization

Administrative structure
Project administration has been undertaken by project secretaries at each center in collaboration with the heads of centers and the DUAG-monitor at the DUAG Coordination Center. Data handling and data storage is undertaken by the DUAG center in collaboration with the clinical centers. General matters concerning ongoing projects, and long-term planning are undertaken by the heads of centers at regular meetings held 2-4 times per year. The center heads also have the general responsibility for data analyses, reporting
and publication of study results, usually with individual members of the DUAG-team as primary responsible persons. At regular intervals, the DUAG Coordination Center issues a DUAG-newsletter that is sent to all active participants. DUAG-6 was carried out with the contribution from one associated psychiatry department in Sweden. In the course of patient recruitment, the DUAG-members meet regularly for joint rating-sessions and for joint scientific meetings.

DUAG Clinical Centers (Study numbers)

- Department of Psychiatry, Odense University Hospital, Odense: (1,2,3,4,5,7)
- Department of Psychiatry, Rigshospitalet, Copenhagen: (1,2,3,4,7)
- Psychiatric University Hospital, Risskov, Aarhus: (1,2,3,4,5,6,7)
- Department of Psychiatry, Hillerød GH, Hillerød: (1,2,3,4,5,6,7)
- Department of Psychiatry, Bornholm GH, Rønne: (1,2)
- Department of Psychiatry, Frederiksberg GH, Copenhagen (2,3,4,5,6,7)
- Department of Psychiatry, Middelfart GH, Middelfart: (3,4)
- Department of Psychiatry, Bispebjerg GH, Copenhagen: (4,5)
- Department of Psychiatry, Aalborg GH, Aalborg: (4,5,6,7)
- Department of Psychiatry, Vordingborg GH, Vordingborg: (4,5)
- Department of Psychiatry, Gentofte GH, Gentofte: (4,5,6,7)
- Department of Psychiatry, Horsens GH, Horsens: (7)
- Department of Psychiatry, Esbjerg GH, Esbjerg: (7)
- Department of Psychiatry, Helsingør GH, Helsingør: (7)
- Department of Psychiatry, Glostrup GH, Glostrup: (7)

DUAG Coordination Center

- Department of Clinical Pharmacology, University of Southern Denmark, Odense (1,2,3,4,5,6)
- Department of Psychiatry, Hillerød GH, Hillerød: (7)

Projects

**DUAG-1**: Comparative trial. Citalopram (40 mg/d) versus clomipramine (150 mg/d), 5 weeks, in depression. N = 102. Inpatients. 1980-84

**DUAG-2**: Comparative trial. Paroxetine (30 mg/d) versus clomipramine (150 mg/d), 6 weeks, in depression. N = 120. Inpatients. 1985-87.

**DUAG-3**: Comparative trial. Moclobemide (300 mg/d) versus clomipramine (150 mg/d), 6 weeks, in depression. N = 115. Inpatients. 1987-90.

**DUAG-4**: Dose-effect study of clomipramine in depression; five fixed dose levels (25, 50, 75, 125, 200 mg/d) for 6 weeks. N = 151. Inpatients. 1990-94.

**DUAG-5**: Comparative trial of prophylactic effect of citalopram versus clomipramine versus placebo in unipolar depression. 2-4 years. In- and outpatients were followed over a period of 7 - 15 months before treatment discontinuation and inclusion in the prophylaxis study. Recruitment started 1997 and the last follow-up was completed by the end of 2006.
with the inclusion of only 59 prophylaxis patients.

**DUAG-6**: Comparative trial of prophylactic effect of lamotrigine versus lithium in bipolar disorder. 2 years, non-blind, randomised. In- and outpatients. Recruitment started in 2000 and was completed in 2006 after inclusion of 155 patients.

**DUAG-7**: Relapse prevention in patients with major depression treated with electroconvulsive therapy comparing a fixed dose range of escitalopram with a fixed dose of nortriptyline. A randomised controlled 6 month double-blind study. Recruitment started in 2009. The study was finalized in 2013.

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**List of publications**


23. Hildebrandt MG, Stage KB, Kragh-Sørensen P; Danish University Antidepressant Group. Gender differences in severity, symptomatology and distribution of melancholia in major depression. Psychopathology 2003;36:204-212.


DUAG Symposium 2015

Monday, 21 September 2015 at the 31ST NORDIC CONGRESS OF PSYCHIATRY in Copenhagen
Time: 13.30 - 15.00

The MINI International Neuropsychiatric Interview and DSM-5 - A DUAG symposium
Chairpersons: Professor David Sheehan, MD, MBA and Associate Professor Erik R. Larsen, MD

Speakers:

- Professor Janet B.W. Williams, PhD: The LEAD approach
- Professor David Sheehan, MD, MBA: The DSM-5 version of the MINI
- Professor Ulrik F. Malt, MD, PhD: The MINI in Norway
- Professor Christer Allgulander, MD: The MINI in Sweden
- Assistant Professor Søren D. Østergaard, MD, PhD: Brief, valid scales for the measurement of response and remission in the corresponding DSM-5 categories

The DUAG (Danish University Antidepressant Group) was established three decades ago for the implementation of methodological procedures at all levels in clinical trials of antidepressants. Concerning clinical assessment scales, DUAG focussed in the first trials on symptom depression scales for outcome measurement (response and remission). We have recently selected the MINI Neuropsychiatric Interview to evaluate to what extent the patient’s clinical picture fulfils the research criteria for ICD-10 or DSM-IV/DSM-5 depression as this instrument was designed to be administered by experienced clinicians.

DUAG has always focussed on the LEAD approach (Longitudinally collected data by Expert utilizing All available Data) as the clinical platform in our trials. Janet Williams, who was behind the development of the LEAD approach will commence this symposium, followed by David Sheehan as one of the architects of the MINI.

In Scandinavia, use of the MINI has obtained a high acceptance in Norway and Sweden. Ulrik Malt and Christer Allgulander will each describe their great work in this respect. Finally, Søren D. Østergaard will give a review over brief rating scales for the dimensional measurement of major depression, psychotic depression and schizophrenia with correspondence to the ICD-10 and DSM-5 categories.
Links

- Dansk Psykiatrisk Selskab
- Dansk Selskab for Affektive Lidelser
- Den Centrale Videnskabsetiske Komité
- Lægemiddelstyrelsen
- Datatilsynet
- Psychiatric Research Unit, CCMH
- The International Society for Bipolar Disorder
- Scandinavian College of Neuropsychopharmacology
- Clinical Trials
- ISAD
- NICE
- EMEA
- Collegium Internationale Neuro Psychopharmacologicum
- European College of Neuro-Psychopharmacology