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ORIGINAL ARTICLE

Assessing the extent of evidence-based therapeutic intervention in a university based family medicine outpatient clinic

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Abstract

***Aim*:** The purpose of the present study was to estimate the proportion of therapeutic interventions which are supported by scientific evidence in a university based family medicine outpatient clinic.

***Methods*:** A retrospective review of patient medical records was done to assess the primary diagnosis and treatment option. A Medline review from 1966 to 2001, standard textbooks and evidence-based medicine online databases including American College of Physician journal club and Cochrane database of systematic reviews were searched to assess the evidence for the chosen intervention. The evidence was then classified as one of three categories developed by the Oxford Center for Evidence-Based Medicine: (i) evidence from randomized controlled trials (RCT); (ii) convicing non experimental evidence; (iii) and interventions without substantial evidence.

***Results*:** Of the 356 primary diagnosis and treatment pairs, 59.6% were supported by evidence from at least one RCT. A total of 19.4% were supported by convincing non experimental evidence, and 75 (21%) were classified as intervention without substantial evidence. As a result, 79.0% of interventions (281/356) met our criteria to be evidenced-based.

***Conclusions*:** Approximately 60% of the interventions in a university based family medicine outpatient practice were supported by evidence from at least one RCT. Although this result is limited to one tertiary hospital outpatient care setting, it could serve as a baseline reference for future assessments of evidence-based family practice.

Key words: evidence-based, family medicine outpatient practice, randomized controlled trials.

Introduction

Despite remarkable advances in biomedical science and health care, there is still a pessimistic view that only a small proportion of medical interventions have a solid scientific foundation. Some studies suggest only 10–20% of medical practices are supported by sound scientific evidence.[1,2]

Previous studies, however, suggested the majority of general practice is based on objective evidence. Ellis *et al*. found 82% of interventions in one inpatient care setting were evidence-based.[2] A further study by Gill *et al*. also reported 81% of treatments were evidence-based in a suburban training general practice.[3] Similar results were found in the surgical field. In an inpatient general surgery, 95% of patients receive treatment based on satisfactory evidence, but the proportion of surgical treatments supported by randomized controlled trial (RCT) evidence was much smaller than that found in general medicine.[4]

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In recent years there has been growing interest in the development of evidence-based medicine, as reflected by the Cochrane Collaboration Study, the publication of a journal such as *Evidence-Based Medicine*, and the numerous papers published on this subject. In Korea, evidence-based medicine is in the early stages. No published studies assessed the extent of medical interventions supported by sound scientific evidence in clinical settings.

The purpose of the present study was to estimate the proportion of therapeutic interventions that are supported by scientific evidence in a university based family medicine outpatient clinic.

Methods

During the week of 1 May to 7 May in 2000 all patient consultations at a university based family medicine outpatient clinic were reviewed by retrospective analysis of medical records. For each consultation, two authors independently designated the primary diagnosis and therapeutic intervention. The primary diagnosis was defined using International Classification of Primary Care (ICPC).[5] The disease or conditions confirmed by diagnostic tests were classified by the International Classification of Disease (ICD-10). If there were several diagnoses, the main one for the patient's visit to the clinic was selected as the primary diagnosis. The primary intervention was treatment that represented the most important attempt to cure, alleviate, and care for the patient in respect of his or her primary diagnosis.

Study design

A Medline search from 1966 to 2001, the American College of Physician journal club and the Cochrane database of systematic reviews were searched for RCT and meta analyses. The filters developed by McKibbon was used to retrieve as much information as possible relevant to the subject from published studies.[6] The search was restricted to published English-language medical reports.

Each treatment was assigned to one of the following three categories developed by Ellis *et al*.[2]

- Category 1, evidence was presumed to be of high quality and was established in one or more RCT or systematic reviews of RCT
- Category 2 was defined by convincing non experimental evidence. This included interventions whose face validity is so great that randomized trials were judged by the research team and consultant to be both unnecessary and, if a placebo would have been involved, unethical. Evidence supported by textbooks was also classified to category 2.
- Category 3, interventions without substantial evidence, which included an intervention in common use but meeting neither the above two criteria

For Category 1 evidence, the strength of evidence was evaluated using the grading system proposed by Shekelle *et al*.[7] This system graded strength of evidence by hierarchy of research design (Table 1).

Table 1 Strength of evidence for treatment decision by Shekelle *et al*.[7]

Category of evidence	
IA	Evidence from meta analysis of RCT
IB	Evidence from at least one RCT
IIA	Evidence from at least one controlled study without randomization
IIB	Evidence from at least one other type or quasi experimental study
III	Evidence from non experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or opinions of respected authorities or both

RCT, randomized controlled trial.

Results

During the study week, a total of 307 patients visited the clinic. After excluding referrals (12 patients) and visits with only diagnostic interventions (10 patients), 285 medical records were reviewed. Among the total consultations, 67% were treated by more than one intervention for each primary diagnosis. Although searching evidence of combined treatment effect is ideal, clinical trials usually focus on the effect of one therapeutic intervention. Therefore, we analyzed the data by combining each primary diagnosis with a single primary treatment to form a diagnostic-treatment pair. As a result, a total 356 primary diagnosis-treatment pairs were retrieved (Table 2). Out of this, 90.3% were drug treatments and the rest were non pharmacologic interventions including observation, exercise, diet therapy, smoking cessation and alcohol abstinence.

A total of 79% of primary diagnosis-treatment pairs (281/356) were judged by our criteria to have received evidence-based interventions (Table 3). Table 4 shows that 59.6% of the primary diagnosis and treatment pairs were based on one or more RCT. Fifty pairs (23.6%) were supported by meta analysis of RCT (evidence from meta analysis of RCT (IA)), and 76.4% were

Table 2 Characteristics of primary diagnosis-primary treatment pairs

Primary diagnosis	ICPC or ICD-10	Number of pair presentations
Acute bronchitis	R73	3
Allergic conjunctivitis	F71	1
Angina pectoris	K74	2
Anxiety disorder/anxiety state	P74	4
Asthma	R96	5
Atopic dermatitis/eczema	S87	3
Bronhiectasis (asymptomatic)	R91	1
Chronic bronchitis/bronchiectasis	R91	4
Chronic bronchitis/bronchiectasis	R91	2
Chronic gastritis, *Helicobacter pylori* infection proved by biopsy	K29.5	2
Chronic hepatitis B	B18.1†	6
Constipation	D12	10
Cough	R05	1
Diabetes non insulin dependent	T90	11
Diarrhea	D11	5
Disease of the esophagus	D84	14
Disorders of stomach function/gastritis	D87	15
Disturbance of sleep/insomnia	P06	1
Dyspepsia/indigestion	D07	29
Emphysema/chronic obstructive disorder	R95	8
Fatty liver	K70.1†	6
Feeling depressed	P03	7
Gastric ulcer	K25.7	1
Hay fever, allergic rhinitis	R79	2
Headache	N01	8
Hip symptoms/complaints	L13	1
Hyperlipidemia	T93	16
Hyperthyroidism/thyrotoxicosis	T85	5
Hyperventilation	R93	4
Hypothyroidism/myxedema	T86	3
Infectious conjunctivitis (viral/bacterial)	F70	10
Iron deficiency anemia	B80	2
Irritable bowel syndrome	D93	5
Jaundice (due to cholangiocarcinoma)	D13	2
Low back symptoms/complaints without radiation	L03	7
NIDDM with neurologic complication	E11.4	6
Obesity	T82	7
Osteoarthritis of knee	L90	6
Osteoporosis	L95	5
Other osteoarthritis	L91	1
Pain, general/multiple sites (cancer)	A01	4
Parkinson disease	N87	1
Sneezing/nasal congestion	R07	1
Somatization disorder	F45.1†	15
Stroke/cerebrovascular accident	K90	1
Symptoms/complications potency	Y07	1
Tinea ungiuum	B35.1	1
Uncompicated hypertension	K86	95
Upper respiratory infection	R74	2
Upper respiratory infection	R74	1
Vertigo/dizziness	N17	3
Total number of primary diagnosis and treatment pairs		356

†Primary diagnosis classified by International Classification of Disease (ICD-10). ICPC, International Classification of Primary Care; NIDDM, Non-insulin dependent diabetes mellitus.

Table 3 The summary of result

Type of evidence	Primary diagnosis-primary treatment pair	
	Numbers	Percent
Good evidence		
Evidence from randomized controlled trials	212	59.6
Convincing nonexperimental evidence	69	19.4
Subtotal	281	79.0
Intervention without substantial evidence	75	21.0
Total	356	100.0

supported by evidence from at least one RCT (IB). Neither RCT nor systematic reviews were found for 69 pairs (19.4%) but these were supported by category 2 (convincing non experimental) evidence (Table 5). Twenty-one percent of the total pairs were classified as specific symptomatic and supportive care without substantial evidence, placing them into category 3 (Table 6).

Discussion

Medical practice has been criticized as not being based on solid evidence, with doubt that primary care practice is less evidence-based than other practice settings. In Korea, however, there are no published studies that examine the extent of evidence-based practice in any clinical settings.

The present study has shown that approximately 80% of interventions within a university based, tertiary hospital family medicine outpatient clinic were based on evidence. This is comparable with the findings from previous studies dealing with general practice.[2,3] Another study for primary care centers serving rural areas reported somewhat lower proportion of evidence-based interventions (42% of interventions were supported by substantial evidence).[8] In the surgical field the proportion of treatments supported by RCT was much smaller than that found in general medicine.[4,9] One of the reasons for this difference can be explained by difficulties encountered in carrying out surgical RCT.

As in other health care specialties, evidence-based practice is beginning to have an impact on the philosophy and workings of primary care. Some practicing clinicians, however, may be doubtful of its relevance to their everyday work, and question whether general practitioners and other members of the primary health care team can realistically adopt a new approach to clinical decision-making, at a time of such high workload and competing priorities. However, this and previous studies suggest that a considerable proportion of primary care related practice has already been evidence-based.

There are a few problems regarding the generalizability of our result. First, the study sample selected only consists of patients encountered during one week of a certain month which may not represent all conditions encountered from the practice population. Nevertheless, we choose a certain period of time, because the characteristics of patients' encounters and number of patients in our clinic are not so variable according to month and seasons. Second, the result of the present study was derived from a tertiary hospital outpatient clinic. Therefore, it cannot reflect the present status of primary practice throughout Korea. Third, the nature of a retrospective study makes it almost impossible to determine whether every intervention was most appropriate for a particular patient in his or her specific physical and psychological situation at that time. There also could be a bias toward overestimations, as interventions supported by solid evidence may well be more likely to be recorded.

Other shortcomings may relate to limited databases for evidence searches. By limiting our search to a database such as Medline, we may fail to find all the evidence available. One possible concern was how we should deal with RCT that are apparently outdated by evidence that another treatment is available, or evidence from other sources suggesting later that a treatment can be harmful. This disparity could be significant because of the previously mentioned rapid growth of reported RCT. However, the primary purpose of the present study was not to evaluate how consciously evidence-based medicine was practised, but to determine to what degree the therapeutic interventions in one family practice setting were supported by scientific evidence. In addition, our literature search may not be perfect. Some 'convincing non experimental' interventions may have been subjected to randomized trials that our search missed and deserve to be promoted to Table 4 (if proved effective) or banished from our list if proven worthless or harmful.

In addition, although using the primary diagnosis-primary treatment pair reduced the complexity of practice, it also lost some of its reality. Clinical problems have many facets, hence diagnoses and interventions are often multiple. The diagnosis-intervention

Table 4 Evidence from randomized controlled trials

Level of evidence	Primary diagnosis	ICPC code	ICD-10 code	Primary treatment	Number of pairs	Reference
IA	Asthma	R96		prednisone	1	Mash B, Bheekie A, Jones PW. Inhaled vs. oral steroids for adults with chronic asthma. *Cochrane Database Syst. Rev.* 2000; **2**: CD002160.
IA	Diabetes non-insulin dependent	T90		metformin	1	Johansen K. Efficacy of metformin in the treatment of NIDDM. Meta-analysis. *Diabetes Care* 1999; **22**: 33–7.
IA	Diarrhea	D11		lactobacillus	2	Van Niel CW, Feudtner C, Garrison MM, Christakis DA. Lactobacillus therapy for acute infectious diarrhea in children: a meta-analysis. *Pediatrics* 2002; **109**: 678–84.
IA	Gastric ulcer, *Helicobacter pylori* infection proved by biopsy		K25.7	triple therapy (lansoprazol, amoxicillin, clarith romycin)	1	Gisbert JP, Gonzalez L, Calvet X *et al*. Proton pump inhibitor, clarithromycin and either amoxycillin or nitroimidazole: a meta-analysis of eradication of *Helicobacter pylori*. *Alim. Pharmacol. Therap.* 2000; **14**: 1319–28.
IA	Hyperlipidemia	T93		lovastatin	1	Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. *BMJ* 2000; **321**: 983–6.
IA	Hyperlipidemia	T93		pravastatin	3	Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary revention of coronary heart disease: meta-analysis of randomised trials. *BMJ* 2000; **321**: 983–6.
IA	Hyperlipidemia	T93		simvastatin	1	Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. *BMJ* 2000; **321**: 983–6.
IA	Low back symptoms/ complaints without radiation	L03		etodolac	2	Tulder MW van, Scholten RJPM, Koes BW, Deyo RA. Non-steroidal anti-inflammatory drugs for low back pain (Cochrane Review). In: The Cochrane Library, 4, 2000.
IA	Low back symptoms/ complaints without radiation	L03		ketoprofen plaster	2	Moore RA, Tramer MR, Carroll D, Wiffen PJ, McQuay HJ. Quantitative systematic review of topically applied non-steroidal anti-inflammatory drugs. *BMJ* 1998; **316**: 1059.
IA	Type 11 Diabetes with neurologic complication		E11.4	amitriptyline	1	Collins SL, Moore RA, McQuay HJ, Wiffen P. Antidepressants and anticonvulsants for diabetic neuropathy and postherpetic neuralgia: a quantitative systematic review. *J. Pain Symptom Manage*. 2000; **20**: 449–58.
IA	Osteoarthritis of knee	L90		ketoprofen plaster	2	Moore RA, Tramer MR, Carroll D, Wiffen PJ, McQuay HJ. Quantitative systematic review of topically applied non-steroidal anti-inflammatory drugs. *BMJ* 1998; **316**: 1059.
IA	Osteoporosis	L95		calcium gluconate	2	Cumming RG, Nevitt MC. Calcium for prevention of osteoporotic fractures in postmenopausal women. *Bone Miner. Res*. 1997; **9**: 1321–9.

Table 4 *Continued*

Level of evidence	Primary diagnosis	ICPC code	ICD-10 code	Primary treatment	Number of pairs	Reference
IA	Osteoporosis	L95		unopposed estrogen	2	Torgerson DJ, Bell-Syer SE. Hormone replacement therapy and prevention of non-vertebral fractures: a meta-analysis of randomized trials. *JAMA* 2001; **285**: 2891–7.
IA	Osteoporosis	L95		estrogen + medroxyprogesterone acetate	1	Torgerson DJ, Bell-Syer SE. Hormone replacement therapy and prevention of non-vertebral fractures: a meta-analysis of randomized trials. *JAMA* 2001; **285**: 2891–7.
IA	Dyspepsia/indigestion	D07		cimetidine	4	Allescher HD, Bockenhoff A, Knapp G, Wienbeck M, Hartung J. Treatment of non-ulcer dyspepsia: a meta-analysis of placebo-controlled prospective studies. *Scand. J. Gastroenterol.* 2001; **36**: 934–41
IA	Pain, general/multiple sites (cancer)	A01		myprodol	4	Eisenberg E, Berkey CS, Carr DB, Mosteller F, Chalmers TC. Efficacy and safety of non-steroidal anti-inflammatory drugs for cancer pain: a meta-analysis. *J. Clin. Oncol.* 1994; **12**: 2756–65.
IA	Parkinson's disease/ paralysis agitans	N87		bromocriptine	1	Ramaker C, Hilten JJ van. Bromocriptine vs. levodopa in early Parkinson's disease (Cochrane Review). In: The Cochrane Library, Issue 4 2002.
IA	Uncompicated hypertension	K86		amlodipine	19	Kloner RA, Vetrovec GW, Materson BJ, Levenstein M. Safety of long-acting dihydropyridine calcium channel blockers in hypertensive patients. *Am. J. Cardiol.* 1998; **81**: 163–9.
IB	Sneezing/nasal congestion	R07		azelastine	1	Grossman J, Halverson PC, Meltzer EO *et al.* Double-blind assessment of azelastine in the treatment of perennial allergic rhinitis. *Ann. Allergy* 1994; **73**: 141–6.
IB	Allergic conjunctivitis	F71		sodium cromoglycate ophthalmic solution	1	Leino M, Ennevaara K, Latvala AL *et al.* Double-blind group comparative study of 2% nedocromil sodium eye drops with 2% sodium cromoglycate and placebo eye drops in the treatment of seasonal allergic conjunctivitis. *Clin. Exper. Allergy* 1992; **22**: 929–32.
IB	Angina pectoris	K74		isosorbid-mononitrate	1	Chrysant SG, Glasser SP, Bittar N *et al.* Efficacy and safety of extended-release isosorbide mononitrate for stable effort angina pectoris. *Am. J. Card.* 1993; **72**: 1249–56.
IB	Angina pectoris	K74		ticlopidine	1	Balsano F, Rizzon P, Violi F *et al.* Antiplatelet treatment with ticlopidine in unstable angina. A controlled multicenter clinical trial. The Studio della Ticlopidina nell'Angina Instabile Group. *Circulation* 1990; **82**: 17–26.
IB	Anxiety disorder/ anxiety state	P74		lorazepam	2	Laakmann G, Schule C, Lorkowski G, Baghai T, Kuhn K, Ehrentraut S. Buspirone and lorazepam in the treatment of generalized anxiety disorder in outpatients. *Psychopharmacol.* 1998; **136**: 357–66.

IB	Anxiety disorder/ anxiety state	P74		sertraline	1	Thase ME, Fava M, Halbreich U *et al*. A placebo-controlled, randomized clinical trial comparing sertraline and imipramine for the treatment of dysthymia. *Arch. Gen. Psychiatry* 1996; **53**: 777–84.
IB	Asthma	R96		fenoterol	3	Richter B, Bender R, Berger M. Effects of on-demand beta2-agonist inhalation in moderate-to-severe asthma. A randomized controlled trial. *J. Intern. Med.* 2000; **247**: 657–66.
IB	Asthma	R96		theophylline	1	Goldstein MF, Chervinsky P. Efficacy and safety of doxofylline compared to theophylline in chronic reversible asthma – a double-blind randomized placebo-controlled multicentre clinical trial. *Med. Sci. Monitor* 2002; **8**: CR297–304.
IB	Atopic dermatitis/ eczema	S87		hydroxyzine	1	Monroe EW. Relative efficacy and safety of loratadine, hydroxyzine, and placebo in chronic idiopathic urticaria and atopic dermatitis. *Clin. Therap.* 1992; **14**: 17–21.
IB	Atopic dermatitis/ eczema	S87		mequitazine	1	Laugier P, Orusco M. Comparative trial of an antihistamine, mequitazine, and placebo. *Curr. Med. Res. Opin.* 1978; **5**: 371–5.
IB	Atopic dermatitis/ eczema	S87		azelastine	1	Henz BM, Metzenauer P, O'Keefe E, Zuberbier T. Differential effects of new-generation H1-receptor antagonists in pruritic dermatoses. *Allergy* 1998; **53**: 180–3.
IB	Chronic gastritis, *Helicobacter pylori* infection proved by biopsy		K29.5	Triple therapy*	2	Svoboda P, Kantorova I, Ochmann J, Doubek J, Kozumplik L, Marsova J. Pantoprazole-based dual and triple therapy for the eradication of Helicobacter pylori infection: a randomized controlled trial. *Hepato-Gastroenterology* 1997; **44**: 886–90.
IB	Constipation	D12		psyllium	1	McRorie JW, Daggy BP, Morel JG, Diersing PS, Miner PB, Robinson M. Psyllium is superior to docusate sodium for treatment of chronic constipation. *Alim. Pharmacol. Therap.* 1998; **12**: 491–7.
IB	Constipation	D12		lactulose	3	Bass P, Dennis S. The laxative effects of lactulose in normal and constipated subjects. *J. Clin. Gastroenterol.* 1981; **3**: 23–8.
IB	Diabetes non-insulin dependent	T90		acarbose	1	Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M. STOP-NIDDM Trail Research Group. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet* 2002; **359**: 2072–7.
IB	Diabetes non-insulin dependent	T90		glimepride	1	Schade DS, Jovanovic L, Schneider J. A placebo-controlled, randomized study of glimepiride in patients with type 2 diabetes mellitus for whom diet therapy is unsuccessful. *J. Clin. Pharmacol.* 1998; **38**: 636–41.
IB	Diabetes non-insulin dependent	T90		insulin	5	Turner R, Cull C, Holman R. United Kingdom Prospective Diabetes Study 17: a 9-year update of a randomized, controlled trial on the effect of improved metabolic control on complications in non-insulin-dependent diabetes mellitus. *Ann. Intern. Med.* 1996; **124**: 136–45.

Table 4 *Continued*

Level of evidence	Primary diagnosis	ICPC code	ICD-10 code	Primary treatment	Number of pairs	Reference
IB	Disease of the esophagus	D84		pantoprazol	1	Richter JE, Bochenek W. Oral pantoprazole for erosive esophagitis: a placebo-controlled, randomized clinical trial. Pantoprazole US GERD Study Group. *Am. J. Gastroenterol.* 2000; **95**: 3071–80.
IB	Disease of the esophagus	D84		cimetidine	1	Wesdorp E, Bartelsman J, Pape K, Dekker W, Tytgat GN. Oral cimetidine in reflux esophagitis: a double blind controlled trial. *Gastroenterol.* 1978; **74**: 821–4.
IB	Disease of the esophagus	D84		famotidine	3	Simon TJ, Berenson MM, Berlin RG, Snapinn S, Cagliola A. Randomized, placebo-controlled comparison of famotidine 20 mg b.d. or 40 mg b.d. in patients with erosive oesophagitis. *Alim. Pharmacol. Therap.* 1994; **8**: 71–9.
IB	Disorders of the stomach function/ gastritis	D87		alumium Magnesium silicate	3	Weberg R, Berstad A. Low-dose antacids and pirenzepine in the treatment of patients with non-ulcer dyspepsia and erosive prepyloric changes. A randomized, double-blind, placebo-controlled trial. *Scand. J. Gastroenterol.* 1988; **23**: 237–43.
IB	Disorders of the stomach function/ gastritis	D87		sucralfate	1	Guslandi M. Comparison of sucralfate and ranitidine in the treatment of chronic nonerosive gastritis. A randomized, multicenter trial. *Am. J. Med.* 1989; **86**: 45–8.
IB	Disorders of the stomach function/ gastritis	D87		cimetidine	1	Nesland AA, Berstad A. Effect of cimetidine in patients with non-ulcer dyspepsia and erosive prepyloric changes. *Scand. J. Gastroenterol.* 1985; **20**: 629–35.
IB	Dyspepsia/indigestion	D07		metoclopramide	1	Dumitrascu DL, Ungureanu O, Verzea D, Pascu O. The effect of metoclopramide on antral emptying of a semisolid meal in patients with functional dyspepsia. A randomized placebo controlled sonographic study. *Roman. J. Inter. Med.* 1998; **36**: 97–104.
IB	Emphysema/chronic obstructive pulmonary disease	R95		theophylline	1	Karpel JP, Kotch A, Zinny M, Pesin J, Alleyne W. A comparison of inhaled ipratropium, oral theophylline plus inhaled beta-agonist, and the combination of all three in patients with COPD. *Chest.* 1994; **105**: 1089–94.
IB	Emphysema/chronic obstructive pulmonary disease	R95		terbutaline	1	Silins RA, Marlin GE. Evaluation of domiciliary treatment with terbutaline by wet nebulization in patients with chronic bronchitis and emphysema. *Aust. NZ J. Med.* 1985; **15**: 230–4.
IB	Feeling depressed	P03		alprazolam	2	Laakman G, Faltermaier-Temizel M, Bossert-Zaudig S, Baghai T, Lorkowski G. Treatment of depressive outpatients with lorazepam, alprazolam, amytriptyline and placebo. *Psychopharmacologia* 1995; **120**: 109–15.

IB	Feeling depressed	P03	amitriptyline	1	Laakman G, Faltermaier-Temizel M, Bossert-Zaudig S, Baghai T, Lorkowski G. Treatment of depressive outpatients with lorazepam, alprazolam, amytriptyline and placebo. *Psychopharmacologia* 1995; **120**: 109–15.
IB	Feeling depressed	P03	etizolam	1	Casacchia M, Bolino F, Ecari U. Etizolam in the treatment of generalized anxiety disorder: a double-blind study vs. placebo. *Curr. Med. Res. Opin.* 1990; **12**: 215–23.
IB	Feeling depressed	P03	fluoxetine	1	Vanelle JM, Attar-Levy D, Poirier MF, Bouhassira M, Blin P, Olie JP. Controlled efficacy study of fluoxetine in dysthymia. *Brit. J. Psych.* 1997; **170**: 345–50.
IB	Feeling depressed	P03	paroxetine	1	Feighner JP, Boyer WF. Paroxetine in the treatment of depression: a comparison with imipramine and placebo. *J. Clin. Psych.* 1992; **53**: 44–7.
IB	Hay fever, allergic rhinitis	R79	cetirizine	1	Nunes C, Ladeira S. Double-blind study of cetirizine and loratadine vs. placebo in patients with allergic rhinitis. *J. Invest. Allergol. Clin. Immunol.* 2000; **10**: 20–3.
IB	Hay fever, allergic rhinitis	R79	triamcinolone nasal spray	1	Condemi J, Schulz R, Lim J. Triamcinolone acetonide aqueous nasal spray vs. loratadine in seasonal allergic rhinitis: efficacy and quality of life. *Ann. Allergy, Asthma, Immunol.* 2000; **84**: 533–8.
IB	Headache	N01	amitriptyline	1	Holroyd KA, O'Donnell FJ, Stensland M, Lipchik GL, Cordingley GE, Carlson BW. Management of chronic tension-type headache with tricyclic antidepressant medication, stress management therapy, and their combination: a randomized controlled trial. *JAMA* 2001; **285**: 2208–15.
IB	Headache	N01	cafergot	1	Friedman AP, Di Serio FJ, Hwang DS. Symptomatic relief of migraine: multicenter comparison of Cafergot P-B, Cafergot, and placebo. *Clin. Ther.* 1989; **11**: 170–82.
IB	Headache	N01	paroxetine	1	Langemark M, Olesen J. Sulpiride and paroxetine in the treatment of chronic tension-type headache. An explanatory double-blind trial. *Headache* 1994; **34**: 20–4.
IB	Hyperlipidemia	T93	gemfibrozil	4	Insua A, Massari F, Rodriguez Moncalvo JJ, Ruben Zanchetta J, Insua AM. Fenofibrate of gemfibrozil for treatment of types IIa and IIb primary hyperlipoproteinemia: a randomized, double-blind, crossover study. *Endocrine Practice* 2002; **8**: 96–101.
IB	Hyperlipidemia	T93	fenofibrate	1	Goldberg AC, Schonfeld G, Feldman EB *et al.* Fenofibrate for the treatment of type IV and V hyperlipoproteinemias: a double-blind, placebo-controlled multicenter US study. *Clin. Therap.* 1989; **11**: 69–83.

Table 4 *Continued*

Level of evidence	Primary diagnosis	ICPC code	ICD-10 code	Primary treatment	Number of pairs	Reference
IB	Hyperthyroidism/ thyrotoxicosis	T85		propranolol	2	Henderson JM, Portmann L, Van Melle G, Haller E, Ghika JA. Propranolol as an adjunct therapy for hyperthyroid tremor. *Euro. Neurol.* 1997; **37**: 182–5.
IB	Hyperthyroidism/ thyrotoxicosis	T85		propylthiouracil	3	Kallner G, Vitols S, Ljunggren JG. Comparison of standardized initial doses of two antithyroid drugs in the treatment of Graves' disease. *J. Inter. Med.* 1996; **239**: 525–9.
IB	Infectious conjunctivitis (viral/bacteral)	F70		fluorometholone ophthalmic solution	2	Leibowitz HM, Hyndiuk RA, Lindsey C, Rosenthal AL. Fluorometholone acetate: clinical evaluation in the treatment of external ocular inflammation. *Ann. Ophthalmol.* 1984; **16**: 1110–5.
IB	Irritable bowel syndrome	D93		lactobacillus	1	Halpern GM, Prindiville T, Blankenburg M, Hsia T, Gershwin ME. Treatment of irritable bowel syndrome with Lacteol Fort: a randomized, double-blind, cross-over trial. *Am. J. Gastroenterol.* 1996; **91**: 1579–85.
IB	Irritable bowel syndrome	D93		tiropamide	1	Galeone M, Stock F, Moise G, Cacioli D, Benazzi E, Riva A. Clinical and instrumental evaluation by multiple colonic manometry of tiropramide, trimebutine and octylonium bromide in the irritable colon: II. Repeated oral administration. *Pharmatherapeutica.* 1986; **4**: 496–509.
IB	Irritable bowel syndrome	D93		amitriptyline	1	Rajagopalan M, Kurian G, John J. Symptom relief with amitriptyline in the irritable bowel syndrome. *J. Gastroenterol. Hepatol.* 1998; **13**: 738–41.
IB	Low back symptoms/ complaints without radiation	L03		thiocolchicoside	2	Marcel C, Rezvani Y, Revel M. Evaluation of thiocolchicoside as monotherapy in low back pain. Results of a randomized study vs. placebo. *Presse Medicale* 1990; **19**: 1133–6.
IB	Low back symptoms/ complaints without radiation	L03		piroxicam	1	Szpalski M, Hayez JP. Objective functional assessment of the efficacy of tenoxicam in the treatment of acute low back pain. A double-blind placebo-controlled study. *Brit. J. Rheumatol.* 1994; **33**: 74–8.
IB	NIDDM with neurologic complication		E11.4	carbamazepine	1	Gomez-Perez FJ, Choza R, Rios JM, Reza A, Huerta E, Aguilar CA, Rull JA. Nortriptyline-fluphenazine vs. carbamazepine in the symptomatic treatment of diabetic neuropathy. *Arch. Med. Rese.* 1996; **27**: 525–9.
IB	Obesity	T82		fluoxetine	1	Goldstein DJ, Rampey AH Jr, Enas GG, Potvin JH, Fludzinski LA, Levine LR. Fluoxetine: a randomized clinical trial in the treatment of obesity. *Intern. J. Obesity Related Metabolic Dis.* 1994; **18**: 129–35.

IB	Osteoarthritis of knee	L90		acetaminophen	1	Williams HJ, Ward JR, Egger MJ, Neuner R, Brooks RH, Clegg DO, Field EH, Skosey JL, Alarcon GS, Willkens RF. Comparison of naproxen and acetaminophen in a two-year study of treatment of osteoarthritis of the knee. *Arthrit Rheumat*. 1993; **36**: 1196–206.
IB	Osteoarthritis of knee	L90		naproxen	2	Williams HJ, Ward JR, Egger MJ *et al*. Comparison of naproxen and acetaminophen in a two-year study of treatment of osteoarthritis of the knee. *Arthrit. Rheumat*. 1993; **36**: 1196–206.
IB	Osteoarthritis of knee	L90		etodolac	1	Dore R, Ballard I, Constantine G, McDonald P. Efficacy and safety of etodolac and naproxen in patients with osteoarthritis of the knee: a double-blind, placebo-controlled study. *Clin. Therap*. 1995; **17**: 656–66.
IB	Osteoporosis	L95		alfacalcidol	4	Tilyard MW, Spears GF, Thomson J, Dovey S. Treatment of postmenopausal osteoporosis with calcitriol or calcium. *N. Engl. J. Med*. 1992; **326**: 357–362.
IB	Osteoporosis	L95		tibolone	1	Rymer J, Robinson J, Fogelman I. Effects of 8 years of treatment with tibolone 2.5 mg daily on postmenopausal bone loss. *Osteoporosis Int*. 2001; **12**: 478–83.
IB	Dyspepsia/indigestion	D07		levosulpiride	1	Corazza GR, Biagi F, Albano O *et al*. Levosulpiride in functional dyspepsia: a multicentric, double-blind, controlled trial. *Ital. J. Gastroenterol*. 1996; **28**: 317–23.
IB	Symptom/complaints of Potency	Y07		sildenafil	1	Padma-Nathan H, Steers WD, Wicker PA. Efficacy and safety of oral sildenafil in the treatment of erectile dysfunction: a double-blind, placebo-controlled study of 329 patients. Sildenafil Study Group. *Int. J. Clin. Pract*. 1998; **52**: 375–9.
IB	Tinea ungiuum		B35.1	itraconazol	1	Gupta AK, Lynde CW, Konnikov N. Single-blind, randomized, prospective study of sequential itraconazole and terbinafine pulse compared with terbinafine pulse for the treatment of toenail onychomycosis. *J. Am. Acad. Dermat*. 2001; **44**: 485–91.
IB	Uncomplicated hypertension	K86		aspirin	19	Hansson L, Zanchetti A, Carruthers SG *et al*. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. *Lancet* 1998; **351**: 1755–62.
IB	Uncomplicated hypertension	K86		captopril	1	Hu Y, Zhu J. Quality of life of patients with mild hypertension treated with captopril: a randomized double-blind placebo-controlled clinical trial. *Chinese Med. J*. 1999; **112**: 302–7.

Table 4 *Continued*

Level of evidence	Primary diagnosis	ICPC code	ICD-10 code	Primary treatment	Number of pairs	Reference
IB	Uncomplicated hypertension	K86		carvedilol	10	Dupont AG, Van der Niepen P *et al*. Effect of carvedilol on ambulatory blood pressure, renal hemodynamics, and cardiac function in essential hypertension. *J. Cardiovascular Pharmacol*. 1987; **10**: S130–6.
IB	Uncomplicated hypertension	K86		cilazapril	2	Prager G, Klein P, Schmitt M, Prager R. Antihypertensive efficacy of cilazapril 2.5 and 5.0 mg once-daily vs. placebo on office blood pressure and 24-h blood pressure profile. *J. Cardiovasc. Pharmacol*. 1994; **24**: S93–9.
IB	Uncomplicated hypertension	K86		felodipine	18	Hansson L. The Hypertension Optimal Treatment study and the importance of lowering blood pressure. *J. Hypertens. Suppl*. 1999; **17**: S9–13.
IB	Uncomplicated hypertension	K86		hydochlorothiazide	1	Jounela AJ, Lilja M, Lumme J *et al*. Relation between low dose of hydrochlorothiazide, antihypertensive effect and adverse effects. *Blood Press*. 1994; **3**: 231–5.
IB	Uncomplicated hypertension	K86		irbesartan	2	Coca A, Calvo C, Garcia-Puig J *et al*. A multicenter, randomized, double-blind comparison of the efficacy and safety of irbesartan and enalapril in adults with mild to moderate essential hypertension, as assessed by ambulatory blood pressure monitoring: the MAPAVEL Study (Monitorizacion Ambulatoria Presion Arterial APROVEL). *Clin. Therap*. 2002; **24**: 126–38.
IB	Uncomplicated hypertension	K86		imidapril	1	van der Does R, Euler R. A randomized, double-blind, parallel-group study to compare the antihypertensive effects of imidapril and nifedipine in the treatment of mild-to-moderate essential hypertension. *J. Int. Med. Res*. 2001; **29**: 154–62.
IB	Uncomplicated hypertension	K86		lisinopril	10	Whelton A, Dunne B Jr, Glazer N *et al*. Twenty-four hour blood pressure effect of once-daily lisinopril, enalapril, and placebo in patients with mild to moderate hypertension. *J. Hum. Hypertens*. 1992; **6**: 325–31.

IB	Uncomplicated hypertension	K86	losartan	1	Byyny RL. Antihypertensive efficacy of the angiotensin II AT1-receptor antagonist losartan: results of a randomized, double-blind, placebo-controlled, parallel-group trial using 24-h blood pressure monitoring. Ambulatory Blood Pressure Monitoring Study Group. *Blood Press. Suppl.* 1996; **2**: 71–7.
IB	Uncomplicated hypertension	K86	manidipine	1	Fogari R, Zoppi A, Lusardi P, Preti P, Poletti L, Mugellini A. Evaluation by 24-h ambulatory blood pressure monitoring of efficacy of manidipine hydrochloride 10, 20 or 40 mg once daily as compared to placebo in treating mild to moderate essential hypertension: a double-blind, randomized, parallel group, placebo-controlled study. *Blood Press. Suppl.* 1996; **5**: 16–23.
IB	Uncomplicated hypertension	K86	pindolol	6	Toth PD, Demeter RJ, Woods JR, Nyhuis AW, Judy WV. Comparison of the effects of pindolol and atenolol on hemodynamic function in systemic hypertension. *Am. J. Cardi.* 1988; **62**: 413–8.
IB	Uncomplicated hypertension	K86	ticlopidine	4	Harbison JW. Ticlopidine vs. aspirin for the prevention of recurrent stroke. Analysis of patients with minor stroke from the Ticlopidine Aspirin Stroke Study. *Stroke* 1992; **23**: 1723–7.
IB	Vertigo/dizziness	N17	dimenhydrinate	2	Marill KA, Walsh MJ, Nelson BK. Intravenous Lorazepam vs. dimenhydrinate for treatment of vertigo in the emergency department: a randomized clinical trial. [Clinical Trial. Journal Article. Randomized Controlled Trial] *Ann. Emer. Med.* 2000; **36**: 310–9.
IB	Vertigo/dizziness	N17	gingko biloba	11	Haguenauer JP, Cantenot F, Koskas H, Pierart H. Treatment of equilibrium disorders with Ginkgo biloba extract. A multicenter double-blind drug vs. placebo study. *Press. Med.* 1986; **15**: 1569–72.
IB	Diabetes non-insulin dependent	T90	gliclazide	1	Salman S, Salman F, Satman I *et al.* Comparison of acarbose and gliclazide as first-line agents in patients with type 2 diabetes. *Curr. Med. Res. Opin.* 2001; **16**: 296–306.

Table 5 Convincing non experimental evidence

Primary diagnosis	ICPC code	Primary treatment	Number of pairs
Acute bronchitis	R73	zipeprol	2
Bronhiectasis (aymptomatic)	R91	quit smokong	1
Anxiety disorder/anxiety state	P74	clonazepam	1
Chronic bronchitis/bronchiectasis	R91	zipeprol	2
Chronic hepatitis B	B18.1†	periodic follow up	3
Constipation	D12	levosulpride	3
Constipation	D12	MgO	1
Diabetes non-insulin dependent	T90	triflusal	2
Diarrhrea	D11	tiropamide	3
Disturbance of sleep/insomnia	P06	etizolam	1
Disorders of stomach function/gastiris	D87	observation	5
Dyspepsia/indigestion	D07	alverine citrate	1
Dyspepsia/indigestion	D07	famotidine	3
Emphysema/chronic pulmonary disease	R95	acerophylline	2
Emphysema/chronic pulmonary disease	R95	fenoterol	1
Emphysema/chronic obstructive disorder	R95	procaterol	2
Fatty liver	K70.1†	alcohol abstinence	2
Hyperlipidemia	T93	exercise and diet control	6
Hypothyroidism/myxedema	T86	levothyroxine	3
Infectious conjunctivitis (viral/bacterial)	F70	oxymycin ophthamic ointment	8
Iron deficiency anemia	B80	sodium ferric gluconate	1
Iron deficiency anemia	B80	ferric sulfate	1
NIDDM with neurologic complication	E11.4	acetaminophen	2
NIDDM with neurologic complication	E11.4	etodolac	1
NIDDM with neurologic complication	E11.4	ketoprofen	1
Obesity	T82	exercise and diet control	6
Somatization disorder	F45.1	diazepam	2
Somatization disorder	F45.1	etizolam	1
Somatization disorder	F45.1	paroxetine	1
Somatization disorder	F45.1	alprazolam	2
Somatization disorder	F45.1	buspirone	2
Stroke/cerebrovascular accident	K90	triflusal	1
Upper respiratory infection	R74	acetaminophen	1
Upper respiratory infection	R74	astemizol	1

†Primary diagnosis classified by International Classification of Disease-10. ICPC, International Classification of Primary Care; MgO, magnesium oxide; NIDDM, non insulin dependent diabetes mellitus

pair can tell only a fraction of the story of a complex interaction. Moreover, 67% of the total consultations used combined treatments with more than two drugs. However, we only analyzed the data as one diagnosis-one treatment pair because searching the evidence of combined treatment effects was not feasible. To reflect a more accurate assessment of evidence-based practice, we need more sophisticated methods that could compare single versus combined treatment effect for each diagnosis.

Conclusion

Approximately 60% of the therapeutic interventions in a tertiary hospital family medicine outpatient clinic were supported by at least one RCT results. Although the results from the present may not accurately reflect the extent of evidence-based family practice in Korea, it could be baseline data for a future study to assess what extent the therapeutic interventions supported by results of RCT in other clinical settings.

Table 6 Intervention without substantial evidence

Primary diagnosis	ICP code	Primary treatment	Number of pairs
Acute bronchitis	R73	fenoterol	1
Chronic bronchitis/bronchiectasis	R91	fenoterol	2
Hip symptoms/complaints	L13	intramuscular stimulation	1
Jaundice (due to cholangiocarcinoma)	D13	biphenyl dimethyl dicarboxylate	1
Jaundice (due to cholangiocarcinoma)	D13	UDCA	1
Cough	R05	zipeprol	1
Chronic hepatitis B	B18.1†	biphenyl dimethyl dicarboxylate	2
Chronic hepatitis B	B18.1†	UDCA	1
Constipation	D12	smecta	1
Constipation	D12	itopride	1
Feeling depressed	P03	diazepam	1
Fatty liver	K70.1†	biphenyl dimethyl dicarboxylate	3
Fatty liver	K70.1†	UDCA	1
Disorders of stomach function/gastiris	D87	allaspan	3
Disorders of stomach function/gastiris	D87	teprenone	2
Disease of the esophagus	D84	rebamipide	5
Disease of the esophagus	D84	teprenone	2
Disease of the esophagus	D84	cisapnde	2
Headache	N01	etizolam	5
Hyperventilation	R93	alprazolam	1
Hyperventilation	R93	amitriptyline	1
Hyperventilation	R93	paroxetine	2
Irritable bowel syndrome	D93	pan-f	1
Irritable bowel syndrome	D93	teprenone	1
Dyspepsia/indigestion	D07	rebamipide	15
Dyspepsia/indigestion	D07	teprenone	4
Other osteoarthritis	L91	thiocolchicoside	1
Somatization disorder	F45.1†	mefanamic acid	2
Somatization disorder	F45.1†	naproxen	1
Somatization disorder	F45.1†	thiocolchicoside	3
Somatization disorder	F45.1†	acetoamiophen	1

†Primary diagnosis classified by International Classification of Disease. ICPC-10, International Classification of Primary Care; UDCA, urusodeoxycholic acid.

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