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# Supplementary file

Anatomical Therapeutic Chemical Classification System (ATC) used in this study

Antibiotics: J01

csDMARDs: L01BA01, L04AX03, L04AA13, P01BA02, L04AD01, L04AX01, A07EC01,

L01AA01, M01CB01, L04AA06

Steroid: H02AB06

Biologics: L04AB02, L04AB01, L04AB04, L01XC02, L04AA24, L04AB05, L04AB06, L04AC07

#### The DNPR

The DNPR has a record of all inpatient hospitalizations in the entire Danish population since 1977 and all instances of contact with hospital outpatient clinics since 1995, including admission and discharge dates and up to 20 discharge diagnoses per contact coded according to the International Classification of Diseases, edition 10 (ICD-10) during the period of this study and ICD-8 during earlier periods (1). It also has a record of CPR numbers, patients' municipalities, identification of the hospital wards, and dates and times of activities performed, including information on the type of examinations, surgeries and treatments. For RA outpatient visits, the use and types of DMARDs and/or biologics are recorded.

The validity of a pneumonia diagnosis in this register has previously been evaluated and found to be high, with a positive predictive value (PPV) of 90% (95%CI: 82-95%) (2).

# The Aarhus University Prescription Database

The Aarhus University Prescription Database records information on prescriptions filled for all reimbursed medications including the CPR number, date of sale and type of drug. The database receives data from all of the community pharmacies in the northern and central regions of Jutland (3). Both DMARDs and prednisolone are eligible for reimbursement.

## **DANBIO**

DANBIO is a nationwide, Danish register where clinical data on patients with rheumatic diseases is recorded. DANBIO was initiated in 2000 as a nationwide voluntary register that was focused on

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patients who received biologics, and information regarding the indications for treatment, treatment efficacy and adverse events was recorded. In 2006, DANBIO was approved by the Danish National Board of Health as a national quality registry, and since then, reporting of patients treated with biologics and newly referred RA patients, regardless of the treatment and disease duration, has been mandatory (4). When an RA patient is seen by a rheumatologist, a "visit" is created in DANBIO. A visit consists of information regarding the current functional status, disease activity, treatment, and visual analogue scale (VAS) scores of pain, fatigue, and of the patient and physician's global assessment.

## The LABKA database

The LABKA database contains results from every blood sample taken from patients living in the study area with full geographical coverage for the northern region of Jutland since 1997 and for the central region since 2000. Data collected in the database include the CPR number, date the blood sample analysis was performed, test results and an identification code for the physician/department requesting the analysis.

### Validity of the RA diagnosis

RA diagnoses recorded in the DNPR may not be entirely accurate (5). To quantify the occurrence of potential coding errors, we reviewed a sample of 190 medical records of pneumonia patients with one or more previous RA registrations in the DNPR from the northern region of Jutland (100 patients with one registration, 45 patients with two registrations, and 45 patients with three or more previous RA registrations). Using the three definitions of RA (clinically confirmed RA based on a rheumatologist's expert opinion, fulfilment of the American College of Rheumatology (ACR) 1987 criteria for RA, or fulfilment of the 2010 ACR/EULAR classification criteria for RA, for patients diagnosed in 2010 or later) a trained rheumatologist confirmed the diagnosis. We confined the validation to the North Jutland Region, as the data quality was considered uniform within regions (6).

We calculated the PPV of an RA diagnosis as the percentage of RA diagnoses in the reviewed hospital record sample that fulfilled the criteria for confirmed RA for each of the three RA definitions.

Of the 1,220 patients identified in the DNPR with RA 637 had a single hospital contact registered with a diagnosis of RA, 255 patients had two registrations and 328 patients had three or more

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registrations. In our validation sample of 190 patients, the PPV of an RA diagnosis was 88% (95% CI: 83-93%). Among patients with three or more registrations, 98% of the RA diagnoses were confirmed, whereas the proportion of patients with a confirmed diagnosis among those with only one registration was 83% (table S1). The ACR 1987 criteria for RA were fulfilled by 81 (42.6%) patients.

The information and validity of the DNPR is of major importance. In a previous study, the estimated PPV of a pneumonia diagnosis based on the DNPR was 90% (2). In the present study, it was 88% for RA diagnosis, which suggests a high validity for RA diagnoses. This is supported by data from a newly published study regarding the validity and completeness of RA diagnosis in DANBIO and the DNPR, which found a PPV of 79% for RA diagnosis in the DNPR (7). However, this was calculated for a total of 2 or more registrations within 90 days. Our data clearly show that the PPV improves with 3 or more registrations.

Number of registrations (Diagnosis in the DNPR)	Fulfilment of the ACR 1987 criteria (yes/no/unknown)	Clinical diagnosis (yes/no/unknown)	Positive predictive value (95% CI)
2 (N=45)	18/0/27	<b>41</b> /4/0	91% (79-98)
≥3 (N=45)	<b>25</b> /1/19	<b>44</b> /0/1	98% (88-100)
Total N=190	<b>81</b> /6/103	<b>168</b> /21/1	88% (83-93)

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#### Supplementary figure 1

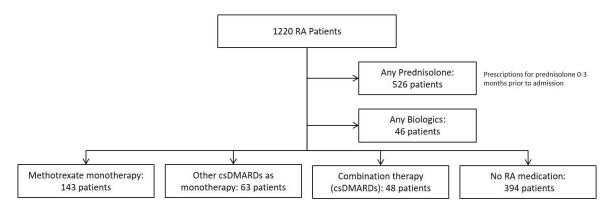


Figure legend: Schematic overview of the hierarchical structure applied to categorize patients according to exposure to prednisolone, csDMARDs and biologics. Each patient could only be in one group.

Based on registered treatment within one year prior to pneumonia admission.

#### References

- 1. Lynge E, Sandegaard JL, Rebolj M. The Danish national patient register. Scand J Public Health 2011;39:30–3.
- Thomsen RW, Riis A, Nørgaard M, Jacobsen J, Christensen S, McDonald CJ et al. Rising incidence and persistently high mortality of hospitalized pneumonia: A 10-year population-based study in Denmark. J Intern Med 2006;259:410–7.
- 3. Ehrenstein V, Antonsen S, Pedersen L. Existing data sources for clinical epidemiology: Aarhus University Prescription Database. Clin Epidemiol 2010;2:273–9.
- 4. Ibfelt EH, Jensen DV, Hetland ML. The Danish nationwide clinical register for patients with rheumatoid arthritis: DANBIO. Clin Epidemiol 2016;8:737–42.
- 5. Pedersen M, Klarlund M, Jacobsen S, Svendsen AJ, Frisch M. Validity of rheumatoid arthritis diagnoses in the Danish National Patient Registry. Eur J Epidemiol 2004;19:1097–103.
- 6. Nickelsen T. Data validity and coverage in the Danish National Health Registry. A literature review. Ugeskr Laeger 2001;164:33–7.
- 7. Ibfelt EH, Sørensen J, Jensen D V., Dreyer L, Schiottz-Christensen B, Thygesen PH et al. Validity and completeness of rheumatoid arthritis diagnoses in the nationwide DANBIO clinical register and

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the Danish national patient registry. Clin Epidemiol 2017;9:627–37.