



## Invited Commentary

## LDL-cholesterol targets as Achilles' heel of 2020 ISH guidelines



2020 International Society of Hypertension (ISH) practice guidelines were published just one year after European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) guidelines on dyslipidaemias [1,2].

As far as LDL-cholesterol targets, ISH guidelines states, that it should be reduced according to risk profile: (1) >50% and <70 mg/dL (1.8 mmol/L) in hypertension with cardiovascular disease (CVD), chronic kidney disease (CKD), diabetes mellitus (DM) or no CVD and high risk; (2) >50% and <100 mg/dL (2.6 mmol/L) in high-risk patients; (3) <115 mg/dL (3 mmol/L) in moderate-risk patients. The reference to this recommendation is based on 2019 ESC/EAS guidelines on dyslipidaemias according to authors, however it is not true. LDL-cholesterol target in the ESC/EAS “very high risk” group is >50% reduction and <55 mg/dL (1.4 mmol/L). To this particular risk category belong many of those called “high-risk first group” in ISH guidelines. Namely, people with hypertension and: documented CVD (clinically or on imaging), those with stroke/transient ischemic attack of central nervous system (TIA) history, peripheral artery disease (PAD), DM (with target organ damage, or at least 3 major risk factor, or early onset of DM type 1 or long DM duration), with severe CKD (estimated glomerular filtration rate, eGFR <30 mL/min/1.73 m<sup>2</sup>), an established ESC calculated SCORE ≥10% for 10-year risk of fatal CVD or just with diagnosis of familial hypercholesterolemia with CVD or another major risk factor. Treating them according to 2020 ISH guidelines would be harmful and misleading if followed old targets.

It is quite important, because 2019 ESC/EAS guidelines introduced even the concept of “extreme high risk group”, stating, that is some patients who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-cholesterol goal <40 mg/dL (1.0 mmol/L) may be considered.

The LDL-cholesterol goal <55 mg/dL (1.4 mmol/L) in 2020 ISG guidelines is only mentioned in the subgroup of hypertension and coronary artery disease (CAD) patients, but as listed above, this is only minority of those considered to be treated according this goal in 2019 ESC/EAS guidelines on dyslipidaemias. The ISH concept of hypertension and diabetes targets (LDL-cholesterol <70 mg/dL for diabetes with target organ damage or <100 mg/dL in uncomplicated diabetes) is also too simplified and too liberal when compared to 2019 ESC/EAS guidelines on dyslipidaemias, as well as 2019 ESC/EASD – European Association for the Study of Diabetes guidelines [3]. The same applies to 2020 ISH LDL-cholesterol targets for the subgroup of hypertension and previous stroke.

We are especially sensitive in Poland to this step back in 2020 ISH guidelines, because we first, before 2019 ESC/EAS guidelines on

dyslipidaemias, introduced the concept of 5 risk groups (low, moderate, high, very high, extremely high) with new LDL-cholesterol targets of accordingly: <115, <100, <70, <55, <35 mg/dL (<3.0; <2.6; <1.8; <1.4; <0.9 mmol/L) as recommended by Polish Cardiac Society (PCS) Working Group on Cardiovascular Pharmacotherapy in December, 2018 [4]. Those LDL-cholesterol targets were also incorporated into Polish

Table 1

Target LDL-cholesterol (LDL-C) levels in relation to the cardiovascular profile introduced in Poland 2018 (reference [4]).

Risk category	Presence of disease, risk factors or 10-year Pol-SCORE risk	Target LDL-C level
Extremely high	Multiple previous cardiovascular events and/or revascularization procedures Stenting for left main coronary artery disease and/or multivessel coronary artery disease (complex percutaneous coronary intervention due to multivessel coronary artery disease) Generalized atherosclerosis — involving multiple vascular beds with additional risk factors Progression of atherosclerotic cardiovascular disease despite achieving and maintaining LDL-C level < 55 mg/dL (<1.4 mmol/L)	<35 mg/dL (<0.9 mmol/L)
Very high	Progression of atherosclerotic cardiovascular disease despite achieving and maintaining LDL-C level < 70 mg/dL (<1.8 mmol/L) Acute coronary syndrome, established coronary, carotid, or peripheral arterial disease Previous revascularization Pol-SCORE risk > 20% Diabetes or stage 3–4 chronic kidney disease with one or more risk factors Familial hypercholesterolemia History of premature atherosclerotic cardiovascular disease (<55 years in men, < 65 years in women) Established cardiovascular disease in patients with diabetes or stage 3–4 chronic kidney disease	<55 mg/dL (<1.4 mmol/L)
High	≥2 risk factors and Pol-SCORE risk 10–20% Diabetes or stage 3–4 chronic kidney disease without other risk factors	<70 mg/dL (<1.8 mmol/L)
Moderate	<2 risk factors and Pol-SCORE risk < 10%	<100 mg/dL (<2.6 mmol/L)
Low	No additional risk factors	<115 mg/dL (<3.0 mmol/L)

LDL-C — low-density lipoprotein cholesterol; SCORE — Systematic COronary Risk Evaluation.

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**Table 2**

Target LDL-cholesterol (LDL-C) levels in relation to the cardiovascular profile in three guidelines published one year after other: 2018 Polish Cardiac Society (PCS) Working Group on Cardiovascular Pharmacotherapy and 2019 Polish Society of Hypertension (PSH) – 2018/2019 PCS/PSH, 2019 European Society of Cardiology/European Atherosclerosis Society – 2019 ESC/EAS, and 2020 International Society of Hypertension – 2020 ISH.

Risk category	2018/2019 PCS/PSH	2019 ESC/EAS	2020 ISH
Extremely high	<35 mg/dL (<0,9 mmol/L)	<40 mg/dL (<1 mmol/L)* * Only for those who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy,	
Very high	<b>LDL</b> <55 mg/dL (<1,4 mmol/L)	<b>LDL</b> <55 mg/dL (<1,4 mmol/L)	<b>LDL</b> <70 mg/dL (<1,8 mmol/L) * * < 55 mg.dL (<1.4 mmol/L) only for those with arterial hypertension and coronary artery disease
High	<70 mg/dL (<1,8 mmol/L)	<70 mg/dL (<1,8 mmol/L)	<100 mg/dL (<1,8 mmol/L)
Moderate	<100 mg/dL (<2,6 mmol/L)	<100 mg/dL (<2,6 mmol/L)	<115 mg/dL (<2,6 mmol/L)
Low	<115 mg/dL (<3,0 mmol/L)	<115 mg/dL (<3,0 mmol/L)	

Society of Hypertension (PSH) guidelines issued in 2019 [5]. In those recommendations we even described different profiles of patients with their different LDL-cholesterol targets, based on some clinical features and Polish version of SCORE calculator (Pol-SCORE) [6]. Those risk categories, still recommended by PSH are presented below (Table 1).

These 2018 PCS Polish recommendations and 2019 PSH guidelines do not differ much in concept from ESC/EAS guidelines on dyslipidaemia, maybe more attention is given to extremely high risk group with broader definition and slightly lower LDL-cholesterol target (<35 mg/dL vs < 40 mg/dL). On the other hand, many differences exist when compared with 2020 ISH guidelines on hypertension, as far as LDL-cholesterol targets are concerned. Therefore this is too big simplification in ISH guidelines. It might be considered as the huge step back in dyslipidaemia knowledge and European guidelines perception and application. It might impact many hypertension patients with DM, PAD, TIA, stroke history, CKD, and many other CVD patients who will be treated to LDL-cholesterol <70 mg/dL instead of <55 mg/dL or even lower targets, as only CAD patients are mentioned in ISH guidelines as those with newer targets. I personally consider it as the real Achilles' heel of 2020 ISH guidelines. To summarize, in Table 2, once again differences in lipid recommendations among: 2018/2019 PCS/PSH, 2019 ESC/EAS, and 2020 ISH guidelines are presented (Table 2).

## References

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Krzysztof J. Filipiak<sup>1</sup>

1st Department of Cardiology, Medical University of Warsaw, Poland  
E-mail address: krzysztof.filipiak@wum.edu.pl.

<sup>1</sup> Polish Society of Hypertension, Immediate Past-President.