

Standardization of total cholesterol measurement in population surveys

Pre-analytic sources of variation and their effect on the total cholesterol distribution and the prevalence of hypercholesterolaemia

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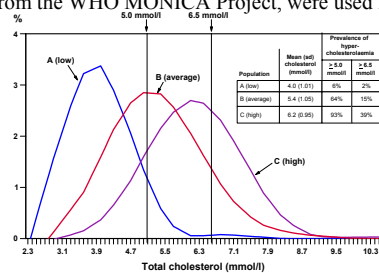
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BACKGROUND AND METHODS

Comparability of the levels of total cholesterol and other lipids, between populations depends on the measurement procedures and the accuracy of the measurements. Comparisons may be difficult or even impossible, if different pre-analytic procedures were used or if the analytic procedures were inaccurate.

We assessed the effect of variations in the pre-analytic procedures on population estimates by reviewing the literature on the effects on individuals and applied these effects on real population distributions.

Simulations were used to demonstrate the potential effect of pre-analytic sources of variation to the total cholesterol distribution and the prevalence of hypercholesterolaemia (total cholesterol ≥ 5.0 mmol/l or ≥ 6.5 mmol/l). Three different population total cholesterol distributions, selected from the WHO MONICA Project, were used for the simulations.



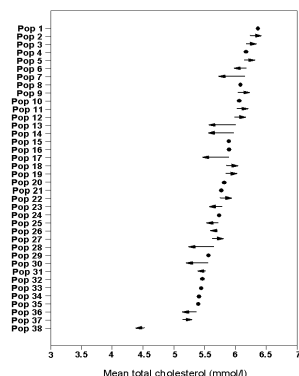
Effects of pre-analytic sources of variation to the total cholesterol levels from the literature review:

- ❖ **Seasonal variation:** 3-5% higher levels during the winter months than during the summer months. (4% used in simulations).
- ❖ **Posture during the blood drawing:** 6% increase when moving from supine to sitting, 9-18% increase when moving from supine to standing. (6% from supine to sitting and 13% from supine to standing used in simulations).
- ❖ **Use of tourniquet:** Increase of 2-5% by prolonged use of tourniquet (i.e. prolonged venous occlusion). (3.5% used in simulations).
- ❖ **Type of blood sample:** Plasma with EDTA (concentration of 4.46 mmol/l) 1-5% lower, with heparin 1% lower, with oxalate 9% lower, with citrate 14% and with fluoride 18% than serum. (For EDTA, 3% used in simulations.)

Potential effect of used pre-analytic procedures to the total cholesterol levels obtained in the final risk factor survey of the WHO MONICA (Multinational MONitoring of trends and determinants in Cardiovascular disease) Project was estimated by adjusting measurements to surveys lasting all year around, sample drawn in sitting posture without prolonged tourniquet use and used blood type to be serum.

RESULTS

The simulations demonstrated that the mean total cholesterol levels and the prevalence of hypercholesterolaemia can change markedly only by the change of pre-analytic procedures. Depending on the population distribution of total cholesterol, the seasonal variation can explain up to 0.3 mmol/l difference in total cholesterol levels and seven percent point difference in the prevalence of hypercholesterolaemia. The difference of same magnitude can be observed also by change of posture during the blood drawing, prolonged use of tourniquet or use of plasma with EDTA instead of serum.



In the WHO MONICA Project, the pre-analytic procedures were very consistent between populations. Therefore, the estimates of total cholesterol mean values from the final risk factor survey did not change markedly after they were adjusted for used pre-analytic procedures.

- ❖ Dot: no adjustment needed
- ❖ Arrow to the right: adjustment increased observed value
- ❖ Arrow to the left: adjustment decreased observed value

CONCLUSIONS

Variation of total cholesterol levels due to differences in procedures during the pre-analytic stage can diminish substantially the reliability and comparability of measurements with other surveys over time and between populations. The effect of pre-analytic variation in the population estimates of total cholesterol can be reduced by standardization and training.

