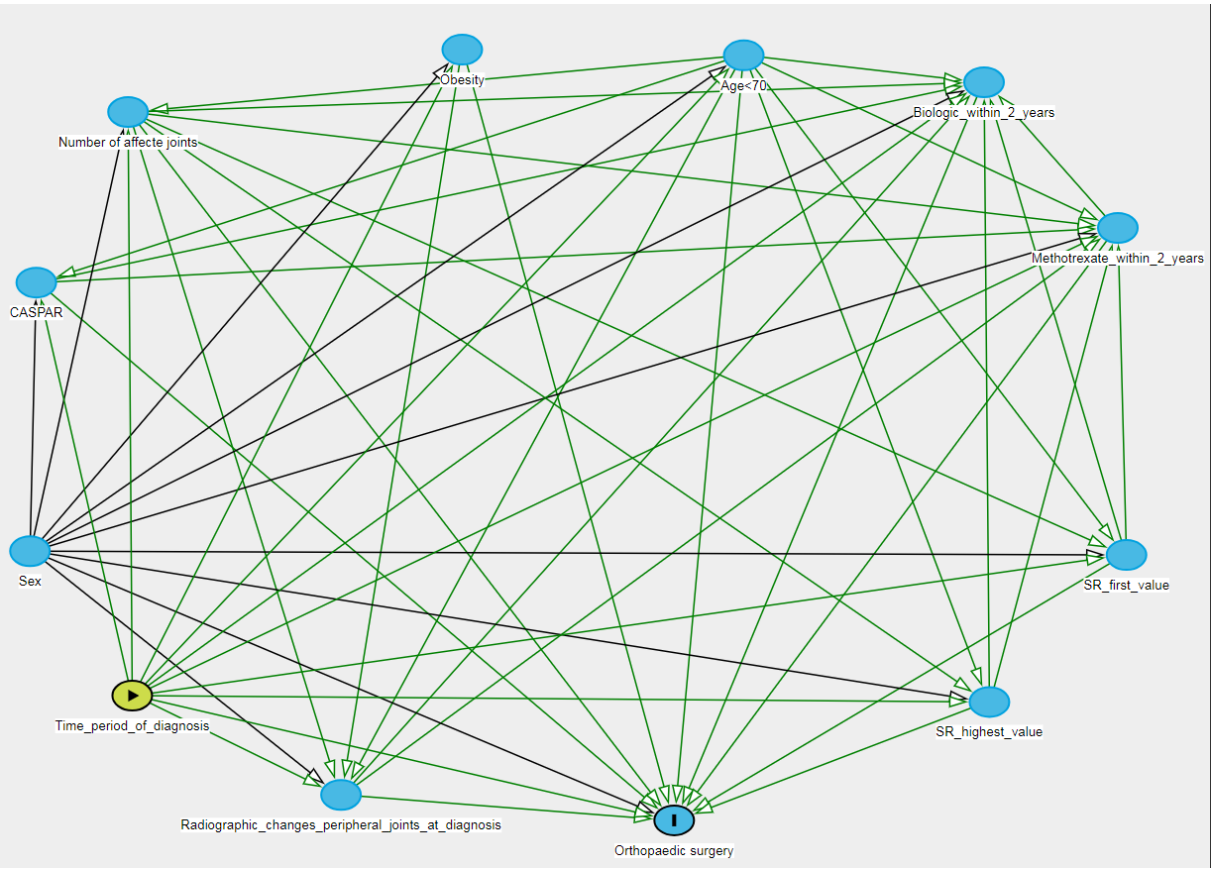
ONLINE SUPPLEMENTARY DATA

A Directed Acyclic Graph (DAG) is a graphic model that depicts a set of hypotheses about the causal process that generates a set of variables of interest. The intention is to minimise bias in empirical studies in epidemiology.

We considered the different exposure variables, and how they could potentially affect one another. This was plotted using the software on www.dagitty.net with the following result (1).




Orthopaedic surgery is the outcome variable. All included exposure variables may potentially affect this outcome. Arrows are drawn according to whether the exposure variables may have an effect on other exposure variables, and visualises causal paths and biasing paths. One may thus find potential biases and which other variables that needs to be included in the Cox regression analyses to minimise bias, for each variable. In example; for “Time period of diagnosis”, no adjustment is necessary to estimate the total effect.

The complete model code is included below.

**Model code**

Age%3C70 1 @0.600,-0.114

Biologic_within_2_years 1 @0.873,-0.084

CASPAR 1 @-0.071,0.243

Methotrexate_within_2_years 1 @0.990,0.352

Number%20of%20affecte%20joints 1 @0.016,-0.025

Obesity 1 @0.333,-0.123

Orthopaedic%20surgery O @0.534,1.088

Radiographic_changes_peripheral_joints_at_diagnosis 1 @0.218,1.048

SR_first_value 1 @0.963,0.671

SR_highest_value 1 @0.833,0.902

Sex 1 @-0.077,0.665

Time_period_of_diagnosis 1 @0.020,0.892

Age%3C70 Biologic_within_2_years CASPAR Methotrexate_within_2_years Number%20of%20affecte%20joints Orthopaedic%20surgery Radiographic_changes_peripheral_joints_at_diagnosis SR_first_value SR_highest_value

Biologic_within_2_years Orthopaedic%20surgery

CASPAR Biologic_within_2_years Methotrexate_within_2_years Orthopaedic%20surgery

Methotrexate_within_2_years Biologic_within_2_years Orthopaedic%20surgery

Number%20of%20affecte%20joints Biologic_within_2_years Methotrexate_within_2_years Orthopaedic%20surgery Radiographic_changes_peripheral_joints_at_diagnosis SR_first_value SR_highest_value

Obesity Orthopaedic%20surgery Radiographic_changes_peripheral_joints_at_diagnosis

Radiographic_changes_peripheral_joints_at_diagnosis Biologic_within_2_years Methotrexate_within_2_years Orthopaedic%20surgery

SR_first_value Biologic_within_2_years Methotrexate_within_2_years Orthopaedic%20surgery

SR_highest_value Biologic_within_2_years Methotrexate_within_2_years Orthopaedic%20surgery

Sex Age%3C70 Biologic_within_2_years CASPAR Methotrexate_within_2_years Number%20of%20affecte%20joints Obesity Orthopaedic%20surgery Radiographic_changes_peripheral_joints_at_diagnosis SR_first_value SR_highest_value

Time_period_of_diagnosis Age%3C70 Biologic_within_2_years CASPAR Methotrexate_within_2_years Number%20of%20affecte%20joints Obesity Orthopaedic%20surgery Radiographic_changes_peripheral_joints_at_diagnosis SR_first_value SR_highest_value

1. Textor J, van der Zander B, Gilthorpe MS, Liskiewicz M, Ellison GT. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. Int J Epidemiol. 2016;45(6):1887-94.