sdLDL-C
Randox sdLDL Cholesterol (sdLDL-C) 
Size Matters: The True Weight of Risk in Lipid Profiling

1. BACKGROUND

Cardiovascular disease (CVD) is recognised as a leading cause of death, with approximately 17.7 million deaths per year, an estimated 31% of all deaths worldwide.

Furthermore, 80% of all CVD deaths are due to heart attacks and strokes.

There is a global commitment to reduce the probability of premature CVD deaths by 25% by 2025; a target set by the United Nations member states.

Globally, the mortality rate for CVD has dramatically declined over the past 20 years, however, in low and middle-income regions, the number of lives lost to CVD is increasing.

The global distribution of CVD is complex and defined by national and regional characteristics as much as by global disease trends. Even with the differences between regions, CVD remains a dominant cause of death, even in those who are under the age of 40. This indicates the need for superior CVD risk markers to include methods that account for uncertainty and heterogeneity.

2. CLINICAL SIGNIFICANCE

LDL Cholesterol (LDL-C) is a low density lipoprotein involved in cholesterol and triglycerides transfer from the liver to peripheral tissues. LDL-C consists of two parts: the bigger part with phenotypic pattern A is light and almost rich in cholesterol (lbLDL-C or large buoyant LDL cholesterol) and the smaller part with more special weight and phenotypic pattern B (sdLDL-C) composed of less cholesterol. The two types of LDL-C vary in size through genetic determination and dietary lipid intake and their atherogenesis varies according to size. These smaller particles can more readily permeate the inner arterial wall and are more susceptible to oxidation.

The below diagrams demonstrate the difference between LDL-C, and sdLDL-C. From this, it can be seen that even if LDL-C levels are the same, sdLDL cholesterol levels can differ. Therefore it is important to assess the quality of LDL-C to assess the level of atherosclerotic cardiovascular disease (ASCVD) risk in patients.

Research indicates that individuals with a predominance of sdLDL-C have a 3-fold increased risk of myocardial infarction (MI). Elevated levels of sdLDL-C are caused by a sedentary lifestyle, a diet high in saturated fat, insulin resistance, pre-diabetes and genetic disposition. Measurement of sdLDL-C allows the clinician to gain a more comprehensive overview of lipid risk factors, enabling treatment to be tailored accordingly. In addition, the high prevalence of sdLDL-C is mainly observed in individuals with familial hyperlipidaemia, non-insulin dependent diabetes mellitus, and central obesity and insulin resistance syndromes.

Even though the overall LDL-C mass is the same for each patient, by measuring sdLDL-C, there are very different treatment considerations required.
3. MANAGEMENT

Reducing sdLDL-C levels will aid in reducing the risk of CVD and MI. High dose statin therapy has been proven to aid in reducing the levels of sdLDL-C as a risk factor for cardiovascular events and high risk patients.\(^1\)

The measurement of LDL-C or the review of levels within arteriosclerotic coronary heart disease (ASCHD) treatment are known within different guidelines (including ATP III, AHA/ ACC, ESC/ EAS and NICE). However doubt remains on the impact of targeting LDL-C only. The inclusion of sdLDL-C within the clinical testing panel will assist in removing this doubt.

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<table>
<thead>
<tr>
<th>Lipoprotein</th>
<th>lbLDL-C</th>
<th>sdLDL-C</th>
</tr>
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<tbody>
<tr>
<td>Priemer (nm)</td>
<td>25.5 – 28.0</td>
<td>22.0 – 25.5</td>
</tr>
<tr>
<td>Hustota (g/cm(^3))</td>
<td>1.019 – 1.044</td>
<td>1.044 – 1.063</td>
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Figure 2 outlines the atherogenic mechanism of sdLDL-C. It can be seen that:

1. sdLDL-C has a lower affinity to the hepatic LDL-C receptor, thus circulating in the blood longer than lbLDL-C.
2. sdLDL-C has a stronger affinity to vessel wall heparin sulphate proteoglycans (HSPGs), which means that sdLDL-C can more readily permeate the arterial wall.
3. sdLDL-C is also liable to oxidation from its physicochemical properties which leads to foam cell formations.

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Table 1: Size and density comparison between lbLDL-C and sdLDL-C\(^1\)
4. **SDLDL CHOLESTEROL AND IT’S APPLICATION TO DIABETES**

Figure 4 illustrates a high prevalence of sdLDL-C particles in patients with type 2 diabetes mellitus (T2DM). It was found that not only the prevalence of sdLDL-C, but also the concentration was substantially increased in patients with T2DM. However, previous studies found that the presence of diabetes did not affect sdLDL-C levels in ASCVD patients. Therefore, these results suggest that sdLDL-C is a powerful predictor of ASCVD for diabetic and nondiabetic populations.

5. **THE NATIONAL LIPID ASSOCIATION (NLA)**

The current lipid panel consists of testing:

- Total Cholesterol
- HDL Cholesterol
- LDL Cholesterol
- Triglycerides
- Risk factors (including age, diet, smoking, QRISK, co-morbidities to view risk and management of risk)

The mission of NLA “is to enhance the practice of lipid management in clinical medicine”. NLA advocate advancing the current lipid testing profile as the traditional tests only detect approximately 20% of all ASCVD patients. Advanced lipid testing is recommended to optimise patient care, which can be achieved through the addition of sdLDL-C.

6. **RANDOX SDLDL-C ASSAY**

**CLEARANCE METHOD**

The Randox sdLDL-C assay utilises the quantitative clearance method which produces results in as little as ten minutes, facilitating faster patient diagnosis and treatment plan implementation. Previously, ultracentrifugation and electrophoresis based methods were options for the measurement of sdLDL-C, which are both laborious and time consuming.

Studies have highlighted that the use of this quantitative method is more informative in assessment, comparison and measurement of the effective parameters in obesity. The method consists of two main reaction steps which are based on the presence of surfactants and enzymes that selectively react with a certain group of lipoproteins. Figure 5 illustrates that the Randox clearance method correlates extremely well with the gold standard method, ultracentrifugation. For this study, 64 samples were taken from healthy people, ASCVD patients and diabetic patients.
7. OTHER BENEFITS OF THE RANDOX ASSAY INCLUDE:

- Direct, automated test is specifically designed for use on automated analysers making the test more convenient and efficient
- Liquid ready-to-use reagents for convenience and ease-of-use
- Applications are available detailing instrument-specific settings for the convenient use of Randox sdLDL-C on a wide range of clinical chemistry analysers
- sdLDL-C controls and calibrator available offering a complete testing package
- The Randox sdLDL-C assay is a niche product, meaning that Randox are one of the only manufacturers to offer sdLDL-C in an automated biochemistry format.

8. CONCLUSION

CVD is a leading cause of death worldwide, with 7 million people living with CVD in the UK. In addition, there is a global commitment to reduce the probability of premature CVD deaths by 25% by 2025. Although there is a declining number of CVD deaths over the past 20 years, the number of lives lost to CVD in low and middle income countries is still increasing.

For these reasons, it is necessary to review the traditional lipid panel outlined in the NLA guidelines to include sdLDL-C. This will enable clinician’s to gain a more comprehensive view of a patient’s CVD risk, allowing them to take the appropriate measures to prevent CVD deaths.

References

11. Liu, M L. (2002). LDL Oxidation and LDL Particle Size in the Development of Atherosclerosis. Department of Medicine, University of Helsinki, Finland.