# Computerized Community Cholesterol Control (4C): Meeting the Challenge of Secondary Prevention

Harel Gilutz MD[1], Lena Novack[2], Pesach Shvartzman MD[3], Julian Zelingher MD MPH[4], Dan Y. Bonneh MD[3,5], Yaakov Henkin MD[1], Maximo Maislos MD[6], Roni Peleg MD[3], Zvi Liss MD MPH[3,5], Gad Rabinowitz PhD[7], Daniel Vardy MD[5], Doron Zahger MD[1], Reuven Ilia MD[1], Niki Leibermann MD[8] and Avi Porath MD MPH[9]

[1]Cardiology Division, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel
[2]Department of Epidemiology and Health Services Evaluation, Ben-Gurion University of the Negev, Beer Sheva, Israel
[3]Department of Family Medicine, Ben-Gurion University of the Negev, and Clalit Health Services Southern District, Beer Sheva, Israel
[4]Department of Medical Planning & Development, Hospital Division, Clalit Health Services, Tel Aviv, Israel
[5]Central Administration, Clalit Medical Services Southern District, Beer Sheva, Israel
[6]Atherosclerosis Service, Soroka Medical Center, Beer Sheva, Israel
[7]Department of Industrial Engineering and Management, Ben-Gurion University of the Negev, Beer Sheva, Israel
[8]Division of Community Medicine, Clalit Health Services, Tel Aviv, Israel
[9]Department of Health Care Policy, Clalit Health Services and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

**ABSTRACT:**
**Background:** Dyslipidemia remains underdiagnosed and under-treated in patients with coronary artery disease. The Computer-based Clinical Decision Support System provides an opportunity to close these gaps.

**Objectives:** To study the impact of computerized intervention on secondary prevention of CAD.

**Methods:** The CDSS was programmed to automatically detect patients with CAD and to evaluate the availability of an updated lipoprotein profile and treatment with lipid-lowering drugs. The program produced automatic computer-generated monitoring and treatment recommendations. Adjusted primary clinics were randomly assigned to intervention (n=56) or standard care arms (n=56). Reminders were mailed to the primary medical teams in the intervention arm every 4 months updating them with current lipid levels and recommendations for further treatment. Compliance and lipid levels were monitored. The study group comprised all patients with CAD who were alive at least 3 months after hospitalization.

**Results:** Follow-up was available for 7448 patients (median 19.8 months, range 6–36 months). Overall, 51.7% of patients were adequately screened, and 55.7% of patients were compliant with treatment to lower lipid level. In patients with initial low density lipoprotein › 120 mg/dl, a significant decrease in LDL levels was observed in both arms, but was more pronounced in the intervention arm: 121.9 ± 34.2 vs. 124.3 ± 34.6 mg/dl ($P < 0.02$). A significantly lower rate of cardiac rehospitalizations was documented in patients who were adequately treated with lipid-lowering drugs, 37% vs. 40.9% ($P < 0.001$).

**Conclusions:** This initial assessment of our data represent a real-world snapshot where physicians and CAD patients often do not adhere to clinical guidelines, presenting a major obstacle to implementing effective secondary prevention. Our automatic computerized reminders system substantially facilitates adherence to guidelines and supports wide-range implementation.

IMAJ 2009;11:23–29

**KEY WORDS:** secondary prevention, computerized reminders, compliance, dyslipidemia, treatment gap

Epidemiological and intervention trials have shown that lowering low density lipoprotein-cholesterol with statins in patients with coronary artery disease significantly improves clinical outcomes [1,2] in a favorable cost-benefit manner [3]. Practice guidelines published as early as 2001 strongly recommend performing a lipoprotein analysis in every patient with proven CAD and reducing the LDL-cholesterol levels to below 100–115 mg/dl [4]. Nevertheless, secondary CAD prevention surveys indicate a wide therapeutic gap between scientific evidence and practice [5]. A specialized and expensive hyperlipidemia clinic intervention achieved better control of multi-risk factors [6]. However, it has been suggested that a computerized feedback system could be used to achieve mass control of treatment goals [7]. Among the many factors that may explain this treatment gap, patient and physician compliance and the health system organization's attitude are probably the most important [8,9].

In recent years, computerized decision support systems have been introduced into medical practice. It has been demonstrated that when used as a preventive care reminder, they enhance clinical performance, permit better drug dosing, and improve preventive care [10-12]. These observations support the application of such systems as a large-scale intervention tool for secondary prevention [13].

A community health information network can facilitate information transfer and introduce treatment recommenda-

---

CAD = coronary artery disease
CDSS = clinical decision support system

LDL = low density lipoprotein

tions [10,14]. This system can be upgraded by integrating a computer-based clinical decision support system, producing a modality supporting primary care teams. However, the effects of the CDSS on patient outcomes have not been adequately studied [15]. We studied the impact of a CDSS mainly on secondary prevention measure outcomes in patients with CAD and dyslipidemia followed by primary care physicians. This was a pilot study to evaluate the feasibility of such a system.

## PATIENTS AND METHODS

Clalit Health Services is the largest of the four health management organizations in Israel. All members of the Southern District Clalit Health Services receive their secondary and tertiary care at the Soroka University Medical Center, a 1000-bed hospital, which also receives the vast majority of readmissions. The CDSS system can integrate data from the hospital discharge diagnosis database, the laboratory database and the Clalit Health Services central pharmacy database. The patients in this particular study were followed in 144 primary care clinics; 32 clinics were excluded from the study because of low capacity. Participating clinics were matched based on geographic location, number and demographics of the listed patients, and number and speciality of physicians, totalling 56 pairs of 112 clinics. The clinics in each pair were randomly assigned to 56 control clinics providing standard care and 56 intervention clinics. The intervention clinics included 204 general practitioners and 396 nurses.

This was a cluster randomized trial comparing the intervention with standard care in primary care clinics. The study protocol was approved by the local ethics committee. The inclusion criteria for participation were as follows:

- Consecutive patients hospitalized at Soroka from January 2000 through December 2003 were screened for CAD diagnoses (ICD-9 codes: 410-414, 428, v36.0, v45.81, and v45.82) (That hospitalization is referred to as the index hospitalization)
- Alive at least 3 months after discharge
- Age 20–80 years
- Followed by Southern District Clalit primary care physicians for at least another 6 months.

The exclusion criteria were:

- Not members of Clalit
- Patients not listed in any of the112 participating clinics
- Patients considered to have significant co-morbidities (> 4.5) according to the Charlson co-morbidities index [16].

The data were collected from three routinely used databases:

- *Admission, Transfer, and Discharge.* This database includes discharge diagnoses, using ICD-9 as well as demographic data and visits to the ambulatory consultation services. All diagnoses of the last 10 years were incorporated into the study database
- *Laboratory Information System.* This includes reports on all laboratory tests ordered by the medical center and by primary care clinics. Lipoprotein panel and creatinine levels within a time window of 6 months (± 3 months of hospitalization) were determined. For patients with acute coronary syndromes a normal lipoprotein panel was considered valid if taken within 24 of admission or at least 1 month after discharge
- *District Pharmacy Information System.* This allows identification of medications dispensed by the Clalit pharmacies.

### THE CDSS SYSTEM

A computer-based clinical decision support system was created for dyslipidemia management based on National Cholesterol Education Program-III [4] and Israeli [17] guidelines for the management of dyslipidemia. The system determined diagnoses that were absolute contraindications for statin therapy (active liver disease, myositis, pregnancy) and excluded these patients from receiving reminders. Clinical conditions that require special attention, e.g., mild renal failure or cirrhosis of the liver, were reported to the GP. This algorithm produced automatic patient-specific reminders for lipid monitoring or treatment.

### INTERVENTION

In the intervention arm, a written reminder with patient-tailored recommendations was mailed to the primary care physicians and nurses. The recommendations were based on the last 6 months data for new patients, and 4 months for patients in periodic follow-up. The reminder indicated the patient's risk factors, lipoprotein values, and known dispensed medications. Lipid-lowering drug treatment was recommended only in patients with LDL > 110 mg/dl and consisted of either statin initiation (simvastatin 20 mg/day), statin up-titration (doubling the last registered dose), changing to a more potent statin or compliance evaluation

For unresponsive and compliant patients it was recommended that they be referred to a metabolic clinic. The primary care teams (physicians and nurses) were asked to identify patients who, according to their judgment, could not receive statins. A log of all the patients was collected after each periodic intervention, and records were maintained.This included patients who had contraindication for statins and were judged not to be reminded. No recommendation was sent to the patients directly.

It was emphasized that the GPs were free to decide whether

---

GP = general practitioner

to accept or refuse the recommendations. As a measure of quality control all the reminders during the first year of activity were reviewed by either a cardiologist or a lipidologist before mailing them out. Patient follow-up was based on the intention to treat and the initial reminder. Health services utilization, medication, admissions, and lipoprotein levels were monitored through the data sources.

Every 4 months the process was repeated, enrolling new patients, evaluating current lipoprotein profile and medication status of the patient's cohort, and updating recommendations.

**PRIMARY ENDPOINTS**

- **Appropriate lipoprotein monitoring.** At least one LDL measurement was expected during each 6 month interval Patients with at least 75% of screened 6 month intervals were considered to have adequate monitoring of LDL levels.
- **Initiation of statin therapy.** Patients were considered to be compliant with statin treatment if they purchased the following minimal number of pills after discharge: ≥ 25 statin tablets in the first 2 months, ≥ 50 tablets in the first 4 months, or ≥ 60 tablets in the first 6 months [18].
- **Optimizing statin treatment.** We evaluated the up-titration of medication doses in appropriate cases, whenever LDL cholesterol was above 110 mg/dl. Statins were divided into three groups according to their maximal LDL-cholesterol reduction potential: a) low potency = less than 30% reduction, b) medium potency = 30–45% reduction, and c) high potency = more than 45% reduction. Recommendations for statin up-titration were sent whenever the measured LDL cholesterol was above 110 mg/dl.
- **Treatment trends.** Negative trends were defined as not receiving statin initially and during the follow-up (in cases where statin treatment was recommended), inappropriate discontinuation of statins, or down-titration. Positive trends were defined as appropriate initiation of statin treatment, appropriate up-titration, or appropriate continuous treatment with statin.
- **LDL level reduction.** LDL levels at the beginning and at the end of follow-up.

**SECONDARY ENDPOINTS**

- All-cause mortality
- Rehospitalizations for major cardiovascular events: cardiovascular mortality, non-fatal myocardial infarction, stroke/transient ischemic attack, coronary artery bypass grafting, catheter-based revascularization procedures, angiography, and unstable angina [1,19]
- All other cardiovascular rehospitalizations: stable angina pectoris, precordial pain, chest pain, defibrillator implantation, pacemaker, arrhythmia, heart failure, newly diagnosed

cerebrovascular atherosclerosis or peripheral vascular disease, chronic ischemic heart disease, syncope, and collapse.

**STATISTICAL ANALYSIS**

Data were analyzed using an SPSS 12.0 package. Descriptive statistics were used for comparison of the groups. All analyses were conducted on an intention-to-treat basis. Inter-group differences for continuous variables were evaluated with the $t$-test and Mann-Whitney test. Univariate analysis with categorical variables was performed by chi-square test and Fisher's exact test. Differences in means for more than two groups were detected by analysis of variance (ANOVA) or Kruskal-Wallis test, as appropriate. Analyses involving repeated measurements were conducted using multivariate analysis of variance (MANOVA). All statistical tests were two-sided and a value < 0.05 was considered significant.

The trial was designed principally to detect any difference between the intervention arm of the study, using a computer-based clinical decision support system versus standard care. The study was designed to have 95% power to detect a 5% difference between the intervention and the control arms in improving monitoring and treatment for dyslipidemia and difference in LDL levels, expecting a relatively high proportion of compliant patients. Multivariate analysis was used to determine the impact of various variables on the primary endpoints and performed by logistic regression. Cox regression was used for the analysis of secondary outcomes, namely, all-cause mortality, major cardiovascular events, and cardiovascular hospitalizations.

## RESULTS

The process of patient selection is presented in Figure 1. A minimum of 6 months follow-up was available for 7448 patients (mean 21.0 ± 8.9 months, median 19.8 months, range 6–36.4 months). Table 1 presents characteristics of the study patients. Patients in the intervention (n=3695) and control groups (n=3753) were similar in most parameters. However, there were significantly more patients with a history of myocardial infarction (33.0% vs. 29.9%, $P = 0.004$) and percutaneous coronary intervention (26.2% vs. 23.8%, $P = 0.019$) in the intervention arm.

**MONITORING AND MONITORING OF LDL-CHOLESTEROL LEVELS**

Initial monitoring was defined as the presence of a lipoprotein profile within 6 months prior to or after the index hospitalization; 6645 patients (89.2%) had such a baseline lipid panel. There were 3854 patients (51.7%) with adequate monitoring. A higher rate of adequate monitoring was documented in the intervention arm (54.8% vs. 48.7%, $P < 0.001$). Multivariate regression analysis of factors affecting monitoring is presented in Table 2. Positive predictive factors

**Table 1.** Demography and medical history of the study groups

| | Intervention (n = 3695) | | Control (n = 3753) | | *P* |
|---|---|---|---|---|---|
| Age (yrs), average ± SD | 65.3 ± 9.8 | | 65.9 ± 10.2 | | 0.002 |
| | **n** | **%** | **n** | **%** | |
| Male | 2320 | 62.8 | 2344 | 62.5 | 0.768 |
| **Clinics** | | | | | |
| Urban | 3113 | 84.2 | 3194 | 85.1 | 0.768 |
| Kibbutz | 144 | 3.9 | 150 | 4.0 | 0.825 |
| Private farms | 187 | 5.1 | 121 | 3.2 | 0.000 |
| Minorities | 251 | 6.8 | 288 | 7.7 | 0.142 |
| **Medical history** | | | | | |
| MI | 1218 | 33.0 | 1121 | 29.9 | 0.004 |
| UA | 1601 | 43.3 | 1682 | 44.8 | 0.196 |
| CHF | 570 | 15.4 | 585 | 15.6 | 0.848 |
| CVA+ | 339 | 9.2 | 309 | 8.2 | 0.150 |
| PVD | 507 | 13.7 | 505 | 13.5 | 0.738 |
| PCI | 968 | 26.2 | 895 | 23.8 | 0.019 |
| CABG | 594 | 16.1 | 631 | 16.8 | 0.391 |
| **MACE during last year** | 1755 | 47.5 | 1770 | 47.2 | 0.773 |
| **Risk factors** | | | | | |
| Dyslipidemia | 2253 | 61.0 | 2245 | 59.8 | 0.308 |
| Hypertension | 2646 | 71.6 | 2739 | 73.0 | 0.186 |
| Diabetes | 1322 | 35.8 | 1347 | 35.9 | 0.919 |
| Obesity | 880 | 23.8 | 837 | 22.3 | 0.121 |
| Active smoker | 1393 | 37.7 | 1392 | 37.1 | 0.603 |
| Charlson index, average ± SD median (min, max) | 4.0 ± 2.0 4.0 (0, 14.0) | | 4.0 ± 2.1 4.0 (0,16.0) | | 0.456 |
| No. of risk factors, median (min, max) | 2.3 (± 1.1) 2 (0; 5) | | 2.3 (± 1.1) 2 (0; 5) | | 0.557 |

CABG = coronary artery bypass grafting, CHF = congestive heart failure, CVA+ = stroke or carotid disease, MI = myocardial infarction, PCI = percutaneous coronary intervention, PVD = peripheral vascular disease, MACE = major cardiac events, UA = unstable angina

**Figure 1.** Trial profile: enrollment and randomization to the 4C program



PCI = percutaneous coronary intevention
CABG = coronary artery bypass graft
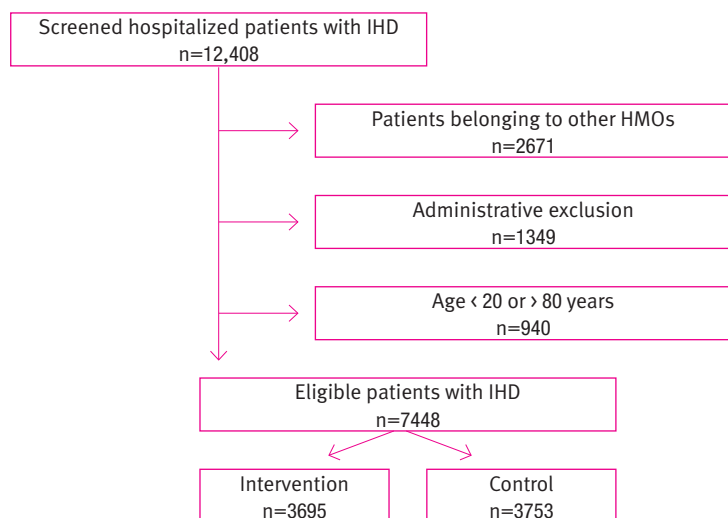
of adequate monitoring were as follows: a history of previous invasive revascularization, having diabetes or dyslipidemia, rehospitalizations, being in the intervention arm, and followed in a kibbutz clinic. Negative predictors of adequate monitoring were active smoking and belonging to a minority ethnic group

In most of the hospitalizations a lipid profile was automatically performed. As the rate of rehospitalizations during the follow-up period was 40%, the effect of the intervention would be distorted. Thus we performed a second multi-regression analysis for 3425 patients who were not rehospitalized, which showed that the independent effect of the intervention on monitoring became even stronger (relative risk = 1.423, confidence interval 1.24–1.64, $P < 0.0001$).

### MEDICATION

The treatment with statin was evaluated at enrollment and thereafter at 6 month intervals. Medication initiation or up-titration was recommended for patients with LDL levels above 110 mg/dl. The results showed that overall positive trends were minimally more prominent in the intervention arm (59.1% vs. 53.7%, $P < 0.003$). This difference constitutes a higher rate of drug initiation (2.5%), up-titration (1.8%) and avoiding drug cessation (1.1%). However, overall up-titration in patients with LDL ≥ 110 mg/dl was poor, both in the intervention arm and in the control arm (8.6% vs. 7.4%, not significant).

Multivariable regression analysis of the factors that affect positive medical treatment behavior is presented in Table 3. The most powerful predictor of positive treatment behavior was having a diagnosis of dyslipidemia, receiving treatment in a kibbutz, and history of mechanical revascularization (PCI more than CABG). Being in the intervention arm had a modest yet significant effect on positive behavior.

Analysis of drug usage (compliance) revealed that 28% of patients were taking > 75% of expected pills, 8% were taking 50–75% of expected pills, 17% were taking 25–49%, and 47% were taking less than 25% of the expected number of pills. This calculation is of crucial importance in evaluating the effect of the intervention on LDL levels since only 28% of patients were taking a clinically meaningful dose of lipid-lowering drugs.

### IMPACT ON LDL LEVELS

The patient cohort was divided according to initial LDL levels: LDL < 110 mg/dl (38.5%), 110–120 mg/dl (9%) and > 120 mg/dl (52.5%). In the group of patients with initial LDL levels above 120 mg/dl a significant decrease in LDL levels was observed in the two groups, which was minimally more pronounced in the intervention arm (from 145.5 ±

22.3 mg/dl to 121.9 ± 34.2, mg/dl, 16.2% reduction) than in the control arm (from 145.8 ± 22.9 to 124.3 ± 34.6, 14.8% reduction; $P < 0.02$).

### CLINICAL IMPACT

Assessing all cardiovascular related rehospitalizations (major and non-major cardiac effects) and all-cause mortality during the first year revealed a modest yet significant decrease of event-free survival in the intervention arm, 57.1% vs. 59.2% ($P < 0.03$).

## DISCUSSION

The results of the 4C Study demonstrate that a modest attenuation of the treatment gap can be accomplished by computerized interventions utilizing adjusted guidelines and appropriate implementation in the community. Primary end points of the study concerning secondary prevention measures were partially achieved in a "real-world" setting that included a non-selected population.

### MONITORING

The intervention had a minimal improvement in lipoprotein profile monitoring. We estimate that in a real-world setting there is a maximum compliance ceiling of about 70% [20,21], thus there is an additional 20% range of further improvement.

### MEDICATION

Clinically meaningful statin treatment was initially documented only in 44% of patients, which corresponds to that reported in the literature [22] and with the ACSIS data for the years 2000–2002 [23]. The intervention had a minor positive effect on "positive behavior" of statin treatment primarily by increasing the percentage of patients receiving treatment. Importantly, up-titrating of statin treatment remained highly unsatisfactory. Receiving treatment in a kibbutz, typically a small and intimate clinic, managed primarily by nurses and with generally more compliant patients, was also highly predictive of better treatment, emphasizing the potential of good compliance in prevention treatment. It should be noted that in cases of apparent non-compliance, the system is unable to differentiate between patient non-compliance with the physician's recommendations, physician non-compliance with the guidelines, or the existence of specific circumstances that make the guideline recommendations inappropriate.

### REDUCTION OF LDL LEVELS

A minimal yet significant ($P < 0.02$) decrease in LDL-cholesterol levels in the intervention arm was documented in patients with initial LDL > 120 mg/dl. It should be reemphasized that our data represent real-world secondary prevention, where at least 40% of patients were not receiv-

**Table 2.** Factors affecting adequate monitoring behavior: results of logistic regression

| Factor | OR | Lower | Upper | P |
|---|---|---|---|---|
| Kibbutz | 2.27 | 1.74 | 2.94 | ‹ 0.001 |
| After CABG | 1.54 | 1.34 | 1.74 | ‹ 0.001 |
| Diabetes | 1.47 | 1.35 | 1.68 | ‹ 0.001 |
| Rehospitalization | 1.48 | 1.34 | 1.63 | ‹ 0.001 |
| Dyslipidemia | 1.47 | 1.33 | 1.62 | ‹ 0.001 |
| After PCI | 1.29 | 1.15 | 1.44 | ‹ 0.001 |
| **Intervention arm** | **1.28** | **1.17** | **1.41** | ‹ 0.001 |
| Charlson Index at baseline | 1.04 | 1.01 | 1.07 | ‹ 0.002 |
| Active smoking | 0.76 | 0.69 | 0.84 | ‹ 0.001 |
| Minority | 0.62 | 0.51 | 0.75 | ‹ 0.001 |

**Table 3.** Factors affecting positive treatment (statin) behavior: results of logistic regression

| | OR | Lower | Upper | P |
|---|---|---|---|---|
| Dyslipidemia | 5.376 | 4.831 | 5.983 | 0.001 |
| Kibbutz | 2.431 | 1.803 | 3.277 | 0.001 |
| After PCI | 1.906 | 1.679 | 2.163 | 0.001 |
| After CABG | 1.396 | 1.21 | 1.61 | 0.001 |
| **Intervention arm** | **1.232** | **1.112** | **1.365** | **0.001** |
| Rehospitalization | 0.722 | 0.626 | 0.833 | 0.001 |

ing a statin. At the end of the follow-up, only a minority of patients were using high dose statins despite having above-target cholesterol levels. This supports the need to initiate high dose statins in all patients, irrespective of the baseline LDL-cholesterol level [2].

### CLINICAL IMPACT

A minimal decease in cardiovascular rehospitalizations in the intervention arm was demonstrated. To date, many CDSS programs have shown some improvement in practitioner performance, yet the effects on patient outcomes remain unclear [24].

### INNOVATION

The 4C study included several innovations:
- **Improvement of medical data integration**. The computerized tool took advantage of three routine collection information systems. Drug consumption was evaluated by following the drugs purchased by the patient (not merely prescriptions issued). Smart manipulation of the laboratory data transformed it from statistical items into operative medical information expressed as automatic recommendations. Such a combination was identified as a predictor of success [25].

- **Real-world approach.** 4C intervention included all administratively eligible CAD patients, a non-selected population. In contrast to clinical trials, in the real world patients often have multisystem co-morbid diseases and related contraindications to statin. We can estimate that at least 10% of patients eligible for a statin based on strict guidelines will be judged by their physicians as not suitable for treatment. This is in addition to another 10–20% of patients who would not comply with the recommendation due to psychosocial and physician-patient communication factors. These numbers represent a "medical ceiling" for strict guideline adherence. It would be reasonable to set a maximum goal of approximately 70–80% guideline adherence. The 4C initial intervention had a modest effect in narrowing the treatment gap by 6%, leaving a potential of 20% for improvement.
- **Negotiating compliance.** Only a minimal additional burden will be tolerated by the GP. We introduced computerized clinical judgment in addition to the existing orthodox guidelines, yielding 'down to earth' clinical recommendations. With this in mind, the initial intervention was recommended only in patients with LDL > 110 mg/dl in order to avoid handling patients with near target level LDL, which would be perceived by the GPs as disturbing and cause mistrust in the system. Manipulating laboratory data based on clinical judgment (e.g., treating cholesterol > 220 mg/dl) avoids unnecessary blood tests, hopefully enhancing compliance. Annual site visits by the principal investigator perpetuated the motivation to fulfill recommendations on the one hand and adjusting the system to the GP's needs on the other.

### 4C INTERVENTION LIMITATIONS

Our trial had several limitations. Firstly, we used only computerized data, including diagnoses, relying on the GPs to validate the clinical information and act accordingly. This, however, would not bias the results as hospital physicians wrote diagnoses for both arms. Second, outcome measures were patient-based, but the interventions were aimed at health professionals. This study did not evaluate separately the impact of system, physician, and patient factors. Thirdly, in this report we present the initial phase of intervention with a very short follow-up. A long-term follow-up of multiple cardiovascular risk factors will allow better understanding of the impact of such CDSS. Finally, the study was not powered to detect clinical outcomes in the real-world setting where compliance approximates 50%.

### CONCLUSIONS

The 4C intervention showed that computer-based clinical decision support systems can moderately enhance second-ary prevention measures and slightly reduce the number of cardiovascular rehospitalizations in a relatively short time. The main treatment obstacles were the low rate of statins administration and a very low rate of drug up-titration. Negotiating compliance with the physicians and creating a positive climate where the GP accepts the recommendation as a supportive intervention are the cornerstones for success. Algorithms that integrate clinical judgment and understanding of phycicians' needs and ability to comply with computerized recommendations are supportive. In view of the limitations noted above there was only a modest improvement in adherence to guidelines with regard to secondary prevention in this system.

A comprehensive cardiovascular risk factors intervention was recently introduced nationwide. A long-term follow-up of the advanced CDSS will allow better evaluation of its impact.

**Correspondence**
**Dr. H. Gilutz**
Dept. of Cardiology, Soroka Medical Center
P.O. Box 151, Beer Sheva 84101, Israel
**Phone:** (972-8) 640-3469
**Fax:** (972-8) 623-9269
**email:** gilutz@bgu.ac.il

**References**

1. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with Coronary Artery Disease: the Scandinavian Simvastatin Survival Study (4S).
   *Lancet* 1994; 344: 1383–9.
2. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial.
   *Lancet* 2002; 360: 7–22.
3. Grover SA, Ho V, Lavoie F, et al. The importance of indirect costs in primary cardiovascular disease prevention: can we save lives and money with statin?
   *Arch Intern Med* 2003; 163: 333–9.
4. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III).
   *JAMA* 2001; 285: 2486–97.
5. Wood D. Recommendations of the Second Joint Task Force of European and other societies on coronary prevention.
   *Eur Heart J* 1998; 19: 1434–503.
6. Harats D, Leibovitz E, Maislos M, et al. for the HOLEM Study Group for cardiovascular risk assessment and treatment to target low density lipo-protein levels in hospitalized ischemic heart disease patients: results of the HOLEM Study.
   *IMAJ* 2005; 7: 355–9.
7. Gavish D, Leibovitz E, Elly I, Shargorodsky M, Zimlichman R. Follow-up in a lipid clinic improves the management of risk factors in cardiovascular disease patients.
   *IMAJ* 2002; 4: 694–7.
8. Benner JS, Glynn RJ, Mogun H, et al. Long-term persistence in use of statin therapy in elderly patients.
   *JAMA* 2002; 288(4): 455–61.
9. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement.
   *JAMA* 1999; 282: 1458–65.

10. Garr DR, Ornstein SM, Jenkins RG, et al. The effect of routine use of computer-generated preventive reminders in a clinical practice. *Am J Prev Med* 1993; 9(1): 55–61.

11. Hunt DL, Haynes RB, Hanna SE, et al. Effects of computer-based clinical decision support systems on physician performance and patient outcomes: a systematic review. *JAMA* 1998; 280(15): 1339–46.

12. Johnston ME, Langton KB, Haynes RB, et al. Effects of computer-based clinical decision support systems on clinician performance and patient outcome. A critical appraisal of research. *Ann Intern Med* 1994; 120(2): 135–42.

13. Balas EA, Austin SM, Mitchell JA, et al. The clinical value of computerized information services. A review of 98 randomized clinical trials. *Arch Fam Med* 1996; 5: 271–8.

14. Shea S, DuMouchel W, Bahamonde L. A meta-analysis of 16 randomized controlled trials to evaluate computer-based clinical reminder systems for preventive care in the ambulatory setting. *JAMA* 1996; 3(6): 399–409.

15. Hunt DL, Haynes RB, Hanna SE, et al. Effects of computer-based clinical decision support systems on physician performance and patient: a systematic review. *JAMA* 1998; 280: 1339–46.

16. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40(5): 373–83.

17. Rubinstein A. Detection and treatment of high blood cholesterol for prevention of coronary artery disease attitude of the Israeli Society of Atherosclerosis. *Harefuah* 1995; 128(9): 551–6 (Hebrew).

18. Jackevicius CA, Mamdani M, Tu JV. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. *JAMA* 2002; 288: 462–7.

19. McCormick LS, Black DM, Waters D, et al., for the AVERT investigators. rationale, design, and baseline characteristics of a trial comparing aggressive lipid lowering with atorvastatin versus revascularization treatments (AVERT). *Am J Cardiol* 1997; 80(9): 1130–3.

20. Campbell NC, Thain J, Dean HG, et al. Secondary prevention in coronary artery disease: baseline survey of provision in general practice. *BMJ* 1998; 316: 1430–4.

21. Gilutz H, Zelingher J, Bonneh D, et al. Is there a ceiling for lipid lowering compliance? Computerized community cholesterol control (4C). 2nd Scientific Conference on Compliance in Healthcare and Research, Washington DC; May 2004 (Abstract).

22. Avorn J, Monette J, Lacour A, et al. Persistence of use of lipid-lowering medications: a cross-national study. *JAMA* 1998; 279(18): 1458–62.

23. Hod H, Gotlieb S, Green M, et al. Trends in management, morbidity and mortality of patients with acute myocardial infarction hospitalized in the last decade. *Harefuah* 2006; 145(5): 326–31, 400 (Hebrew).

24. Garg AG, Adhikari NK, McDonald H, et al. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes. A systematic review. *JAMA* 2005; 293: 1223–38.

25. Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. *BMJ* 2005; 330: 765.