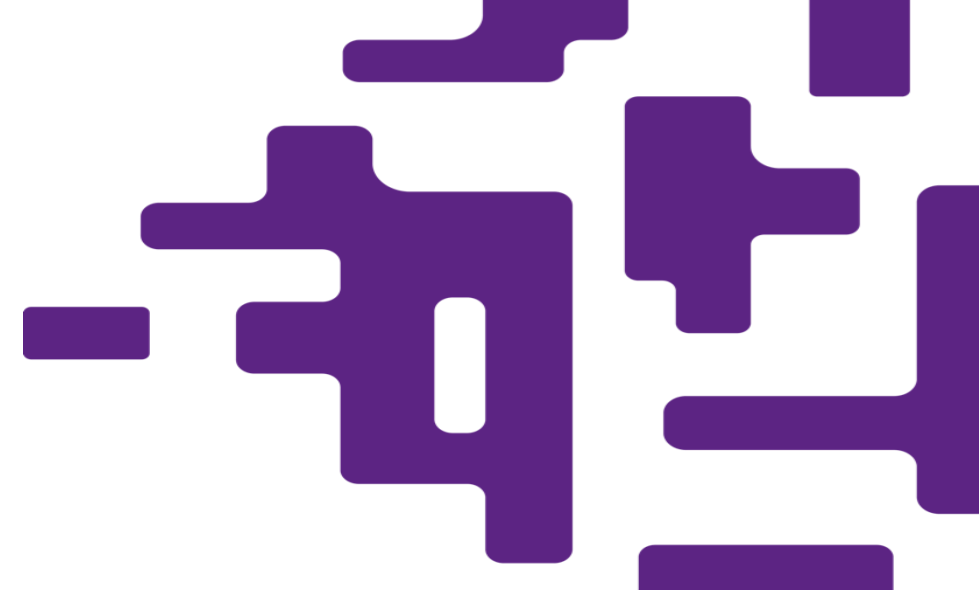




NORMENT

Norsk senter for forskning
på mentale lidelser



Immunsystemet: Mulighet for behandling av mentale lidelser med betennelsesdempende medisiner

Nils Eiel Steen

Overlege og professor



UNIVERSITETET
I OSLO



Oslo
universitetssykehus



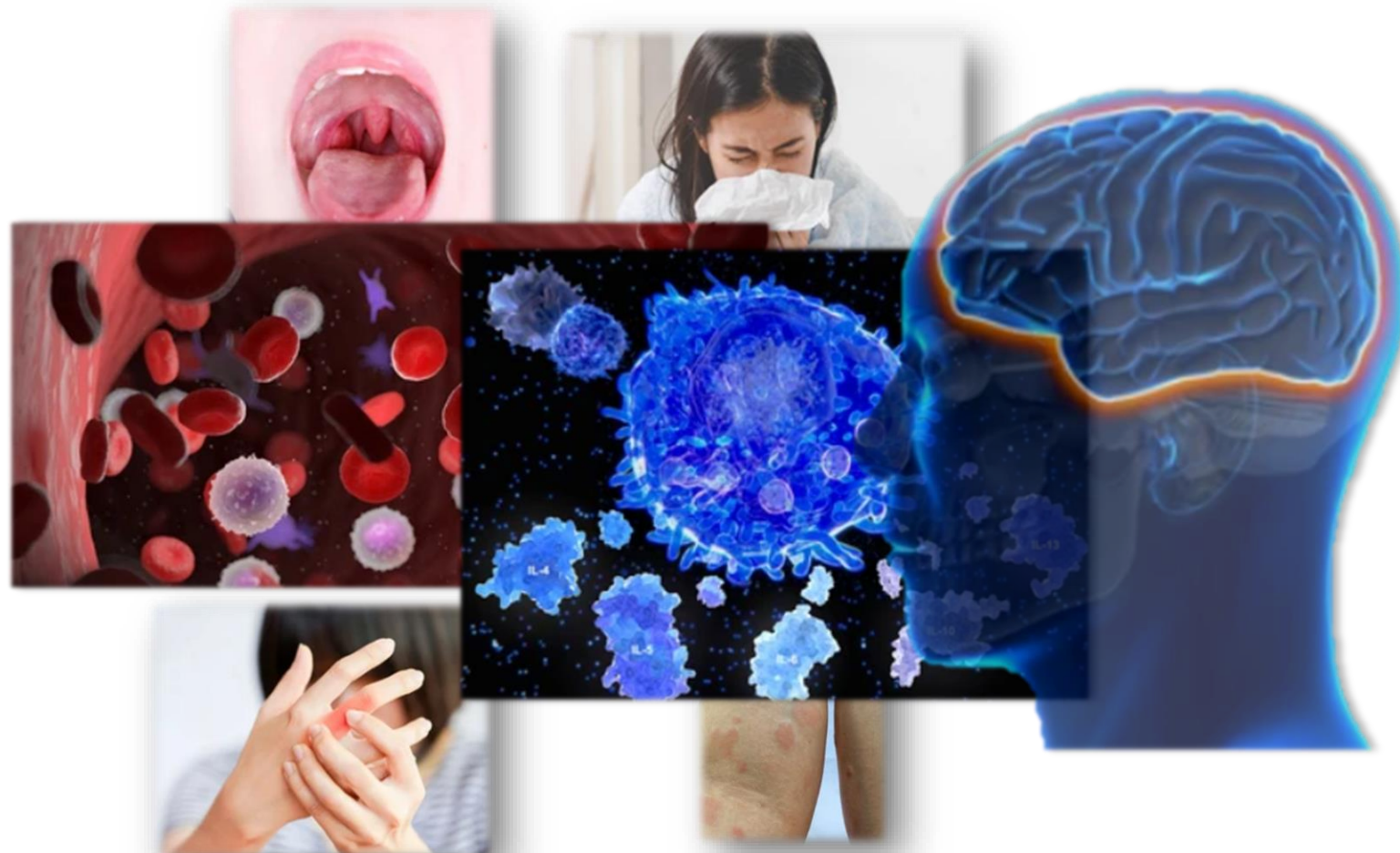
UNIVERSITETET I BERGEN



HELSE BERGEN
Haukeland universitetssjukehus



Betennelse – mekanisme



Bilder fra Shutterstock

Håp: Betennelse kan behandles

Det finnes medisiner

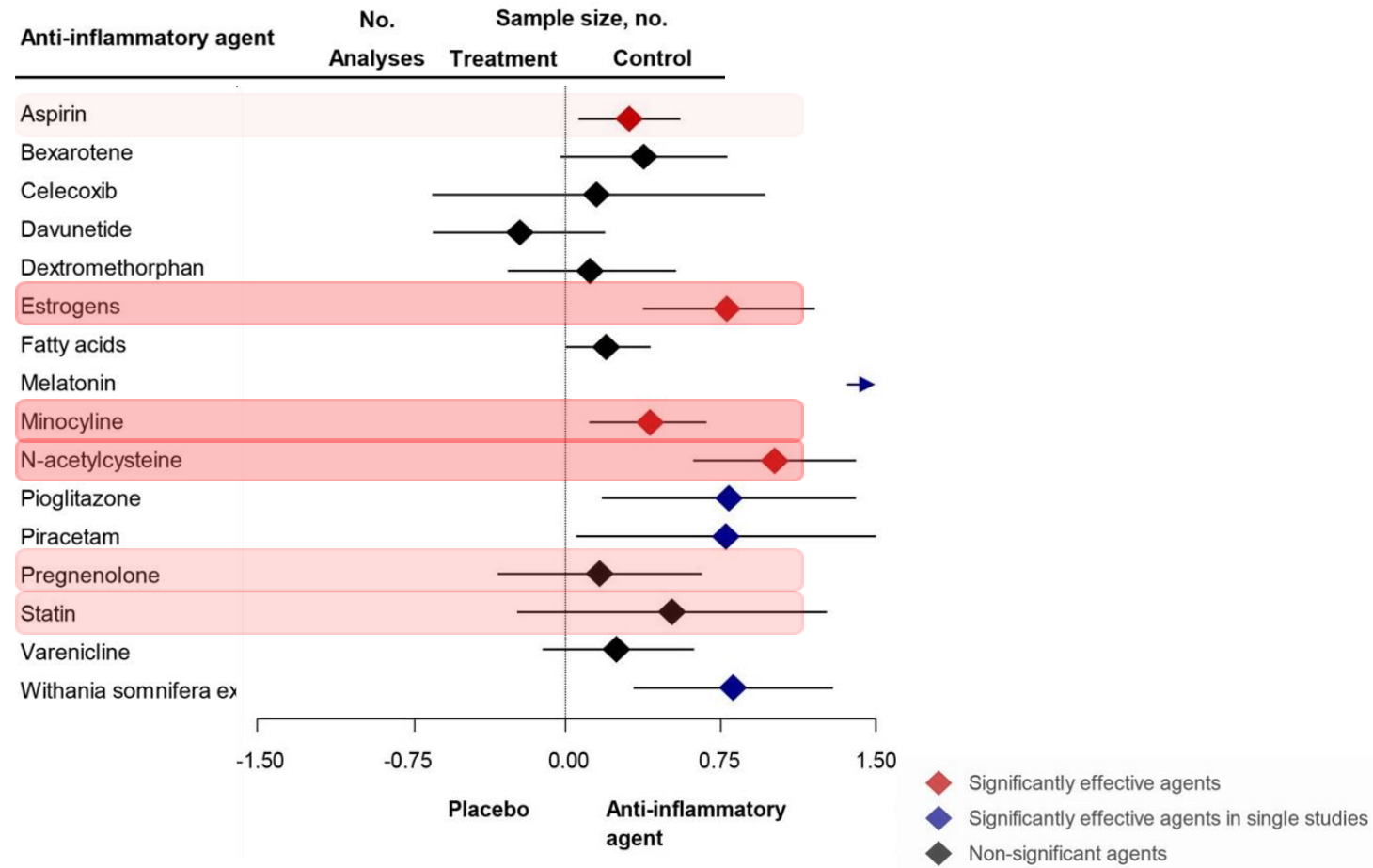
Flere typer medisiner

Medisiner

| Inflammatory components | Crosses BBB | Actions in the brain |
|--------------------------|-------------|--|
| Antipsychotics | ++ | Dopamine receptor blockade (D2), 1BDNF |
| Aspirin | +/- | PGI, TNF- α , COX-1, COX-2 |
| Bexarotene | ++ | Complement system (indirectly) |
| Celecoxib | ++ | COX-2, PGI |
| Corticosteroids | +/- | Inhibition of many steps in innate and specific immune response |
| Cytostatics | +/- | Diverse, e.g. for MTX: TNF- α |
| Davunetide | ++ | TNF- α |
| Dextromethorphan | ++ | Microglia inhibition |
| Estrogens | ++ | IL-1 β , IL-6, TNF- α , NF- κ B, NO |
| Fatty acids | ++ | Zinc, TNF- α , COX-2, IL-1 |
| Leptin | ++ | Pro- and anti-inflammatory effects (e.g. IL-4, IL-10, IFN- γ) |
| Macrolides/tetracyclines | ++ | IL-1 β , NO |
| Melatonin | ++ | NO, IL-1 β , TNF- α , NF- κ B |
| Minocycline | ++ | Microglia inhibition, IL-1 β , IL-6, TNF- α , IFN- γ |
| Monoclonal antibodies | +/- | Act on specific inflammatory cytokines |
| N-acetylcysteine | ++ | IL-1 β , IL-6, TNF- α |
| Pioglitazone | ++ | NF- κ B |
| Piracetam | +/- | IL-1 β , TNF- α , MPO |
| Pregnenolone | ++ | IL-6, TNF- α |
| Statins | ++ | CRP, IL-6 |
| Transplantation adjuncts | +/- | Diverse, e.g. IL-1/2/6, TNF- α |
| Ticagrelor | ++ | IL-1 β , TNF- α , NF- κ B |
| Thrombinomifera | ++ | COX-2, NF- κ B |

Bilder fra N Çakici et al, Psychol Med. 2019 og Shutterstock

Randomiserte studier - Schizofreni



Figur (omarbeidet) fra N Çakici et al, Psychol Med. 2019

Randomiserte studier - Schizofreni

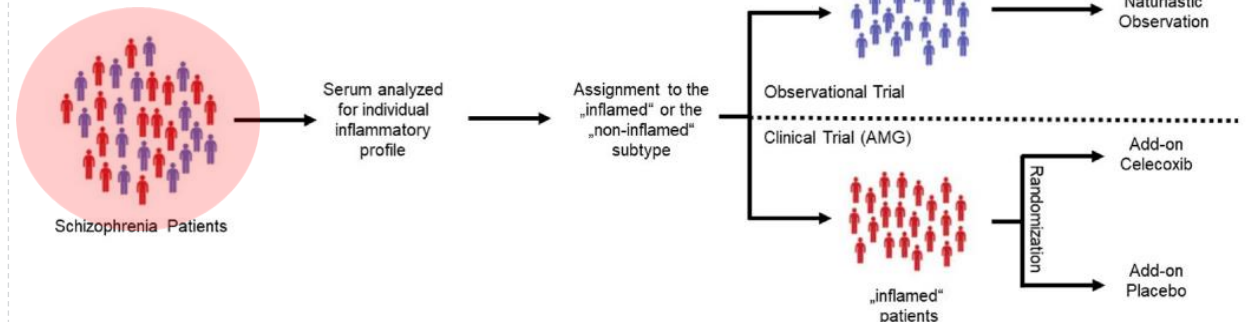
R. Jeppesen, et al.

Brain, Behavior, and Immunity 90 (2020) 364–380

Table 3

Overview of main results from meta-analyses.

| | Effect size | 95% CI |
|---|--------------|----------------|
| Total psychopathology (MD, PANSS)* | -4.57 | -5.93 to -3.20 |
| Total psychopathology (MD, BPRS) * | -3.85 | -6.63 to -1.07 |
| Total psychopathology (SMD) * | -0.29 | -0.40 to -0.19 |
| Psychotic symptoms (MD, PANSS) * | -0.53 | -0.88 to -0.18 |
| Psychotic symptoms (MD, BPRS) | -1.52 | -3.05 to 0.01 |
| Psychotic symptoms (SMD) * | -0.13 | -0.21 to -0.05 |
| Negative symptoms (MD, PANSS) * | -1.29 | -1.84 to -0.74 |
| Negative symptoms (SMD) * | -0.23 | -0.35 to -0.12 |
| Gen. psychopathology (MD, PANSS) * | -1.50 | -2.27 to -0.72 |
| Gen. psychopathology (SMD) * | -0.16 | -0.26 to -0.06 |
| Cognition (SMD) | -0.03 | -0.17 to 0.11 |
| Working memory * | 0.21 | 0.03 to 0.40 |
| Attention | -0.02 | -0.26 to 0.21 |
| Executive functions | 0.01 | -0.14 to 0.15 |
| Processing speed | 0.11 | -0.03 to 0.26 |
| Verbal fluency | 0.02 | -0.16 to 0.20 |



Figur (omarbeidet) fra Strube et al, J Neural Transm (Vienna) 2023

Randomiserte studier – Bipolar lidelse

Network meta-analysis comparisons for the response rate and remission rate.

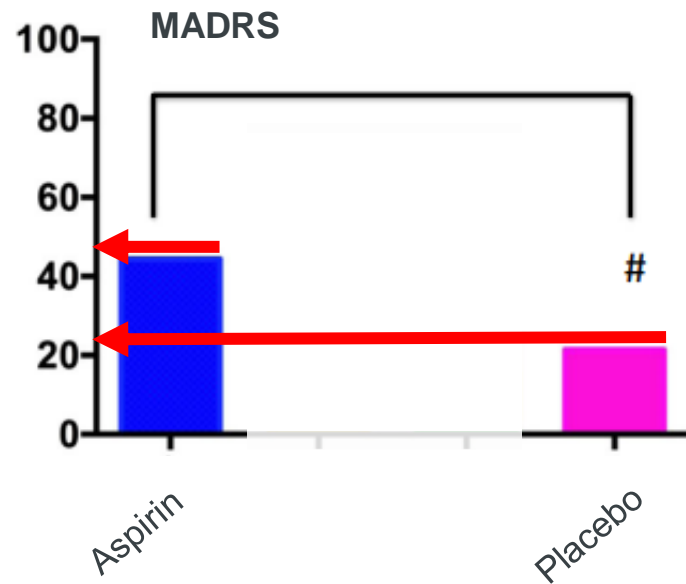
Xu et al, Asian J Psychiatr. 2023

| | | | | | | | |
|--------------|--------------|---------------|--------------|--------------------|--------------------------|---------------|---------------|
| NSAIDs | 0.80 | NA | 1.36 | 20.97 | 1.52 | 0.56 | <u>3.93</u> |
| | (0.07,9.24) | | (0.24,7.74) | (0.68,647.50) | (0.09,24.67) | (0.01,29.42) | (1.15,13.43) |
| 0.68 | NAC | NA | 1.71 | 26.33 | 1.91 | 0.71 | 4.94 |
| (0.19,2.49) | | | (0.11,25.70) | (0.56,1229.93) | (0.07,50.88) | (0.01,53.14) | (1.03,41.38) |
| 0.16 | 0.23 | Omega-3 FA | NA | NA | NA | NA | NA |
| (0.01,4.67) | (0.01,7.12) | | | | | | |
| 1.02 | 1.49 | 6.44 | Minocycline | 15.37 | 1.11 | 0.41 | 2.83 |
| (0.31,3.34) | (0.32,7.00) | (0.20,210.31) | | (0.41,577.19) | (0.05,22.93) | (0.01,25.58) | (0.53,11.78) |
| 2.52 | 3.69 | 15.93 | 2.48 | Pioglitazone | 0.07 | 0.03 | 0.19 |
| (0.41,15.42) | (0.56,24.25) | (0.42,600.01) | (0.34,18.20) | | (0.00,4.22) | (0.00,3.75) | (0.01,4.61) |
| 0.64 | 0.94 | 4.06 | 0.63 | 0.25 | TNF- α inhibition | 0.37 | 2.53 |
| (0.08,4.99) | (0.11,7.79) | (0.09,173.70) | (0.07,5.76) | (0.02,2.89) | | (0.00,33.84) | (0.21,31.51) |
| 0.12 | 0.18 | 0.78 | 0.12 | <u>0.05</u> | 0.19 | CoQ10 | 7.00 |
| (0.01,1.07) | (0.02,1.67) | (0.02,35.56) | (0.01,1.23) | <u>(0.00,0.61)</u> | (0.01,2.87) | | (0.16,301.54) |
| 2.33 | <u>3.42</u> | 14.75 | 2.29 | 0.93 | 3.63 | <u>18.85</u> | Placebo |
| (0.96,5.65) | (1.23,9.52) | (0.56,387.85) | (0.68,7.70) | (0.19,4.47) | (0.57,23.12) | (2.63,135.00) | |

Response rate Comparison Remission rate

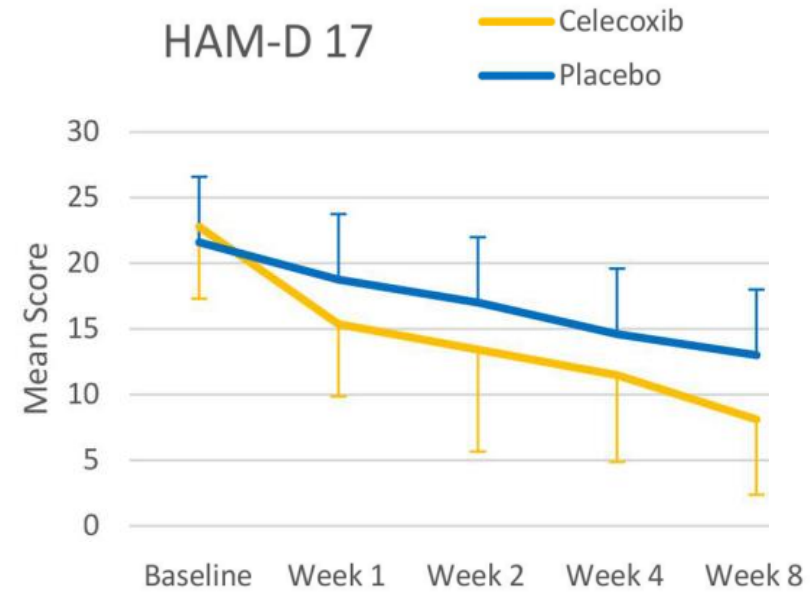
Randomiserte studier – Bipolar lidelse

% respondere, depresjon



Figur (omarbeidet fra Savitz et al, Transl Psych 2018)

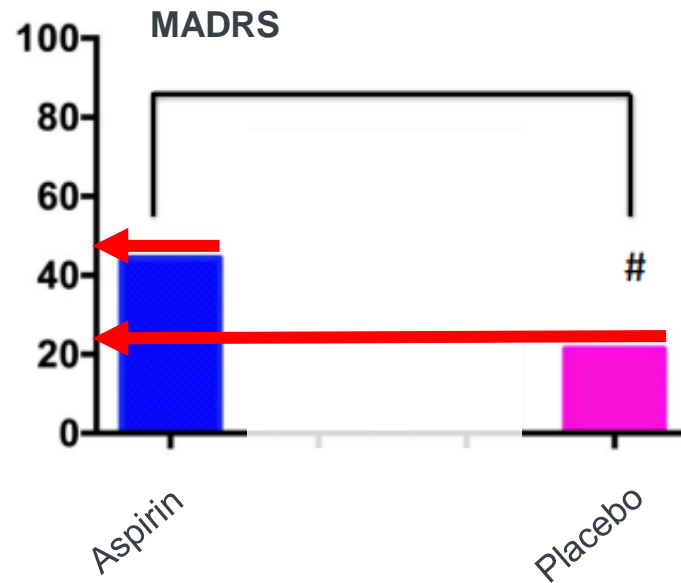
Behandlingsresistent depresjon



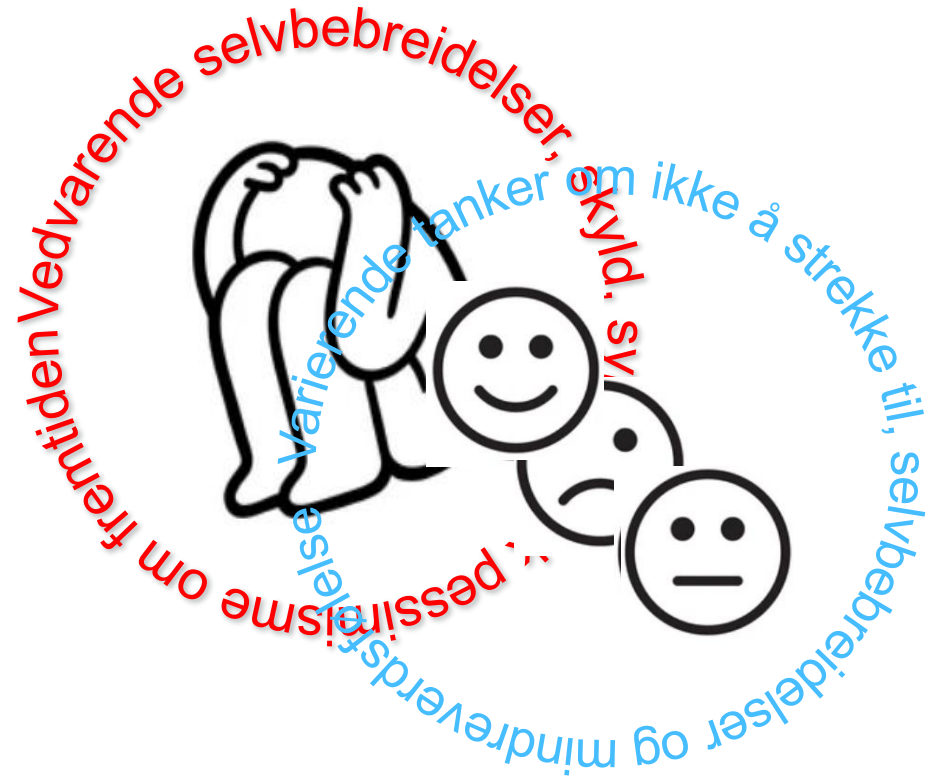
Figur (omarbeidet) fra Halaris et al, J Affect Disord 2020

Randomiserte studier – Bipolar lidelse

% respondere, depresjon



Figur (omarbeidet fra Savitz et al, Transl Psych 2018)





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