OPEN ACCESS

GAVIN PUBLISHERS

Current Trends in Medical Diagnostic Methods

Research Article

Bolodeoku J Curr Trends Med Diagn Meth: CTMDM-106.
DOI: 10.29011/ CTMDM-106.100006

Biological Variation of Self-Monitoring of Blood Cholesterol (SMBC) Using Portable Handheld Point of Care Testing Devices: 3in1, Cardio Chek PA and Elemark

John Bolodeoku*

Honorary Consultant Physician, Lipid Clinic, Department of Cardiology, Basingstoke & North Hampshire Hospital, United Kingdom

***Corresponding author:** Dr John Bolodeoku, Honorary Consultant Physician, Lipid Clinic, Department of Cardiology, Basingstoke & North Hampshire Hospital, Basingstoke Hampshire, UK. Tel: +4407765401135 Email: John.bolodeoku@hhft.nhs.uk

Citation: Bolodeoku J (2018) Biological Variation of Self-Monitoring of Blood Cholesterol (SMBC) Using Portable Handheld Point of Care Testing Devices: 3in1, Cardio chek PA and Elemark. Curr Trends Med Diagn Meth: CTMDM-106. DOI: 10.29011/ CTMDM-106.100006

Received Date: 12 November, 2018; **Accepted Date:** 19 November, 2018; **Published Date:** 28 November, 2018

Keywords: Biological Variation of Lipids; Cardio Chek; Elemark; Self-Testing Cholesterol Devices; 3in1

Introduction

Currently Point of Care Testing (POCT) has revolutionized the self-testing of a number of parameters such as blood pressure, glucose and lipids. Point of care testing provides significant benefits to patients:

- The tests are usually minimally invasive as most of them require only a small amount of blood usually collected from the finger and requires no sample preparation [1].
- The tests are usually completed within 5 minutes, leading to a reduction in the result turnaround time, thereby allowing a quicker decision being made [2,3].
- The patient being involved with their testing improves their compliance, adherence to treatment and therapeutic control [4,5]
- The self-testing also allows the patients to make less visits to the laboratory or GP practice to have their bloods taken [4,5,6]

Well-known examples are the self-testing of blood pressure in patients with hypertension. Studies have shown that self-monitoring results in small, but significant reductions in blood pressure and better adherence to treatment [7]. Self-Monitoring of Blood Glucose (SMBG) has been shown to be helpful in 4 distinct ways: First, both patient and clinician are able to ascertain high or low levels of glucose and thereby make the necessary therapeutic adjustments. Second, SMBG provides the patients the chance to detect or confirm whether they have a hyper or hypo incident. Third, the SMBG devices also provide patient education and disease management information. Fourth, SMBG helps motivate the patients [8]. There are a number of point of care cholesterol measuring systems on the market, such as Accutrend Plus, Bene Check Plus, Cardio Chek PA, Cholestech LDX, Veri-Q and 3in1, these measuring devices range from portable handheld lipid blood testing devices to compact desktop analyzers that can measure a number of lipid fractions and ratios on whole blood, plasma or serum collected from the finger or venous blood. The method of analysis uses reflectance or biosensor technology with single-use, disposable, dry reagent test strips, rotors or cassettes. The lipid fractions and ratios can be measured individually or as multiple tests: a full lipid profile would consist of total cholesterol, HDL-Cholesterol and triglyceride. Calculated lipid fractions and ratios such as total cholesterol/HDL ratio and calculated LDL-Cholesterol can be estimated with some of the measuring systems [9,10]. Two cholesterol point of care testing devices have been Cholesterol Reference Method Laboratory Network (CRMLN) certified: Cholestech LDX® System (Alere, UK) and Professional CardioChek PA (Polymer Technology Systems Inc, Indiana, US, BHR Pharmaceuticals Ltd., Nuneaton, UK) [9]. Lipid and lipoprotein concentration vary during the normal course of daily activity. Studies have demonstrated that within person variability is sufficient to make an individual move in and out of the pre-defined risk categories defined by the respective lipid guidelines. It is expected that after initiating pharmacological interventions such as statins, fibrates, bile acid sequestrants and more recently, PCSK9 inhibitors, the patients are expected to have follow up laboratory tests done at 6 weeks, -3 months, -6 months and yearly. However, the practice is that patients have these blood tests done for their next visit to the outpatient lipid clinic and usually requires the patients visit their local hospital laboratory or General Practice (GP) to have their bloods taken and the lipids estimated prior to their visit to the outpatient lipid clinic. One important factor to take into consideration, if the cholesterol self-testing devices are to be considered as useful for monitoring patients, is the ability to simulate the within

person day to day variation, especially if these devices are going to be used for helping both the patient and clinician in being able to ascertain lipid levels after initiation of medication, at the appropriate time, and thereby make the necessary therapeutic adjustments. The expected within person biological variation for total cholesterol (2.5% - 10.9%), for HDL-cholesterol (3.6% - 12.4%), for LDL-cholesterol (7.8% -13.6%) and for triglyceride (12.9% - 40.8%) (11-14).

In this study, the within person day to day variation of lipids: Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL-C), Triglyceride and calculated Low Density Lipoprotein Cholesterol (LDL-C) was assessed using three portable handheld blood lipid testing devices: The CardioChek PA which is FDA 510(K) declared, CLIA waived, and CE labelled; the 3in1 which is a handheld portable point of care whole blood analyser dedicated to testing glucose, cholesterol and triglycerides and is CE certified; and the elemark™ which is a mobile blood testing device capable of testing Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL-C), Triglyceride and calculated Low Density Lipoprotein Cholesterol (LDL-C) which is undergoing CE approval.

Keywords: Biological Variation of Lipids; Cardio Chek; Elemark; Self-Testing Cholesterol Devices; 3in1

Materials & Methods

Biological Variation Study

Finger prick (capillary) whole blood samples were taken from a single subject between 7.30 and 10.00 am (fasting) on 12 days (Day 3,5,7,9,13,15,17,19,23,26,29 and 31) over a 2-month period see (Figure 1). Total Cholesterol and Triglyceride estimations were carried out on the 3in1 device immediately after being taken, according to manufacturer's instructions. The mean, Standard Deviation (SD), Coefficient of Variation Percent (CV%) of the total number of estimations was calculated. Finger prick (capillary) whole blood samples were taken from a single subject between 7.30 and 10.00 am (fasting) on 14 days (Day 3,5,7,9,13,15,17,19,23,26,29,31,34 and 37) over a 2-month period see (Figure 1). Total Cholesterol, HDL-Cholesterol, LDL-Cholesterol and Triglyceride estimations were carried out on the Cardio CheK PA device immediately after been taken, according to the manufacturer's instructions. The mean, Standard Deviation (SD), Coefficient of Variation Percent (CV%) of the total number of estimations was calculated. Finger prick (capillary) whole blood samples were taken from a single subject between 7.30 and 10.00 am (fasting) on 16 days (Day 3,5,7,9,13,15,17,19,23,26,29,31,34,37,39 and 41) over a 2-month period see (Figure 1). Total Cholesterol, HDL-Cholesterol, LDL-Cholesterol and Triglyceride estimations were carried out on the elemark™ device immediately, according to manufacturer's instructions. The mean, Standard Deviation (SD), Coefficient of Variation Percent (CV%) of the total number of estimations was calculated.

1	11	21	31	41
2	12	22	32	42
3	13	23	33	43
4	14	24	34	44
5	15	25	35	45
6	16	26	36	46
7	17	27	37	47
8	18	28	38	48
9	19	29	39	49
10	20	30	40	50
	1 finger prick sample tested on elemark			
	2 separate finger prick samples tested on elemark and Cardio Check PA			
	3 separate finger prick samples tested on elemark, Cardio Check PA and 3in1			

Figure 1: Shows the testing schedule (days) over a 2-month period that finger prick samples were taken and device tested.

Comparative Study

As 3 separate finger prick samples were taken and tested on the 3 devices (3in1, CardioChek PA and elemark™) on Days 3, 5,7,9,13,15,17,19,23,26,29,31. The daily and means of the total cholesterol and triglyceride were calculated to compare the results between the 3 devices.

Results

Biological Variation Study

The mean concentrations for total cholesterol estimated in the healthy volunteer was 5.00 mmol/l, 4.24 mmol/l and 5.74 mmol/l using the 3in1, CardioChek PA and elemark™, respectively over the 2-month period - Day 3,5,7,9,13,15,17,19,23,26,29 and 31) (Figure 2,3,4). The estimated within person day to day variation (CV%) for total cholesterol was 7.0%, 9.4% and 5%, using the 3 in 1, CardioChek PA and elemark™, respectively over the 2-month period (Tables 1,2,3). With the elemark™ having the lowest biological variation and the CardioChek PA the highest. The mean concentrations for triglyceride estimated in the healthy volunteer was 0.9 mmol/l, 0.82 mmol/l and 1.11 mmol/l using the 3in1, CardioChek PA and elemark™, respectively over the 2-month period – Day 3,5,7,9,13,15,17,19,23,26,29,31,34 and 37 (Figure 2,3,4). The within person day to day variation (CV%) for triglyceride was 34.1%, 23% and 30%, using the 3 in 1, CardioChek PA and elemark™, respectively over the 2-month period (Tables 1,2,3). With the CardioChek PA having the lowest biological variation and the 3in1 the highest. The mean concentrations for HDL-cholesterol estimated in the healthy volunteer was 1.48 mmol/l and

1.79 mmol/l using the CardioChek PA and elemark™, respectively over the 2-month period - Day 3,5,7,9,13,15,17,19,23,26,29,31,34 ,37,39 and 41 (Figure 3,4). The within person day to day variation (CV%) for LDL-cholesterol was 7% and 13%, using the CardioChek PA and elemark™, respectively over the 2-month period (Tables 1,2,3) with the CardioChek PA having the lowest biological variation. The mean concentrations for LDL-cholesterol estimated in the healthy volunteer was 2.38 mmol/l and 3.5 mmol/l using the CardioChek PA and elemark™, respectively over the 2-month period (Figure 3,4). The within person day to day variation (CV%) for LDL-cholesterol was 14% and 13%, using the CardioChek PA and elemark™, respectively over the 2-month period (Tables 1,2,3) with the elemark™ having the lowest biological variation.

Comparative Study

The total cholesterol estimations for Days 3,5,7,9,13,15,17,19,23,26,29,31 of the CardioChek PA were consistently lower than the estimation from the elemark™ and the 3in1. The estimated mean of the total cholesterol was 5.77 mmol/l, 4.28 mmol/l and 5.00 mmol/l for the elemark™, CardioChek PA and 3in1, respectively (Figure 5,6). Using the total cholesterol normal range of 5.2 nmol/l, the elemark™ would have identified the healthy volunteer as having a high level of cholesterol with a mean 5.77 mmol/l, whilst the CardioCheK PA and 3in1 would have identified the healthy volunteer as having a normal level of cholesterol. The total triglyceride estimations for Days 3,5,7,9,13,15,17,19,23,26,29,31 of the CardioChek PA were not consistently lower than the estimations from the elemark™ and the 3in1. The mean of the triglyceride was 1.03 mmol/l, 0.8 mmol/l and 0.9 mmol/l for the elemark™, CardioChek PA and 3in1, respectively (Figure 7,8). Using the triglyceride normal range of <2.0 mmol/l, all three devices would have identified the healthy volunteer as having a normal triglyceride.

Figures 2-4: Showing daily finger lipid measurements in healthy volunteer using 3in1, CardioChek PA and elemark.

3in1

	Mean	SD	CV%
Total Cholesterol	5.008333	0.350216	6.992673
Triglyceride	0.9	0.307482	34.16472

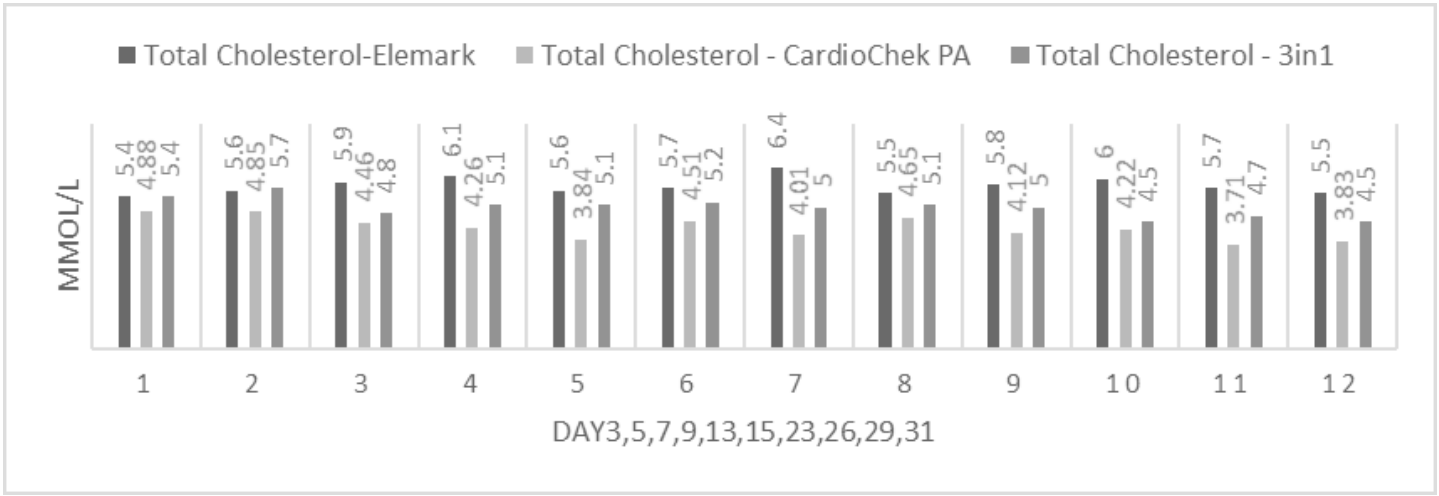
CardioChek PA

	Mean	SD	CV%
Total Cholesterol	4.24	0.4	9.4
HDL-Cholesterol	1.48	0.1	7
Triglyceride	0.82	0.2	23
LDL-Cholesterol	2.38	0.3	14

Elemark™

	Mean	SD	CV%
Total Cholesterol	5.74	0.3	5
Triglyceride	1.11	0.3	30
HDL-Cholesterol	1.79	0.2	13
LDL-Cholesterol	3.5	0.5	13

Tables 1-3: Showing the mean, standard deviation (SD) and coefficient of variation percent (CV%) of the daily finger lipid measurements in healthy volunteer using 3in1, CardioChek PA and elemark™.



Figures 5: Showing bar chart of the daily finger lipid (total cholesterol) measurements in Days 3,5,7,9,13,15,17,19,23,26,29,31 of a healthy volunteer using elemark, CardioChek PA and 3in1.

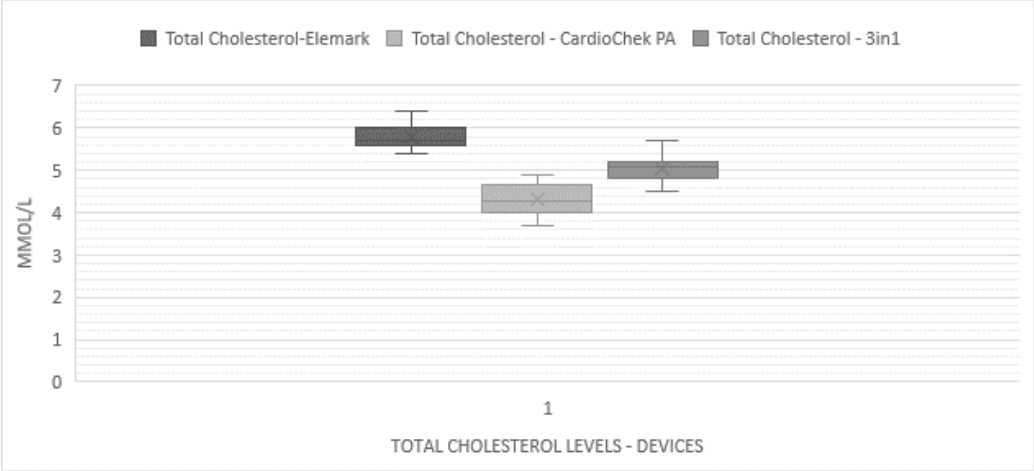


Figure 6: Showing a whisker plot of the daily finger lipid (total cholesterol) measurements in Days 3,5,7,9,13,15,17,19,23,26,29,31 of a healthy volunteer using elemark™, CardioChek PA and 3in1.

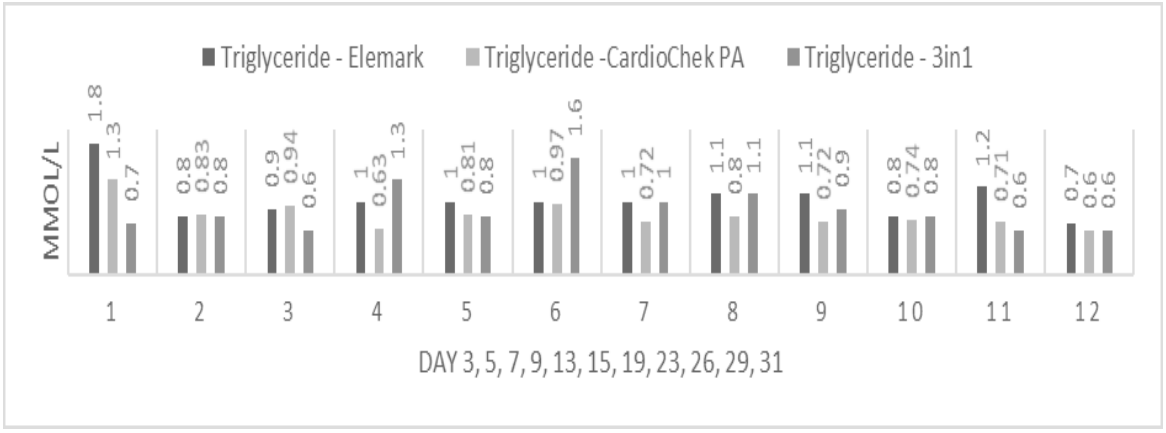


Figure 7: Showing bar chart of the daily finger lipid (triglyceride) measurements in Days 3,5,7,9,13,15,17,19,23,26,29,31 of a healthy volunteer using elemark™, CardioChek PA and 3in1.

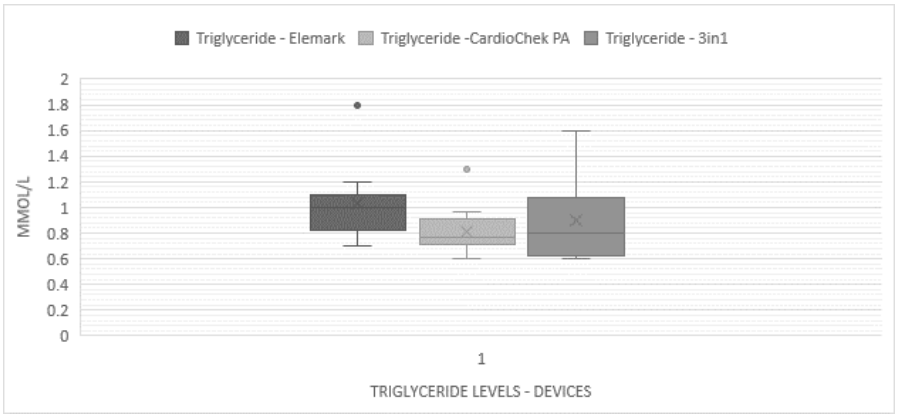


Figure 8: Showing a whisker plot of the daily finger lipid (triglyceride) measurements in Days 3,5,7,9,13,15,17,19,23,26,29,31 of a healthy volunteer using elemark™, CardioChek PA and 3in1.

Discussion

The potential of these new devices warrants further investigation into how they can be potentially of use in the treatment pathways for our patients attending lipid clinics and being monitored. If patients can perform their own tests and carry out at least 2 estimations after their lipid lowering drugs have been administered, and these results transmitted to care giver or provider, consultations and interventions could be carried out with the patients, without them having to go to their local general practice or laboratory to have their routine blood tests for cholesterol estimation. In understanding the potential of these devices, if they are able to measure lipids in a healthy volunteer and be consistent with the expected within person biological variation for total cholesterol (2.5% - 10.9%), for HDL-cholesterol (3.6% - 12.4%), for LDL-cholesterol (7.8% -13.6%) and for triglyceride (12.9% - 40.8%) [11-14] this would provide us with comfort in accepting them. Previously, the CardioChek PA demonstrated in a healthy volunteer that the biological variation (CV%) of the estimated total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride fell within the intra-individual variation determined in healthy volunteers [15]. In this study, 2 more point of care cholesterol testing devices (3in1 and elemark™) were investigated alongside the CardioChek PA and their estimations produced very similar observations with their estimated total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride also falling within the intra-individual variation determined in healthy volunteers. The elemark™ produced the lowest biological variation for total cholesterol, whilst the CardioChek PA produced the lowest biological variation for triglyceride. HDL-cholesterol and LDL-cholesterol was not measured on the 3in1 device and therefore only the performance of CardioChek PA and the elemark™ were used for these parameters. The CardioChek PA produced the lowest biological variation for HDL-cholesterol whilst the elemark™ produced the lowest biological variation for LDL-cholesterol. Although no direct head to head study has been carried out using these devices, looking at the means of the cholesterol and triglyceride estimations from the 3 devices (elemark™, CardioChek PA and 3in1) on Days 3,5,7,9,13,15,17,19,23,26,29 and 31, when 3 separate finger prick samples were taken and the cholesterol estimation made on the separate devices immediately after been taken, the actual and mean values differ significantly between the devices with the estimations from the CardioChek PA being lower than those from the elemark™ and 3in1. Using the total cholesterol normal range of 5.2 nmol/l, the elemark™ would have identified the healthy volunteer as having a high level of cholesterol with a mean 5.77 mmol/l, whilst the CardioCheK PA and 3in1 would have identified the healthy volunteer as having a normal level of cholesterol [16]. This observation still poses the question if these point of care devices are accurate enough. Of the 3 devices, the CardioCheK PA appears to be the one studied more in the literature. A study which compared the CardioChek PA and a desk top analyser the Cholestech LDX, indicated that the Cholestech LDX analyser demonstrated slightly better reproducibility than the CardioChek PA [17]. The CardioChek PA has also been demonstrated to show good correlation with a laboratory method [18]. The elemark™ is a new device currently ongoing CE certification, this device is able to generate data and share it easily with care givers, healthcare professionals, etc. A review carried out in the United States on point of care cholesterol monitors, suggests that there may be a role for them in pharmacies, and they offer potential advantages such as ease of use, portability, increased patient access, low cost, fewer physician or laboratory visits and instant results [19]. Further comparative studies with laboratory tests need to be carried out with these point of care testing devices before they can have a place in the routine monitoring of patients on lipid lowering interventions.

References

1. Crook MA (2000) Near patient testing and pathology in the new millennium. Journal of Clinical Pathology 53: 27-30.
2. Kilgore ML, Steindel SJ, Smith JA (1998) Evaluating stat testing options in an academic health centre: therapeutic turnaround time and staff satisfaction. Clin Chem 44: 1597-1603.
3. Rainey PM (1998) Outcomes assessment for point-of-care testing. Clin Chem 44: 1595-1596.
4. Price CP (2001) Regular review: Point of care testing. BMJ 322: 1285-1288.
5. Hobbs R (1996) Near patient testing in primary care. BMJ; 312: 263-264.
6. Price CP (2003) Delivering clinical outcomes. Point-of-Care-Journal of Near Patient Testing and Technology 2: 151-157.
7. Cottrell E, Chambers R, O'Connell P (2012) Using simple telehealth in primary care to reduce blood pressure; a service evaluation. BMJ Open 2: e001391.
8. Klonoff DC (2007) Benefits and Limitations of self-monitoring of blood glucose. J Diabetes Sci Technol 1: 130-132.
9. Pluddermann A, Thompson M, Price CP, Wolstenholme J, Heneghan C (2011) Point of care testing for the analysis of lipid panels. Br J Gen Pract 65: e224–e226.
10. (2017) Centre for Evidence Based Purchasing. CEO catalogue search. London. Department of Health.
11. Hammond J, Wentz P, Statland BE, Phillips JC, Winkel P (1976) Daily variation of lipids and hormones in sera of healthy subjects. Clinica Chimica Acta 73: 347-352.
12. Demacker PNM, Schade RWB, Jansen RTP, Laar AV (1982) Intra-individual variation of serum cholesterol triglycerides and high density lipoprotein cholesterol in normal humans. Atherosclerosis 45: 259-266.
13. Gidding SS, Stone NJ, Bookstein LC, Laskarzewski PM, Stein EA (1998) Month to month variability of lipids, lipoproteins and apolipoproteins and the impact of acute infection in adolescents. The Journal of Pediatrics 133: 242-246.
14. Bookstein L, Gidding SS, Donovan M, Smith FA (1990) Day to day

variability of serum cholesterol, triglyceride and high density lipoprotein cholesterol levels. Arch Intern Med 150: 1653-1657.

15. Bolodeoku J (2017) Self-monitoring blood cholesterol (SMBC) testing: within person day to day variation in a healthy volunteer. Medical Research Archives 5.

16. Glasziou PP, Irwig L, Kirby AC, Tonkin AM, Simes RJ (2014) Which lipid measurement should we monitor? An analysis of the LIPID study. BMJ Open 4: e003512.

17. Shephard MD, Mazzachi BC, Shephard AK (2007) Comparative performance of two point of care analysers for lipid testing. Clinical Laboratory 53: 561-566.

18. Bubner TK, Laurence CP, Gialamas A, Worley P, Beilby JJ, et al. (2009) Effectiveness of point of care testing for therapeutic control of chronic conditions results from the POCT in general practice trial. Medical Journal of Australia 190: 624-626.

19. Taylor JR, Lopez LM (2004) Cholesterol point of car testing. Annals of Pharmacotherapy 38: 1252-1257.