Clinical Chemistry 45:10
1752–1761 (1999)

Test Utilization and Outcomes

Common Diagnostic Test Panels for Clinical Evaluation of New Primary Care Outpatients in Japan: A Cost-Effectiveness Evaluation

Yuzuru Takemura,[1,4*] Haku Ishida,[2] Yuji Inoue,[3] and J. Robert Beck[1]

Background: **The Japan Society of Clinical Pathology (JSCP) has developed a guideline for common diagnostic test utilization in new primary care outpatients. To determine the scientific and economic validity of the JSCP panel testing system, we analyzed cost-effectiveness parameters of test panels advocated.**

Methods: **The "Essential Laboratory Tests" panel (2) [ELT(2) panel], a package of common diagnostic tests added to the ELT(1) baseline health-status screening panel, was applied to 540 new outpatients who visited the Comprehensive Medicine Clinics in an academic medical center during 1991 to 1997. A "useful result" (UR) of testing was defined as a finding that contributed to a change in a physician's diagnosis- or decision-making, relating to a "tentative initial diagnosis" (TID) obtained from history and physical examination alone.**

Results: **Clinical usefulness was demonstrated in 259 patients with ELT(2), in whom 398 URs were generated. Clinical effectiveness (UR/TID) ranged from 1.65 (hematological) to 0.088 (neurological disease), with a cost disparity from ¥1251 (~$10) to ¥23 037 (~$200) per UR. A total of 1137 tests generated URs. We further assessed the clinical effectiveness and economic efficiency (cost/UR) of ELT(1) and restructured panels. Use of the ELT(1) alone generated 244 URs in 167 patients. The poor efficiency of the ELT(1) panel was markedly improved with the addition of certain ELT(2)-specific tests in liver/pancreatobiliary, metabolic/endocrine, and cardiovascular disease groups.**

Conclusions: **A wide disparity in the utility of ELT panels in different patient groups does not support the JSCP recommendation of their routine use for new outpatients. Selective test combinations should be used in selected patient groups.**

The Japan Society of Clinical Pathology (JSCP)[5] organized a subcommittee, named "The Uses of Clinical Laboratory Tests in Daily Primary Care", in 1988 to investigate efficient and appropriate combinations of laboratory tests for the initial clinical evaluation of new patients. The concept is based on the placement of common diagnostic tests into a conventional, efficacious diagnostic complex to compete against the rapid expansion of diagnostic test usage in the past two decades in Japan. The subcommittee has been establishing guidelines for efficacious test utilization in common clinical areas and in organ-directed or disease-specific conditions. The former has led to two "Essential Laboratory Test" (ELT) panels, which are directed toward new outpatients with some defined symptoms in primary care medicine. The ELT, according to the JSCP, should be performed at the initial clinical evaluation of new outpatients in parallel with a history and physical examination *(1)*. The ELT are composed of two panels, ELT(1) and ELT(2) (Table 1); JSCP intends the ELT(1) basic panel to be universally ordered in every new outpatient as routine testing to obtain minimally essential information for a disease or patient status, whereas the ELT(2) panel tests, including chest and abdominal plain x-rays and electrocardiograms (ECGs), should be per-

[1] Department of Pathology and Information Technology Program, Baylor College of Medicine, Houston, TX 77030-3498.
[2] Department of Clinical Pathology, Kawasaki Medical School, Kurashiki, Okayama 701-0192, Japan.
[3] Department of Medical Informatics, Yamaguchi University School of Medicine, Ube, Yamaguchi 755-8505, Japan.
[4] Department of Laboratory Medicine, National Defense Medical College, Tokorozawa, Saitama 359-8513, Japan.
*Address correspondence to this author at: Department of Pathology and Information Technology, Baylor College of Medicine, One Baylor Plaza, Room 126E, Texas Medical Center, Houston, TX 77030-3498. Fax 713-790-7052; e-mail takemura@bcm.tmc.edu.
Received May 19, 1999; accepted July 8, 1999.

[5] Nonstandard abbreviations: JSCP, Japan Society of Clinical Pathology; ELT, Essential Laboratory Test; ECG, electrocardiogram; TID, tentative initial diagnosis; CRP, C-reactive protein; CBC, complete blood count; LDC, leukocyte differential count; RBC, red blood cell; ESR, erythrocyte sedimentation rate; UR, useful result; ALP, alkaline phosphatase; AST, aspartate aminotransferase; and ALT, alanine aminotrasferase.

Table 1. Components of the Essential Laboratory Test (ELT) panels advocated by the Japan Society of Clinical Pathology.

ELT (1): Tests required anytime, anywhere
Dipstick urinalysis: protein, occult blood, glucose
ESR and CRP
Hematology: WBC[a] count, RBC count, hemoglobin, hematocrit
Chemistry: total protein, albumin, albumin/globulin ratio
ELT (2): Performed at hospital admission or when necessary at the initial clinical evaluation of new outpatients
Urinalysis: color, turbidity, pH, specific gravity, protein, glucose, occult blood, nitrites, leukocyte esterase, sediment
ESR and CRP (or sialic acid)
Hematology: WBC count, RBC count, hemoglobin, hematocrit, RBC indices (MCV, MCH, MCHC), platelet count, peripheral blood smear examination
Chemistry: total protein, serum protein fraction profile, total cholesterol, triglycerides, glucose, AST, ALT, LD, ALP, GGT, serum urea nitrogen, creatinine, uric acid
Serological examination: hepatitis B virus surface antigen-antibody, hepatitis C virus antibody, serological tests for syphilis
Fecal occult blood
Chest or abdominal plain x-ray
ECG

[a] WBC, white blood cell; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; LD, lactate dehydrogenase; GGT, γ-glutamyltransferase.

formed selectively to focus the initial clinical diagnosis if necessary.

Our preliminary study demonstrated that the clinical usefulness[6] of the ELT for a physician's diagnosis- or decision-making was classified into (*a*) establishment of an initial clinical diagnosis in a patient with an undetermined pre-test diagnosis; (*b*) negation and/or correction of a pre-test diagnosis; (*c*) confirmation of a pre-test diagnosis; and (*d*) estimation of the nature or degree of seriousness of a disease as well as evaluation of a patient's general condition *(2)*. The ELT may lead to proper treatment for, and management of, a patient on the basis of a more accurate diagnosis without time delay and save time for the next diagnostic evaluation when the ELT is used as the basis for on-site testing. In fact, one study demonstrated that panel chemistry testing led to fewer return visits of patients to clinics and substantially lower costs than with selective testing *(3)*. Panel testing is also much more informative and more convenient to patients who need not be subjected to multiple blood samplings.

Another advantage in panel testing has been cost: the direct charges to the patient or payer are often lower when profile testing is done than when a selected smaller group of tests is ordered *(4)*. Lehmann and Leiken *(5)* compared "a la carte" test ordering with panel testing for a common set of analytes in 1985 and found a 32% cost saving from ordering the panel, with few false-positive test results. However, the advances in discrete chemical analyzers have continued, and programmable machines can now match the frugality of high-throughput continuous flow analyzers in most settings. Others have shown that unbundling component tests saved costs *(6)*. With the recent interest in cost-effective resource utilization, there have been several attempts to reduce test volume, eliminating unnecessary diagnostic tests and procedures *(7–13)*. Panel testing has been changed toward more carefully selected individual tests or small groups of tests in the United States *(14, 15)*. Reimbursement is granted only to limited small panels based on automated multichannel analyzers under the Medicare billing regulations that became effective in April 1998 *(16)*. In contrast to the United States under the fixed-fee reimbursement system, charges for clinical laboratory testing are still reimbursed on a cost basis in Japan, although the government has attempted to introduce generalized cost-containment programs for medical care. Considering the social and economic forces against current laboratory testing, persuasive utilization of a panel testing system must depend on its distinct cost-effectiveness, at least for selected patient groups.

Lack of evidence of the validity of the JSCP-advocated ELT test panels urged us to study their clinical effectiveness and economic efficiency for clinical evaluation of new outpatients in primary care medicine. After careful evaluation of cost and effectiveness in different disease categories, our efforts were directed toward the development of highly efficient new test combinations that can provide maximal effectiveness at a minimal cost increment. In this study, we focused on the utility of the ELT for establishing a diagnosis and physicians' decision-making against primary diseases related to patients' complaints. Disease screening or case-finding efficiency in general patient populations was analyzed only tangentially.

Patients and Methods

PATIENTS

Among all new outpatients who visited the Comprehensive Medicine Clinics, National Defense Medical College, Tokorozawa, Japan, and its affiliated hospital from June 1991 to March 1997, 540 patients (250 males, 290 females; ages, 9–83 years) who had some defined symptoms and who were seen by physicians certified by the Japanese Boards of Internal Medicine and Clinical Pathology were entered in this study. Patients were eligible irrespective of their symptoms or disease categories, without any selection process. Those referred from physicians in other medical facilities with test results and/or tentative clinical diagnoses were excluded in advance from the study or not evaluated in the analyses. Patients were universally

[6] Definitions for descriptions used specifically: clinical usefulness, values of testing contributing to physician's diagnosis- or decision-making; clinical effectiveness, the number of URs per TID (UR/TID) in each disease category; economic efficiency, the cost required per UR generated (cost/UR) in each disease category; cost-effectiveness, incremental cost for tests added/additional UR generated (Δcost/ΔUR).

given a diagnostic test package corresponding to the ELT(2) panel (Table 1) with the addition of serum cholinesterase after a history and physical examination. The diagnostic sensitivity, specificity, and positive predictive values of the individual panel components were analyzed in our preliminary study and described elsewhere *(17)*. Chest and abdominal plain x-rays, ECGs, fecal occult blood tests, and serological tests for hepatitis-related virus antigen or antibody and syphilis were optional choices. Diagnoses were divided into the "tentative initial diagnosis" (TID), which was made tentatively by the primary care physician from the history and physical examination alone, and the "initial clinical diagnosis", which was established after integrating the results of diagnostic tests. The TID was made at the first visit of a patient to the outpatient clinic, and the initial clinical diagnosis was established at that patient's next visit to the same clinic. Physicians participating in the clinical practice were not given information relating to the test results, irrespective of ELT(1) or ELT(2), at the time of initial clinical evaluation (the TID process), except for emergency cases. A diagnosis related to a patient's chief complaint was defined as the "primary diagnosis", whereas those uncovered with abnormal test results that were unexpectedly elicited by the enforcement of the ELT and not related directly to a patient's illness, were defined as "additional diagnoses".

ASSAY METHODS

Dipstick urinalysis was performed with Ames reagent strips (Multistix SGL; Miles-Sankyo). Serum samples were collected for analyses of chemistry test items, C-reactive protein (CRP), and sialic acid by an automated multichannel analyzer (model 736; Hitachi). Because sialic acid is considered as a delayed responder to inflammation and to show a different movement in the inflammation process from CRP, this test was also adopted in the ELT(2) panel. Serum protein profiles (protein fractions) were determined after electrophoresis of sera on a cellulose acetate membrane by an automated analyzer (model CTE1200; Johkoh). The complete blood count (CBC) was measured by an automated blood cell counter equipped with a function for leukocyte differential counts (LDCs; model E-5000; Sysmex). This instrument can also measure red blood cell (RBC) indices, including mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration. Microscopic examination of peripheral blood smears was performed on samples with any abnormalities in CBC or qualitative abnormalities detected by the analyzer. The standard Westergren method was used for measurement of the erythrocyte sedimentation rate (ESR). Chest and abdominal plain x-rays, ECGs, and fecal occult blood tests were ordered optionally if necessary. Serological tests for hepatitis-related virus antigen or antibody and syphilis were also optional and not evaluated. Triglyceride values were excluded for diagnosis-making or assessment of clinical usefulness of ELT because of large fluctuations related to postprandial status, although random blood glucose values were evaluated in this study.

DETERMINATION OF USEFUL RESULT, CLINICAL EFFECTIVENESS, COSTS, AND COST-EFFECTIVENESS

The clinical usefulness of the ELT was determined by assessing the impact of its results on a physician's diagnosis- or decision-making. A "useful result" (UR), which is the unit of usefulness of the ELT and is classified into four categories, was assigned according to criteria shown in Table 2. For determination of URs, patients' medical records were reviewed closely to find any changes or modifications in the clinical diagnosis of, treatment for, or management of, a patient before and after interpretation of test results. Additional ordering of organ- or disease-specific diagnostic tests and reference to a specialist after interpretation of the ELT were also counted as URs. A UR in any category was deemed to have equivalent weight in this study, and a patient may have had more than one UR. Three physicians participated the determination of URs; one of these physicians was a participant in the initial clinical practice of the patients. The diagnosis- and decision-making of that physician or other physicians were strictly reviewed by the other two physicians examining the URs assigned. The clinical effectiveness of the ELT is

Table 2. Criteria for assignment of a useful result (UR).

Classification of usefulness of Essential Laboratory Tests	Criteria for UR assignment
(1) Establishment of the initial clinical diagnosis among patients with undetermined tentative initial diagnoses (TIDs)	Newly established diagnosis corresponding to patient's clinical illness after interpretation of test results
(2) Negation or correction of a TID	Difference between a TID and the initial clinical diagnosis
	Negative test results for a TID
(3) Confirmation of a suspected TID	Test results supporting a TID
(4) Evaluation of the nature or degree of seriousness of a disease	Test data that could estimate the nature or degree of seriousness of a disease and followed by:
	(*a*) Any change or modification in the treatment for a patient
	(*b*) Any change in the management of a patient
	(*c*) Further ordering of organ- or disease-specific tests
	(*d*) Reference to a specialist, or transfer of the patient to a specialist clinic

expressed as the number of URs per TID in each disease category.

Because of a lack of availability of cost data at the National Defense Medical College Hospital, costs[7] were calculated by considering all expenditures required to obtain test results at the Kawasaki Medical School Hospital (Kurashiki, Japan), which is a tertiary hospital similar to the National Defense Medical College Hospital with respect to size, geographic location, and surrounding population distribution. These include costs for test reagents and analyzer operation, equipment amortization, and personnel expenses for medical technologists. Indirect costs were excluded. The economic efficiency of the ELT is defined as the cost required per UR generated in each disease category. The cost-effectiveness was determined as incremental cost for tests added to the ELT(1) baseline panel per additional UR generated.

SIMULATION STUDIES

The test package performed for 540 new outpatients included all components of the ELT(1) panel. We modified the accumulated database to contain patients' chief complaints, TIDs, and test data of ELT(1) items alone but not to include initial diagnoses obtained from interpretation of all test items actually performed; we then reestablished the initial diagnosis, assigning URs based on the ELT(1) in individual patients. The results were compared with those obtained from test components corresponding to the ELT(2). We further extended the study to pursue a test combination that can provide maximal effectiveness at a minimal cost increment in each disease category, analyzing the UR generated and costs required after certain ELT(2)-specific test components were added to the ELT(1) basic panel.

In this study, RBC indices, which can be calculated by CBC data in the ELT(1), were moved to the ELT(1), although the JSCP guideline incorporates them into the ELT(2).

Results

UR DETERMINATION

Histories and physical examinations generated 633 effective TIDs (excluding those in patients previously diagnosed at, or with test results performed at, other medical facilities) among 540 new outpatients. Integration of the test results with TID produced 692 primary initial clinical diagnoses and 276 additional diagnoses, the latter being unrelated to patients' chief complaints but uncovered as a result of the disease-screening effect of the test package. A "true" UR yielded by the tests was limited to those between a given TID and the primary initial clinical diagnosis. Table 3 compares the type and number of URs generated by the ELT(1) and ELT(2). A patient may have more than one UR with ELT panel testing, particularly as increasing test components are performed. Consider, for example, a patient who had a TID of fever of unknown origin but who demonstrated pneumonia by chest x-ray with a markedly increased CRP value and leukocytosis with striking neutrophilia. Three URs that contributed to a physician's diagnosis- and decision-making could be assigned in this case: (*a*) establishment of the initial clinical diagnosis; (*b*) evaluation of the degree of seriousness of the disease; and (*c*) evaluation of the nature of the disease (possibly bacterial infection). The latter two led to hospitalization of the patient and administration of antibacterial chemotherapeutic agent(s) according to the chemosusceptibility of the causative microorganisms. Clinical usefulness was demonstrated in 259 patients with the ELT(2), in whom 398 URs were generated against 633 TIDs, whereas the use of the ELT(1) panel alone yielded 244 URs in 167 patients.

CLINICAL EFFECTIVENESS AND ECONOMIC EFFICIENCY OF THE ELT PANELS

The clinical effectiveness and economic efficiency of the ELT(1) and ELT(2) panels in each disease category are shown in Table 4. The clinical effectiveness of the ELT(2) ranged from 1.65 UR/TID (hematological) to 0.088 UR/TID (neurological disease group), and the cost per UR generated was distributed (from ¥1251 to ¥23 037 per UR) between these two disease groups. Comparison of the ELT(1) with the ELT(2) demonstrated substantial decreases in clinical effectiveness: UR/TID with the ELT(1) was 0.39 overall compared with 0.64 with the ELT(2). The ELT(1) generated UR/TID ratios of only 0.080 and 0.18 in metabolic/endocrine and liver/pancreatobiliary disease groups, whereas the ELT(2) generated UR/TID ratios of 0.68 and 1.30, respectively. Remarkable increases in clinical effectiveness with the ELT(2) led to improved cost efficiency, which decreased from ¥11 426/UR and ¥5126/UR with the ELT(1) to ¥3263/UR and ¥1482/UR with the ELT(2) for the metabolic/endocrine and liver/pancreatobiliary disease groups, respectively, producing

Table 3. Type and number of useful results (URs) generated by Essential Laboratory Test (ELT) panel testing among 540 new outpatients.

	No. of URs	
Type of ELT	**ELT(1)**	**ELT(2)**
Establishment of the initial clinical diagnosis among patients with undetermined tentative initial diagnoses (TIDs)	25	41
Negation or correction of a TID	41	80
Confirmation of a suspected TID	24	55
Evaluation of the nature or degree of seriousness of a disease, following by physician's decision-making	154	222
	244 (167 cases)	398 (259 cases)

[7] Costs (¥) can be converted to US dollars at a rate of US $1.00 ≅ ¥120.00 on May 1, 1999.

Table 4. Clinical effectiveness and economic efficiency of the Essential Laboratory Test (ELT) panels among 540 new outpatients.

			ELT(1)				ELT(2)				
Patient group	No. of patients	No. of TIDs[a,b]	No. of URs	Total cost,[c] ¥	UR/TID	Cost/UR, ¥	No. of URs	Total cost, ¥	UR/TID	Cost/UR, ¥	ΔCost/ΔUR, ¥
Infectious or inflammatory diseases	180	177	121	160 796	0.68	1329	179	367 050	1.01	2051	3556
Gastrointestinal diseases	87	84	21	77 869	0.25	3708	31	154 431	0.37	4982	7656
Neurological diseases	58	57	3	53 360	0.053	17 787	5	115 187	0.088	23 037	30 914
Cardiovascular diseases	57	60	7	52 631	0.12	7519	27	149 394	0.45	5533	4838
Metabolic/endocrine diseases	43	25	2	22 851	0.080	11 426	17	55 477	0.68	3263	2175
Liver/pancreatobiliary diseases	42	33	6	30 758	0.18	5126	43	63 706	1.30	1482	890
Hematological diseases	29	23	36	20 843	1.57	579	38	47 543	1.65	1251	13 350
Renal/urinary tract diseases	10	9	10	8515	1.11	852	13	20 022	1.44	1540	3836
Respiratory diseases	10	7	8	6627	1.14	828	9	19 411	1.29	2157	12 784
Others	83	80	7	73 557	0.088	10 508	14	171 428	0.18	12 245	13 982
Diagnosis undetermined	77	78	23	72 102	0.29	3135	28	171 581	0.36	6128	19 896
Total	676	633	244	579 909	0.39	2377	404[d]	1 335 230	0.64	3305	4721

[a] TID, tentative initial diagnosis; UR, useful results.
[b] Excluded patients with TIDs diagnosed previously or with test results performed in other medical facilities.
[c] Costs (¥) can be converted to US dollars at a rate of $1.00 ≅ ¥120.00 on May 1, 1999.
[d] Six URs were overlapped in multiple disease categories.

the best cost-effectiveness (Δcost/ΔUR) for the ELT(2) in the liver/pancreatobiliary disease group (¥890/additional UR). A similar decrease in cost/UR with the ELT(2) was also demonstrated in the cardiovascular disease group, although the disparity was not as large [from ¥7519 with the ELT(1) to ¥5533/UR with the ELT(2)]. In patients with neurological problems, there were very few URs generated with the ELT(1) or the ELT(2); therefore, this group yielded the poorest clinical effectiveness and the lowest economic efficiency with testing in both ELT panels. In contrast, the ELT(1) yielded the best UR/TID (1.57) in the hematological disease group at a cost of only ¥579/UR, but additional ELT(2) test items scarcely produced incremental URs. The ELT(2) was substantially less cost-effective in the gastrointestinal disease group (¥7656) than in the infectious or inflammatory disease group (¥3556/additional UR).

test panel components contributing to generation of URs

In total, 1137 tests contributed to 398 URs generated among 540 new outpatients with 633 TIDs. Basic diagnostic tests constituting the ELT(1) made up 44% of the total tests contributing to UR. Fig. 1 illustrates the frequency of test components contributing to UR. Not only test values out of reference intervals but also those within them, indicating negative results against a TID, could contribute to UR because the latter may have URs for negation and/or correction of the TID. Chest and abdominal x-rays, ECGs, and fecal occult blood tests, which were optional choices in this study, were ordered in 198, 17, 79, and 53 patients, respectively, and their contribution rates were 13.6%, 35.3%, 17.7%, and 5.7%, respectively.

Because the clinical usefulness of individual tests varied depending on the disease category of TID, we further analyzed the pattern and frequency of tests contributing to the generation of URs in each disease category (Fig. 2). Basic components in the ELT(1) panel were major contributors to the generation of URs in hematological diseases, whereas ELT(2)-specific test items primarily produced URs in liver/pancreatobiliary, metabolic/endocrine, cardiovascular, and renal/urinary tract disease groups. In infectious or inflammatory diseases, major contributing test components were inflammation indicators: the usefulness of the LDC, sialic acid, and protein fraction profile in the ELT(2) panel overlapped with that of CRP, leukocyte count, and ESR in the ELT(1) panel; thus, there was a relatively small increment in URs produced only by ELT(2)-specific test items [121 and 179 URs with the ELT(1) and ELT(2) panels, respectively], despite the dominance of ELT(2)-specific test items contributing to UR. A similar effect was observed in the renal/urinary tract disease group. The frequency of tests generating URs was extremely low irrespective of ELT(1) or ELT(2) test items in neurological and other (miscellaneous) disease categories, reflecting the very low clinical effectiveness of the ELT panels in the aggregate in these groups.

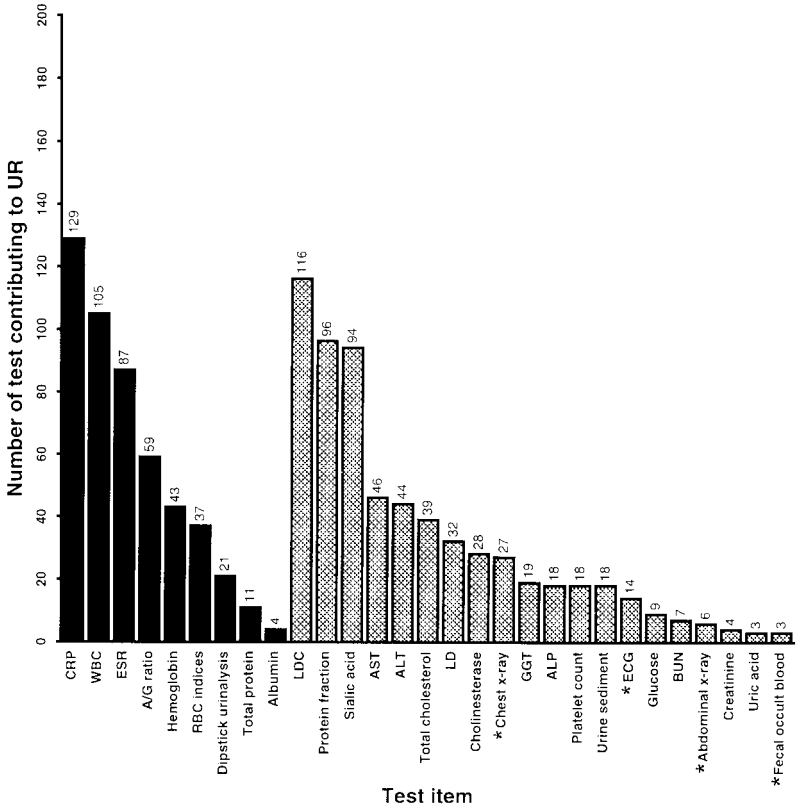

Fig. 1. The ELT components and their frequency of contribution to generation of URs.

Filled columns indicate ELT(1) component tests; *hatched columns* are those of ELT(2)-specific test items. The *number* at the top of each column is the frequency of contribution for that test. A total of 1137 tests contributed to 398 URs. *A/G ratio*, albumin/globulin ratio; *BUN*, serum urea nitrogen; *GGT*, γ-glutamyltransferase; *LD*, lactate dehydrogenase. *, optional tests that were ordered.

simulation studies for cost-effective test combinations in selected patient groups

Considering individual test components that were major contributors to the generation of URs (Fig. 2), we attempted to seek more effective test combinations, adding some ELT(2) test items to the ELT(1) baseline panel. Substantial increases in clinical effectiveness with the ELT(2) were observed in infectious or inflammatory, cardiovascular, metabolic/endocrine, liver/pancreatobiliary, and renal/urinary tract disease groups (Table 4), indicating that certain test items in the ELT(2) panel have substantial effectiveness in these disease groups. Table 5 demonstrates the cost-effectiveness parameters of redesigned panels of common diagnostic tests based on the ELT(1) in these five disease categories. As expected in Fig. 2, clinical effectiveness and economic efficiency were improved to a great extent by the addition of five automated analyzer-based chemistry tests and a protein fraction profile to the ELT(1) in liver/pancreatobiliary diseases at a cost-effectiveness of ¥192/additional UR. Addition of only three chemistry tests [alkaline phosphatase (ALP), total cholesterol, and glucose] to the ELT(1) produced fairly improved clinical effectiveness at ¥91/additional UR in metabolic/endocrine diseases. Although chest x-rays and ECGs with the ELT(1) increased clinical effectiveness more than threefold (from 0.12 UR/TID to 0.43 UR/TID) in cardiovascular diseases, cost/UR was only moderately decreased (from ¥7519/UR to ¥4159/UR) because of higher costs for both tests (¥877 and ¥699 per test, respectively). In infectious or inflammatory and renal/urinary tract disease groups, cost/UR increased as the number of added test items increased.

Discussion

In the present study, we investigated the clinical effectiveness and economic efficiency of test panels composed of common diagnostic tests for clinical evaluation of new primary care outpatients with some defined symptoms. The utility of the panels for case-finding or screening of new diseases unrelated to patients' illness was not evaluated in this study. Because cost data may be influenced by the prevalence of various diseases among the test population, it would be desirable to use the cost data obtained from the hospital in which the study was carried out, if these were available.

According to the JSCP guideline, individual new outpatients receive the ELT(1) panel as routine testing to obtain basic information at the initial clinical evaluation. Additional tests should be selected from the ELT(2) panel at the initial visit if necessary, and then organ-directed or disease-specific diagnostic approaches would follow the ELT in a step-by-step manner *(1)*. However, the guideline

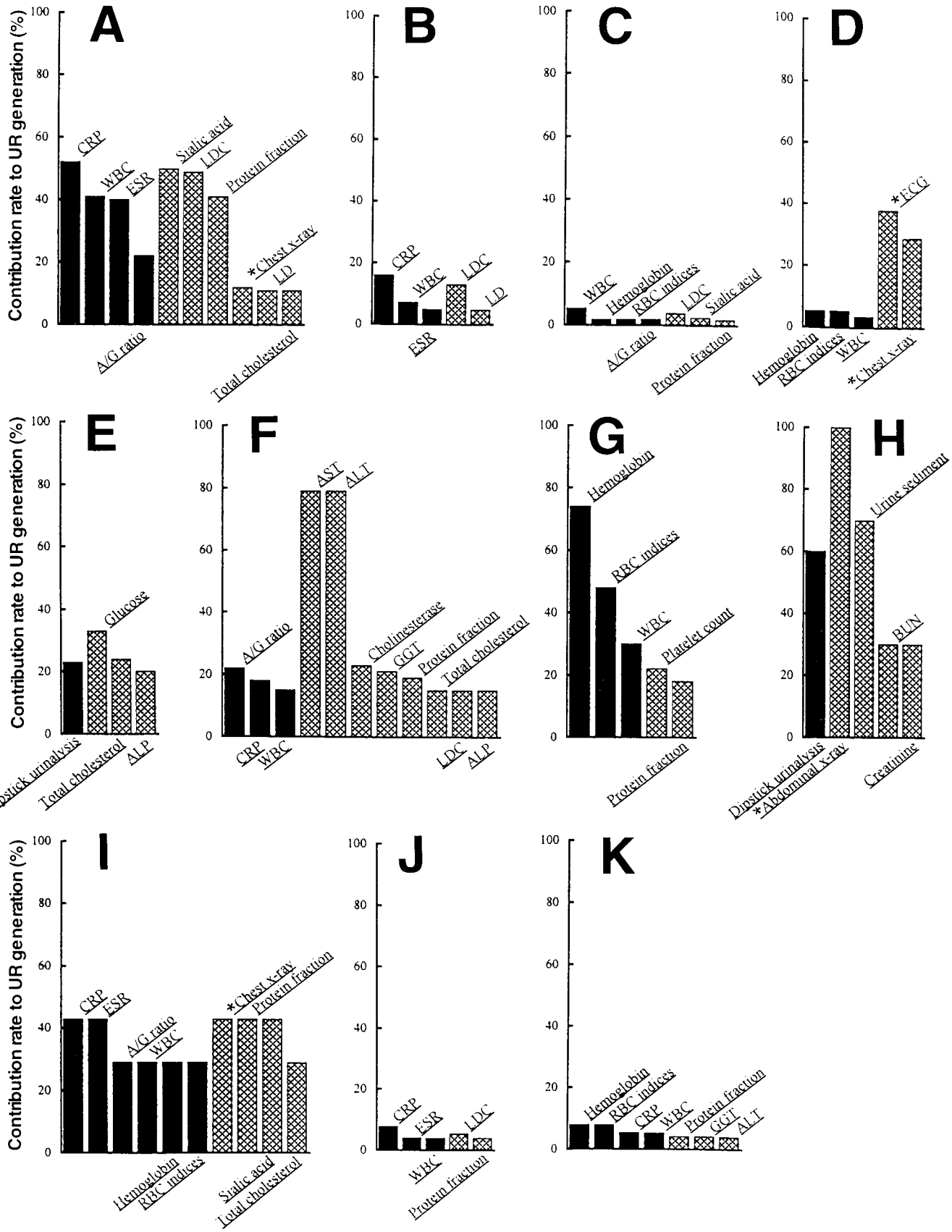
A
B
C
D
E
F
G
H
I
J
K
Contribution rate to UR generation (%)
0
20
40
60
80
100
CRP
WBC
ESR
Sialic acid
LDC
Protein fraction
*Chest x-ray
LD
A/G ratio
Total cholesterol
Hemoglobin
RBC indices
*ECG
Glucose
Dipstick urinalysis
Total cholesterol
ALP
AST
ALT
Cholinesterase
GGT
Platelet count
Urine sediment
BUN
*Abdominal x-ray
Creatinine

Table 5. Clinical effectiveness and economic efficiency of redesigned test combinations for selected patient groups.

Patient group	TID[a]	Test combination	No. of URs	Total cost, ¥[b]	UR/TID	Cost/UR, ¥	ΔCost/ΔUR, ¥
Infectious or inflammatory diseases	177	ELT(1)	121	160 796	0.68	1329	
		ELT(1) + LDC	138	169 009	0.78	1225	483
		ELT(1) + LDC, AST, ALT, LD,[b] ALP, chest x-ray	154	246 411	0.87	1600	2594
		ELT(2)	179	367 050	1.01	2051	3556
Cardiovascular diseases	60	ELT(1)	7	52 631	0.12	7519	
		Chest x-ray, ECG alone	21	55 502	0.35	2643	
		ELT(1) + chest x-ray, ECG	26	108 133	0.43	4159	2921
		ELT(2)	27	149 394	0.45	5533	4838
Metabolic/endocrine diseases	25	ELT(1)	2	22 851	0.08	11 426	
		ELT(1) + ALP, total cholesterol, glucose	13	23 851	0.52	1835	91
		ELT(2)	17	55 477	0.68	3263	2175
Liver/pancreatobiliary diseases	33	ELT(1)	6	30 758	0.18	5126	
		AST, ALT alone	27	11 253	0.82	417	
		ELT(1) + AST, ALT	32	31 060	0.97	971	12
		ELT(1) + AST, ALT, ALP, GGT, cholinesterase, protein fraction	41	37 488	1.24	914	192
		ELT(2)	43	63 706	1.3	1482	890
Renal/urinary tract diseases	9	ELT(1)	10	8515	1.11	852	
		ELT(1) + urine sediment, BUN, creatinine, abdominal x-ray	13	13 909	1.44	1070	1798
		ELT(2)	13	20 022	1.44	1540	3836

[a] TID, tentative initial diagnosis; UR, useful result; LD, lactate dehydrogenase; GGT, γ-glutamyltransferase; BUN, serum urea nitrogen.
[b] Conversion rate for ¥ to US $ is ¥120.00 = US $1.00 (May 1, 1999).

does not refer to the following fundamental issues on the basis of clinical evidence: *(a)* How efficacious is the guideline with regard to clinical effectiveness and performance cost when the ELT is applied to every new outpatient? *(b)* Does the guideline have the same weight in effectiveness and economic efficiency in patients in different disease categories? *(c)* To elicit maximal effectiveness at reasonable cost, which test items should be selected from the ELT(2) panel for a patient with specific symptoms and sign? The above questions arose in part from our preliminary studies, which indicated that the clinical usefulness of the ELT varied depending on disease categories *(2, 18)*. In addition, the limited value of routine laboratory panel testing has been reported previously in the literature *(19)*. Furthermore, in the current trend of cost-effective resource utilization throughout the world *(14, 15, 20–22)*, more careful use of laboratory tests, based on distinct cost-effectiveness, is now consensus in many countries. These were the incentives that we sought to analyze: not only the clinical effectiveness, but also the economic efficiency of the JSCP test panels.

The usefulness of the ELT was not equivalent among common diseases seen in primary care medicine; in fact, there was a large disparity in clinical effectiveness and economic efficiency of the ELT in different disease categories (Table 4). TIDs can be classified into four groups according to clinical effectiveness and economic efficiency of the ELT: *(a)* neurological and other (miscellaneous) disease groups, in which little or no effectiveness of ELT was demonstrated; *(b)* liver/pancreatobiliary, metabolic/endocrine and cardiovascular disease groups, in which the limited effectiveness of the ELT(1) panel was remarkably improved by application of the ELT(2) panel, demonstrating an excellent cost-effectiveness of the ELT(2) panel; *(c)* infectious or inflammatory and renal/urinary tract disease groups, in which the ELT(2) increased clinical effectiveness but decreased cost efficiency (increased cost/UR); and *(d)* hematological and respiratory disease groups or gastrointestinal disease and diagnosis-undetermined groups, in which excellent (hematological and respiratory disease groups) or limited (gastrointestinal disease and diagnosis-undetermined groups) clinical effectiveness of the ELT(1) panel was not demonstrably improved by application of the ELT(2) panel. Our results clearly indicate that the ELT panels are not cost-effective for certain patients, such as those with neurological problems. In fact, a careful history and physical examination would be much more helpful for the establishment of

Fig. 2. Contribution rates of the ELT(1) and ELT(2) items to generation of URs in each disease category.

Filled columns indicate numbers of ELT(1) component tests; *hatched columns* are ELT(2)-specific test items. (*A*), infectious or inflammatory diseases (626 tests contributed to generation of 179 URs in patients with 177 TIDs); (*B*), gastrointestinal diseases (69 tests for 31 URs in 84 TIDs); (*C*), neurological diseases (10 tests for 5 URs in 57 TIDs); (*D*), cardiovascular diseases (35 tests for 27 URs in 60 TIDs); (*E*), metabolic/endocrine diseases (45 tests for 17 URs in 25 TIDs); (*F*), liver/pancreatobiliary diseases (125 tests for 43 URs in 33 TIDs); (*G*), hematological diseases (68 tests for 38 URs in 23 TIDs); (*H*), renal/urinary tract diseases (41 tests for 13 URs in 9 TIDs); (*I*), respiratory diseases (29 tests for 9 URs in 7 TIDs); (*J*), other (miscellaneous) diseases (38 tests for 14 URs in 80 TIDs); (*K*), diagnosis undetermined (51 tests for 28 URs in 78 TIDs). *WBC*, white blood cell; *LD*, lactate dehydrogenase; *A/G ratio*, albumin/globulin ratio; *GGT*, γ-glutamyltransferase; *BUN*, serum urea nitrogen.

clinical diagnosis than would routine laboratory panel testing in the majority of patients in this group; thus, these patients should be forwarded directly to organ-specific tests without application of the ELT. Similarly, the limited effectiveness of ELT(2)-specific test components in patients with gastrointestinal diseases might allow a physician to forward these patients for further diagnostic approaches without consideration of ELT(2) test items. Although there is a well-recognized consensus on important roles for platelet counts and LDCs or chest x-rays in establishing diagnoses of hematological diseases or respiratory diseases, respectively, the ELT(2) panel in the aggregate generated only slight additional effectiveness in these disease groups. This may be attributed to the relatively small number of patients entered in these groups. Movement of the RBC indices back to the ELT(2) panel would improve the effectiveness of the ELT(2) in the hematological disease group.

Excellent (liver/pancreatobiliary and metabolic/endocrine diseases) or fair (infectious or inflammatory, renal/urinary tract and cardiovascular diseases) cost-effectiveness of the ELT(2) panel led to a possibility of establishing more efficient test panels, which yield equivalent clinical effectiveness at a minimal cost increment, for these patient groups by adding certain ELT(2) test items to the ELT(1) basic panel. Taking into account test components largely contributing to UR generation (shown in Fig. 2), we analyzed the cost-effectiveness parameters of redesigned test combinations proposed for these disease groups (Table 5). The best cost-effectiveness was given by a combination of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) with ELT(1) in liver/pancreatobiliary diseases, and clinical effectiveness could be further improved with the incorporation of six automated chemistry tests into ELT(1) (1.24 UR/TID at a cost of ¥914/UR). Although testing of AST and ALT alone without the ELT(1) was reasonably effective (0.82 UR/TID) at a low cost (¥417/UR), this served only to confirm or negate liver diseases and was not informative for possible alternative diseases corresponding to clinical illness or for estimation of the patient's general physical condition. In the metabolic/endocrine disease group, addition of only three chemistry tests to the ELT(1) panel appreciably improved the clinical effectiveness and economic efficiency, with a cost-effectiveness of ¥91/additional UR, although this should take into account the small number of patients in this group and the distribution of patients leaning largely against thyroid diseases and diabetes mellitus. Major contributors to UR generation were chest x-rays and ECGs in cardiovascular diseases; addition of these items to the ELT(1) increased the clinical effectiveness 3.5-fold but reduced costs by less than 50% per UR because of the much higher performance costs for these tests than the automated multichannel analyzer-based test items. Even taking into account that costs were increased as tests were added to obtain adequate clinical effectiveness in infectious or inflammatory and renal/urinary tract disease groups, our findings clearly lead to the conclusion that there are substantial advantages to using selected test panels for the different groups of patients, at least for disease groups mentioned above.

Recently, laboratory testing performed in testing sites outside the main centralized clinical laboratory in a hospital (alternative site or point-of-care testing) has been growing in the United States because of the importance of timely diagnostic results obtained within patient care sites *(23–25)*. The ELT(1) panel with the addition of some common tests from the ELT(2) panel can be applied to new outpatients as point-of-care satellite laboratory testing, either manually or using smaller-sized, automated discrete instruments. The immediate availability of data at the initial clinical evaluation might offer an increased convenience to patients (e.g., fewer return visits to clinics) and lead to a prompt and optimized diagnostic-therapeutic process in new primary care outpatients. Utility of the JSCP panel test system must be elicited in this setting, and in fact, the guideline recommends that the ELT(1) panel be performed in parallel with a history and physical examination *(1)*. The integrated patient-physician-laboratory relationship based on patient-focused principles is an ultimate goal of the JSCP guideline. Cost-benefit evaluation of ELT panels in this setting should be the next project undertaken in this research.

Another social and economic aspect of ELT panel testing is the effect on cost-containment for diagnostic tests. Recent advances in laboratory technology as well as changes in the healthcare system and reimbursement practices in the United States have stimulated increased use of diagnostic tests in hospital outpatient facilities or nonhospital settings such as physicians' office laboratories during the past two decades *(14, 26–28)*. However, payment on a cost-reimbursed basis for hospital outpatient and office-based laboratory testing has raised issues of possible overuse of diagnostic tests because of financial incentives to hospital administrators and practitioners *(29)*. Unlike the United States, in which cost containment has been achieved through government policies or managed care, the ELT guidelines themselves aim to constrain test volumes and unnecessary spending.

In conclusion, this study provides some insights for cost-effective utilization of common diagnostic tests in primary care medicine. Although the ELT panels offer much relevant clinical information, the wide disparity of effectiveness of the ELT shown in different patient groups does not match the JSCP's recommendation for their routine use for all new outpatients. Furthermore, our finding that clinical effectiveness of the ELT(1) basic panel can be enhanced and made cost-efficient by adding some specified ELT(2) test items in selected patient groups certainly indicates the necessity for selective test combination corresponding to each patient group. We proposed such redesigned panels with distinct cost-effectiveness for testing new outpatients in this study.

This study was supported in part by grants from the Clinical Pathology Research Foundation of Japan and from the Pfizer Health Research Foundation. We are grateful to Yasumasa Kajihara, Reishi Izumi, Katsunori Koguchi, Mitsugi Okura, and Kuniki Takamatsu at Kawasaki Medical School, Kurashiki, Japan for providing cost data for x-ray tests and laboratory tests. We also thank Hiroyuki Kobayashi, Nobuo Kugai, and Hirokazu Matsuta at the National Defense Medical College, Tokorozawa, Japan for their assistance in collecting clinical data.

References

1. Hashimoto N. Essential laboratory tests: a proposal. In: Subcommittee of the Uses of Clinical Laboratory Tests in Daily Primary Medical Care, the Japan Society of Clinical Pathology, ed. The uses of clinical laboratory tests in daily primary medical care, 1st ed. Tokyo, Japan: The Japan Society of Clinical Pathology, 1989: 1–16.
2. Takemura Y, Hayashi K, Kugai N, Sekiguchi S. Usefulness of "Essential Laboratory Tests" for the establishment of the initial diagnosis in new outpatients [Japanese, English abstract]. Jpn J Clin Pathol 1992;40:55–60.
3. Lehmann C, Leiken AM. Influence of selective vs panel chemistry tests on cost and diagnostic time. Am J Med Technol 1982;48: 833–6.
4. Cebul RD, Beck JR. Biochemical profiles: applications in ambulatory screening and preadmission testing of adults. In: Sox HC Jr, ed. Common diagnostic tests: use and interpretation, 2nd ed. Philadelphia, PA: American College of Physicians, 1990:344–66.
5. Lehmann C, Leiken A. Cost of laboratory ordering strategies. Lab Med 1985;15:759–60.
6. Golden WE, Pappas AA, Lavender RC. Financial unbundling reduces outpatient laboratory use. Arch Intern Med 1987;147: 1045–8.
7. Tierney WM, Miller ME, McDonald CJ. The effect on test ordering of informing physicians of the charges for outpatient diagnostic tests. N Engl J Med 1990;322:1499–504.
8. Tierney WM, McDonald CJ, Hui SL, Martin DK. Computer predictions of abnormal test results: effects on outpatient testing. JAMA 1988;259:1194–8.
9. Grossman RM. A review of physician cost-containment strategies for laboratory testing. Med Care 1983;21:783–802.
10. Shapiro MF, Hatch RL, Greenfield S. Cost containment and labor-intensive tests: the case of the leukocyte differential count. JAMA 1984;252:231–4.
11. Gortmaker SL, Bickford AF, Mathewson HO, Dumbaugh K, Tirrell PC. A successful experiment to reduce unnecessary laboratory use in a community hospital. Med Care 1988;26:631–42.
12. Solomon DH, Hashimoto H, Daltroy L, Liang MH. Techniques to improve physicians' use of diagnostic tests: a new conceptual framework. JAMA 1998;280:2020–7.
13. van Walraven C, Goel V, Chan B. Effect of population-based interventions on laboratory utilization. JAMA 1998;280:2028–33.
14. Takemura Y, Beck JR. The effects of a fixed-fee reimbursement system introduced by the federal government on laboratory testing in the United States. Jpn J Clin Pathol 1999;47:1–10.
15. Kricka LJ, Parsons D, Coolen RB. Healthcare in the United States and the practice of laboratory medicine. Clin Chim Acta 1997; 267:5–32.
16. Root CB. Medicare coding and reimbursement for clinical laboratory services. Clin Chem 1998;44:1713–27.
17. Takemura Y, Kobayashi H, Kugai N, Sekiguchi S. The results of the "Essential Laboratory Tests" applied to new outpatients—re-evaluation of diagnostic efficiencies of the test items. Jpn J Clin Pathol 1996;44:555–63.
18. Hayashi K, Takemura Y, Hanba Y, Mori S, Kugai N, Sekiguchi S. Laboratory tests in primary care medicine: pre-clinical, ambulatory screening test system on the basis of the patient's chief complaints in the initial diagnosis making [Japanese, English abstract]. Jpn J Clin Pathol 1993;41:767–72.
19. Sox HC Jr, ed. Common diagnostic tests: use and interpretation, 2nd ed. Philadelphia, PA: American College of Physicians, 1990: 441pp.
20. Conn RB, Snyder JW. Changes in the American health care system: crisis in the clinical laboratory. Clin Chim Acta 1997;267: 33–49.
21. Valdiguié PM, de Graeve JS, Guerre JP. Laboratory medicine in France: a jeopardized situation. Clin Chim Acta 1997;267:51–62.
22. Bais R, Wyndham LE. The changing face of pathology—an Australian perspective. Clin Chim Acta 1997;267:63–85.
23. Cousar JB, Peters TH. Laboratories in patient-centered units. Clin Lab Med 1994;14:525–38.
24. Handorf CR, McLendon WW. Opportunities and challenges of laboratory testing at alternative sites. JAMA 1995;274:1308–9.
25. Kost GJ. Guidelines for point-of-care testing: improving patient outcomes. Am J Clin Pathol 1995;104(Suppl 1):S111–27.
26. Crawley R, Belsey R, Brock D, Baer DM. Regulation of physicians' office laboratories: the Idaho experience. JAMA 1986;255:374–82.
27. Helbing C, Latta VB, Keene RE. Hospital outpatient services under Medicare, 1987. Health Care Financing Rev 1990;11:147–58.
28. Benge H, Bodor GS, Younger WA, Parl FF. Impact of managed care on the economics of laboratory operation in an academic medical center. Arch Pathol Lab Med 1997;121:689–94.
29. Schroeder SA, Showstack JA. Financial incentives to perform medical procedures and laboratory tests: illustrative models of office practice. Med Care 1978;16:289–98.