Table 1. LM in RA - summary

Stratification of LM according to CVR

- LM is navigated by lipid parameters and CVR. However, due to limited evidence, optimal strategies for CVR estimation and LM in RA are uncertain.
- We propose a new algorithm for CVR estimation/LM (Figure 1).
    - Patients with **"Low-risk RA"** (seronegative, non-erosive RA, without extraarticular manifestations, in long-term remission, with well-preserved physical function, not currently using glucocorticoids, and without high cumulative disease activity and glucocorticoid dose) should follow LM recommendations for the general population, but all should optimally have LDL-C<3 mmol/L (115 mg/dL). **"High-risk RA"** reclassifies patients into a higher ESC CVR-category, requiring lower LDL-C targets than those recommended for the general population.
        - Thus, RA patients should ideally have LDL-C levels <3 mmol/L (115 mg/dL), but many (including "high-risk RA") <2.6 mmol/L (100mg/dL), and some <1.8 mmol/L (70mg/dL).
    - When using SCORE, appropriate version for the respective country should be used, preferably the version that includes HDL-C (http://www.heartscore.org).
    - All diabetics >40 years of age should use statins. This treatment may be considered also in younger diabetics with pronounced CVR (30).

- In order to correctly treat patients with very-high CVR, and given the tendency to atypical clinical CVD picture in RA, proactive approach to diagnosing CVD is critical.
- Ultrasonographic detection of carotid plaques can facilitate determining very-high CVR and may be particularly important in "high-risk RA". It can be meaningful in low to high ESC CVR-categories.
- The overall situation, including comorbidities, treatment, lifestyle and socioeconomic status, should be considered in CVR estimation.

Lipid assessment

- Lipid monitoring in RA should include TC, LDL-C, HDL-C and TG levels, and can be performed under non-fasting conditions. If non-fasting TGs ≥2.3 mmol/L (200 mg/dL), fasting TG assessment should be performed.
- Lp(a) screening should be considered.
- Non-HDL-C may be superior to LDL-C as CVR marker, especially in patients with high TG and low LDL-C, and in non-fasting samples.
- We recommend lipid assessment in RA regardless of age, at least every five years in "low-risk RA", and annually in "high-risk RA".
- More frequent assessment should be considered in patients with severe lipid abnormalities and poor therapeutic response, rapidly progressing RA or CVR estimate close to thresholds mandating lower LDL-C targets.

- Reassessment is indicated after changes significantly influencing CVR (e.g., lifestyle modifications, initiation of DMARD or high-dose glucocorticoid treatment).
- The assessment should be performed also during low RA-activity, when hypercholesterolemia can be uncovered, e.g. 1-4 months after initiation of DMARDs.
    - For interleukin-6 inhibitors, assessment of lipid profile is recommended 4-8 weeks after initiation of therapy, and subsequently at 6 months intervals.
- Intensive CVR screening/LM might not be appropriate in some individuals, e.g. those with short life-expectancy or predisposed to adverse effects.

Therapeutic interventions

- RA patients should receive adequate counseling and support regarding diet, physical activity and other beneficial lifestyle modifications.
- Pharmacological treatment of hypercholesterolemia should be performed primarily by statins.
    - The optimal form of statin regimen in RA is unknown, but statins with profound anti-inflammatory effects (e.g., atorvastatin or rosuvastatin) may be particularly beneficial.
- If goal LDL-C cannot be reached through lifestyle and statins, other LMTs (PCSK9, ezetimibe, fibrates) should be considered, following general recommendations.
- Treatment of other lipid aberrations, including high TG and Lp(a) levels, should follow general recommendations.

- Control of RA activity may ameliorate some alterations of lipid homeostasis, such as Lp(a) levels, lipoprotein functions and cellular cholesterol transport, and decrease overall CVR.

Implementation of LM

- LM in RA can be administered by general practitioners, in collaboration with, e.g., cardiologists, endocrinologists, lipidologists, dietitians, nurses and physical therapists. Rheumatologists should take the lead and ensure that adequate LM is provided.
- There should be focus on education of patients and health care providers about CVR/LM in RA.

Figure