

Clinical Research and Methods

Practitioner Empathy and the Duration of the Common Cold

David P. Rakel, MD; Theresa J. Hoefft, PhD; Bruce P. Barrett, MD, PhD;
Betty A. Chewing, PhD; Benjamin M. Craig, PhD; Min Niu, MS

Objective: This study's objective was to assess the relationship of empathy in medical office visits to subsequent outcomes of the common cold. **Methods:** A total of 350 subjects ≥ 12 years of age received either a standard or enhanced physician visit as part of a randomized controlled trial. Enhanced visits emphasized empathy on the part of the physician. The patient-scored Consultation and Relational Empathy (CARE) questionnaire assessed practitioner-patient interaction, especially empathy. Cold severity and duration were assessed from twice-daily symptom reports. Nasal wash was performed to measure the immune cytokine interleukin-8 (IL-8). **Results:** Eighty-four individuals reported perfect (score of 50) CARE scores. They tended to be older with less education but reported similar health status, quality of life, and levels of optimism. In those with perfect CARE scores, cold duration was shorter (mean 7.10 days versus 8.01 days), and there was a trend toward reduced severity (mean area under receiver-operator characteristics curve 240.40 versus 284.49). After accounting for possible confounding variables, cold severity and duration were significantly lower in those reporting perfect CARE scores. In these models, a perfect score also correlated with a larger increase in IL-8 levels. **Conclusions:** Clinician empathy, as perceived by patients with the common cold, significantly predicts subsequent duration and severity of illness and is associated with immune system changes.

(Fam Med 2009;41(7):494-501.)

Practitioner-patient interactions have been discussed at length in the medical literature,¹⁻³ but there are limited data about their specific influence on medical outcomes, particularly regarding patients' perceptions of empathy in clinical encounters. There is evidence, however, that empathy is a positive component in practitioner-patient interactions. In 2001, Di Blasi et al published a systematic review of "context effects on health outcomes" that looked at influences of the practitioner-patient interaction. This review, which included 25 randomized trials, concluded that "One relatively consistent finding is that physicians who adopt a warm, friendly, and reassuring manner are more effective than those who keep consultations formal and do not offer reassurance."⁴

The feeling of empathy between practitioner and patient includes a combination of complex interactions

that are difficult to define. Mercer⁵ defines empathy as the ability to understand the patient's situation, perspective, and feelings (and their attached meanings); to communicate that understanding and check its accuracy; and to act on that understanding with the patient in a helpful and therapeutic way. Empathy is a foundational ingredient that defines holistic, relationship-centered care that is the essence of the biopsychosocial model in primary care.^{6,7} Preliminary research on the health benefits of empathy in the therapeutic encounter shows promising correlations with satisfaction, compliance, and enablement.⁸⁻¹⁰ Further data and better methodology are needed to assess potential influences on medical outcomes.

Our objective was to assess the relationship of empathy in the medical consultation to subsequent outcomes for patients with the common cold. We will present interim data from the "PEP trial" (Physician, Echinacea, and Placebo: A Randomized Controlled Trial in a Common Cold Model) related to the association between empathy in clinical encounters and the subsequent duration and severity of the common cold.

From the School of Medicine and Public Health (Drs Rakel, Barrett, and Hoefft), School of Pharmacy (Dr Chewing), and Department of Statistics (Ms Niu), University of Wisconsin; and H. Lee Moffitt Cancer Center and Research Institute, Tampa, Fla (Dr Craig).

Methods

The larger PEP trial was designed to assess pill-related placebo effects and practitioner-patient interaction effects on the common cold. Articles describing conceptual framework¹¹ and methodology¹² for this trial are available. The study was approved by the Health Sciences Institutional Review Board at the University of Wisconsin.

Subjects and Setting

The study took place in two settings: a primary care clinic in Verona, Wis, and the Employee Health Clinic at St. Mary's Hospital in Madison, Wis. Study clinicians received special training for this research and were not the subjects' primary care providers.

Patients were eligible to be enrolled in the study if they were at least 12 years of age and answered "yes" to the question, "Do you think that you have a cold?" They also needed to report one of the following four symptoms: (1) nasal discharge (runny nose), (2) nasal obstruction (nasal congestion, stopped up nose, stuffiness), (3) sneezing, and (4) sore throat (raw throat, scratchy throat). They were not eligible if any of these symptoms arose more than 36 hours prior to the intake evaluation.

Six clinicians were involved in the study (five family physicians and one family nurse practitioner). Two were women (one physician and one nurse practitioner), and the rest were male.

Instruments and Measures

Consultation and Relational Empathy. The Consultation and Relational Empathy (CARE) measure is a questionnaire designed to measure several aspects of the clinical encounter related to empathy.^{13,14} CARE assesses empathy from the patient's perspective and has been validated in primary care settings. Patients completed the CARE measure once, directly following their clinician visits at the time of enrollment.

CARE assesses 10 areas of consultations to see if clinicians (1) made patients feel at ease, (2) allowed them to "tell their story," (3) really listened, (4) were interested in them as a whole person, (5) fully understood their concerns, (6) showed care and compassion, (7) were positive, (8) explained things clearly, (9) helped them take control, and (10) helped create a plan of action. For each item, clinicians are rated on a scale from 1–5, from poor to excellent. Ratings are summed to produce a possible CARE score range from 0–50, 50 being a perfect score.¹³

Clinicians were also asked to rate the practitioner-patient interaction with two questions assessing how much they liked the patient and how connected they felt to the patient. Both questions were answered on a 0–100 visual analog scale (VAS).

Outcome Measures. Outcome measures collected assess the self-rated severity of the common cold, illness duration from enrollment in the study, and the individuals' immune responses. The Wisconsin Upper Respiratory Symptom Survey (WURSS-44)^{15,16} was self-reported by the patient at enrollment. A shorter version, the WURSS-21, was reported twice daily to assess severity over time. Overall cold severity was determined as the area under the time-severity curve (AUC) delineated by the WURSS-21 scores. Duration was assessed from enrollment as the number of days the individual continued to report "yes" to "Do you think you still have a cold?" before reporting two consecutive "no" responses to this question. If the individual still reported a cold on the last day of the study (day 14), the duration of the cold totaled 14 days.

Immune response was evaluated by measuring concentration of interleukin 8 (IL-8) from nasal wash specimens at enrollment and at a follow-up visit approximately 48 hours later. IL-8, an inflammatory cytokine found in nasal secretions, rises rapidly with viral upper respiratory infection and then falls over days to weeks. It is one of the best single markers of immune response in community-acquired upper respiratory infection, as it correlates well with symptoms, and can be reliably measured.

Optimism and Quality of Life. Study participants filled out questionnaires assessing their level of optimism (LOT)¹⁷ and perceived stress (PSS-4)¹⁸ at enrollment and again 2 days later. Health-related quality of life was assessed every day with the physical and mental subscales of the SF-8¹⁹ and with the feeling thermometer, a 100-mm visual analogue scale derived from the EuroQol.²⁰ The first item of the WURSS ("How sick do you feel today?") was also considered to indicate overall health and was analyzed separately. These measures and several demographic variables were used to assess possible differences between individuals reporting high or lower CARE scores (Table 2).

Procedures

Recruitment. Members of the general public were recruited through multiple methods: advertisements in daily and weekly newspapers, flyers, e-mails, word of mouth, and a Web site. These materials noted the importance of telephoning study staff at the first sign of a cold. Study staff screened callers, scheduled appointments, distributed surveys, and performed nasal washes. Subjects came in three times: at the start of their colds, 48 hours later, and when their colds had ended. They saw a study clinician once, at the first visit.

Randomization. Participants were randomized to: (1) no practitioner-patient interaction, (2) "standard" practitioner-patient interaction, and (3) "enhanced"

Table 1
Evaluation Tools

<i>Study Tool</i>	<i>What the Tool Measured</i>	<i>Format</i>	<i>Result (Sum Score/Range)</i>
CARE Questionnaire	Perceived empathy	10 questions Likert scale	10–50
Clinician Questionnaire	How much clinician “liked” and felt “connected to” the patient.	2 questions Visual Analog Scale	0–100
WURSS-21 (AUC)	Severity and duration of the cold	WURSS-21: 21 questions assessed twice daily Likert scale	0–3,920
IL-8	Cytokine associated with immune response	Biological marker for inflammation	15.6 pg/mL to no upper limit
<i>Tools to Assess Confounding Variables</i>			
LOT	Optimism	6 questions Likert scale	0–24
PSS	Perceived stress	4 questions Likert scale	0–16
SF-8 (MCS, PCS)	Quality of life (mental and physical)	8 questions Likert scale	MCS 17.9–59.3 PCS 19.5–58.6
WURSS-21	Baseline health	21 questions Likert scale	0–140
“How sick today?”	Baseline sickness	1 question Likert scale	0–7
Feeling thermometer	Assessment of personal health	1 question Visual analog scale	0–100

CARE—Consultation and Relational Empathy Questionnaire

WURSS—Wisconsin Upper Respiratory Symptom Survey

AUC—Area under the curve

IL-8—Interleukin-8

LOT—Life Orientation Test

PSS—Perceived Stress Scale

practitioner-patient interaction. Statistical staff prepared random assignments; clinicians learned to which group they had been assigned from the study packet they received upon entering an examining room. For the “no interaction” group, subjects saw study staff but were not seen by a clinician. The “standard” visit included the basic ingredients of a clinical encounter including history and present illness, relevant past medical history, focused physical exam, and diagnosis. The “enhanced” visit included the above with five added ingredients of the practitioner-patient interaction hypothesized to have a positive effect on health. These can be summarized using the PEECE mnemonic: (P) Positive prognosis, (E) Empathy, (E) Empowerment, (C) Connection, and (E) Education. These domains were chosen because of their prominence in the practitioner-patient interaction literature.^{21–41} In this study, only the empathy scores for the standard or enhanced visits were evaluated. At the time of submission, the study is still blinded, and we are not able to show the distribution of CARE scores associated with each of these randomized groups.

Clinician Training. Each of the clinicians completed training from an acting coach to establish common reproducible behaviors assigned to a standard or an enhanced visit. The foundational mind-set that the clinician was taught before entering the room was to create a different degree of “connectedness,” depending on the participant’s assignment to a standard or enhanced visit. For the standard encounter, the practitioner tried to prevent a connection from forming by keeping the visit short, with limited touch and eye contact. The enhanced visit focused on creating a connection or bond to enhance the interaction, with emphasis on the domains embodied in the PEECE acronym described earlier. In short, the enhanced visit attempted to “stack the deck” in favor of using nonspecific variables to facilitate health and healing.

Data Analysis

Student’s *t* tests and chi square tests were used to assess potential differences between those reporting higher and lower scores on the CARE measure. Linear regression assessed the relationship between the

dichotomous CARE measure and two of the outcomes: AUC cold severity and the changes in IL-8 value between baseline and the 48-hour follow-up visit. There was no graduated dose correlation between outcome measures and CARE scores except when the results were dichotomized to perfect (50) and non-perfect (<50) CARE scores. A Cox-proportional hazard model assessed the duration of the cold by looking at the rate at which colds are ending based on level of the CARE measure. All regression models were adjusted for potential confounders, specifically age, gender, race, education, optimism, perceived stress, and time from first symptom to enrollment. Further description of potential confounders can be found in Tables 1 and 2.

Results

Only two individuals were lost to follow-up. They were included in the analysis of baseline differences but were excluded from analysis of cold outcomes.

Patients who gave their clinical encounters perfect CARE scores at baseline subsequently had shorter

duration of colds and a trend to lower severity of their colds. This predictive association did not, however, hold across CARE scores below the perfect score level. Based on these findings, we reviewed the data of perfect score (84) and non-perfect score (264) respondents (Figure 1). (Two non-perfect score respondents were lost to follow-up.)

Individuals with perfect CARE scores were typically older, reported less than college/postgraduate education, were more racially diverse, and tended to report lower perceived stress (Table 2). Individuals reporting perfect CARE scores did not, however, differ from other participants on several important baseline characteristics. They had a similar male/female ratio and rated themselves similarly on optimism as assessed via the Life Orientation Test (LOT)⁴² and on several baseline reports of health status including WURSS-21 Feeling Thermometer rating and the SF-8 (Table 2).

Because the larger PEP study remained blinded and we were unable to correlate CARE scores with the standard or enhanced groups, we evaluated the clinician ratings of “liking” and “feeling connected to” the patients to see if these data correlated with perfect CARE scores. Clinicians reported liking and feeling more connected to those patients who gave their encounters perfect CARE scores (77.7 versus 72.4, $P < .002$ and 69.0 versus 59.8, $P < .001$ respectively). Each of the six clinicians in the study saw a comparable proportion of individuals reporting perfect CARE scores, suggesting that a perfect score is not correlated with one clinician being naturally more empathetic than another.

Cold outcomes were more favorable among individuals reporting perfect CARE scores in data that is unadjusted for differences (Table 3). Analysis of AUC scores showed lower overall severity colds among those subjects giving perfect CARE scores (mean 240.40 versus 284.49), but the difference is not statistically significant. The mean cold duration from time of enrollment was almost 1 day shorter among this group (mean 7.10 versus 8.01, $P < .032$). Figure 2 also highlights this difference in cold duration from enrollment to the end of their cold.

The mean change in IL-8 from baseline to follow-up was higher in those reporting perfect scores (mean change 562.18 versus 220.14, $P = .180$). This difference, however, was not statistically significant.

When analyses were adjusted for potential demographic and psychosocial confounders, results indicate that AUC cold severity was milder (P value .037) and colds ending sooner (P value .017) among those reporting perfect CARE scores (Columns 4 and 5, Table 3). Adjusted analysis of change in IL-8 values between baseline and 48 hours post-enrollment showed a significantly larger rise for those individuals reporting perfect CARE scores (P value .015). One IL-8 value determined too high for accurate measurement was

Table 2

Group Differences at Enrollment Based on Perfect CARE Score

	<i>Perfect Score n=84</i>	<i>< Perfect Score n=266</i>	
	<i>Mean (SD) or %</i>	<i>Mean (SD) or %</i>	<i>P Value</i>
Demographic			
Age	37.32 (16.17)	33.69 (14.12)	.052
% male	34.1	36.5	.694
% caucasian	84.7	93.6	.011
Education (%)			
< High school	6.49	6.00	
High school	20.8	5.60	
Some college	39.0	29.6	
College/post-graduate	33.8	58.8	<.001
Health status			
WURSS-21	45.39 (26.67)	44.82 (23.38)	.859
“How sick?”	3.73 (1.48)	3.56 (1.32)	.129
Feeling thermometer	61.72 (22.00)	62.17 (18.33)	.851
SF-8 (MCS)	48.11 (9.54)	48.18 (8.75)	.950
SF-8 (PCS)	43.64 (9.88)	43.85 (7.88)	.840
Psychosocial			
Optimism	22.98 (4.23)	22.57 (3.82)	.415
Perceived stress	4.65 (3.33)	5.26 (3.01)	.108

SD—standard deviation

WURSS-21—Wisconsin Upper Respiratory Symptom Survey

SF-8—Short Form-8 Health Survey

winsorized⁴³ to take the value of the next highest value in these analyses. When this outlier was included in a censored regression, study results did not differ.

Discussion

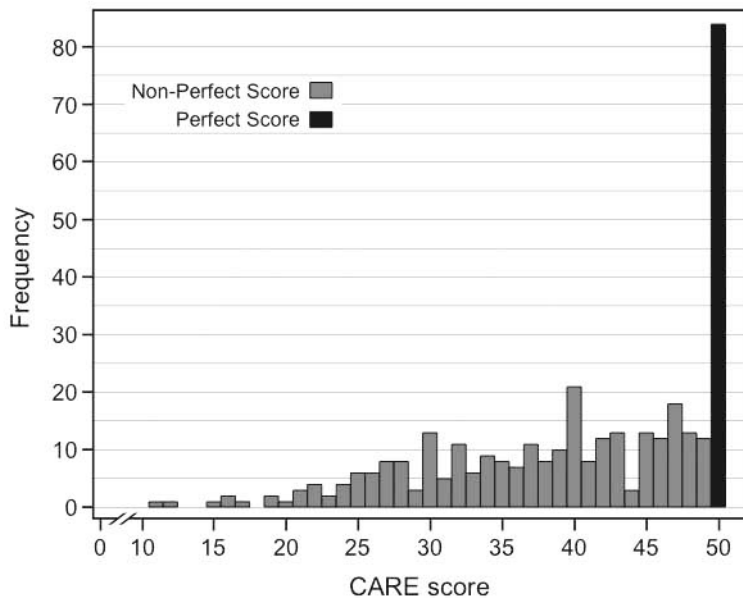
We found that perfect scores on the CARE instrument, which measures the effects of empathy in the clinical encounter, predicted the duration of subsequent illness from the common cold. Adjustment for potential confounders did not reduce the strength of the observed predictive relationship. Although not statistically significant, perfect scores also showed a trend toward improved severity and the degree of rise of IL-8 levels from nasal washings.

A patient rating of a perfect score on the CARE instrument at the time of consultation was associated with a 0.91 day (7.10 versus 8.01) shorter duration of illness, a 16% reduction in overall cold severity (AUC 240.4 versus 284.5), and more than double the rise in the immune biomarker IL-8 (562.2 versus 220.1).

To help determine if these associations are the result of clinician empathy or the unique characteristics of patients giving perfect scores, we looked at individual characteristics including age, race, education, stress, and optimism. When these factors were included in our analysis, we found that a perfect CARE score was still associated with a shorter cold and less severe symptoms. Reporting a perfect CARE score did not significantly correlate with quality of life ratings (SF-8) or ratings of personal health (ie, feeling thermometer, “How sick are you?”) at enrollment. Thus, we were unable to find unique characteristics of

Figure 1

Graph of CARE Score Distribution (n=350): Perfect Score (n=84) Versus Non-perfect Score (n=266)



CARE—Consultation and Relational Empathy questionnaire

Table 3

Group Cold Outcome Differences Based on Perfect CARE Score

	Perfect Score n=84 [1]	< Perfect Score n=264 [2]	[3]	[4]	[5]	[6]
<i>Cold Outcome</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>P Value</i>	<i>Adjusted Difference in Means^a</i>	<i>P Value Adjusted for Confounding Variables^a</i>	<i>95% CI</i>
Duration	7.10 days (3.50)	8.01 days (3.36)	.032	0.375*	.017	(0.068 to 0.682) [†]
Severity	240.40 (226.31)	284.49 (219.88)	.118	- 66.58	.037	(-129.24 to -3.918) [†]
Change in IL-8	562.18 (2,871.66)	220.14 (1,602.60)	.180	663.52	.015	(127.72 to 1,199.32) [†]

CARE—Consultation and Relational Empathy questionnaire

SD—standard deviation

CI—confidence interval

[] Column number

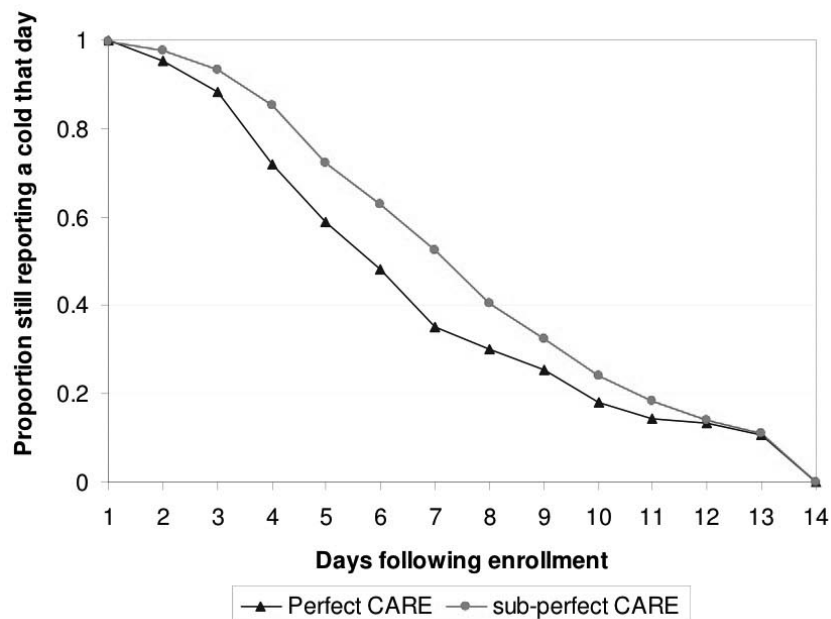
* Cox proportional hazard model coefficient represents a % higher rate at which colds are ending

^a Adjusting for age, gender, race, education, optimism, perceived stress, hours since first symptom, and squared hours since first symptom

[†] P<.05

Figure 2

Kaplan-Meier Survival Curve: Time to End of the Common Cold



Log rank test for equality of survivor functions P value .0803.

This unadjusted graphic of time after enrollment until the end of the individual's cold shows the proportion with a cold is typically less within the perfect CARE score group when compared to the non-perfect CARE score groups.

individuals giving perfect scores that could account for the associations with illness duration, severity and IL-8 levels, and even after controlling for possible confounders, the association of a perfect CARE score with reduced duration and severity remains (Table 3). We therefore conclude that the empathetic interaction between patient and clinician may indeed influence subsequent illness.

Why did these changes only occur within patients who gave perfect CARE scores and not with "sub-perfect scores"? Why was there no graduated "dose-response relationship"? A possible explanation for this lack of dose-response relationship is that if a "connection" between clinician and patient happened in the consultation, the patient gave a perfect score. Anything less than a perfect score may not correlate with such a connection taking place where empathy was expressed or felt. This may suggest that the perception of empathy by patients may be more of an "on or off" phenomenon than a graduated response. We either feel empathy or we don't.

Those reporting perfect CARE scores also had more robust IL-8 responses at 48 hours after intake than

those who gave a non-perfect score. Inflammatory/immune cytokines such as IL-8, which are released in response to viral infections, indicate an active immune response to the offending organism.⁴⁴⁻⁴⁶ Our observation that IL-8 rose faster among those giving perfect CARE scores links the subjective rating of a positive emotion (empathy) with an objective measure of immune response. Specific negative emotional states such as stress and depression can increase susceptibility to the common cold, suggesting that negative emotions may have a negative effect on immune function.⁴⁷⁻⁴⁹ Data presented here suggest that a consultation rated high in empathy, a positive emotion, is associated with an enhanced immune response and a shorter illness. These findings suggest that IL-8 holds promise for future research in relation to empathy's effect on immune pathways.

The positive benefits of perceived empathy on the common cold can be put into perspective when compared to anti-viral studies showing similar modest effect sizes. For a drug to be beneficial for a self-limited illness such as the common cold, it needs to show efficacy, ease of dosing, and few side effects.⁵⁰ The best effect from a drug studied to date (pleconaril) reduced the duration by about 1 day but worked only for picornavirus-associated colds and caused nausea and diarrhea.^{50,51} Empathy has a similar effect without side effects in all-cause colds and was found beneficial after only one dose of human empathy.

Limitations

While the data presented here come from a randomized controlled trial, allocation remains concealed at the time of writing. Therefore, this study is best described as a prospective cohort, and hence while associations and predictive capacity can be assessed, we cannot assess causality. Since we can only interpret findings as associations, another interpretation is that the patients who feel better or have had less severe colds also perceive and transmit greater empathy and connectedness with their clinicians. A challenge in this work is disentangling the effects of physical status from reported empathy.

An additional limitation is that neither the clinical setting nor the provider was one with whom the patient

already had a relationship. All clinicians were new to the patients. Prior relationships with practitioners who knew them well may have further enhanced the positive effects of empathy.

Conclusions

We found that when patients with a common cold rated encounters with clinicians as “perfect” on a measure of empathy, the patients had a significantly shorter duration of illness and trend toward lesser severity of illness and higher levels of immune response as measured by IL-8. This finding is in need of replication. Until then, including empathy in the clinical encounter has little potential for harm and has positive influences that extend beyond the medical consultation. A “connection” also enhances continuity and builds a foundation for relationship-centered primary care within the patient’s medical home.

Acknowledgments: Financial support: This article describes the methods and rationale for an ongoing randomized controlled trial sponsored by the National Center for Complementary and Alternative Medicine at the National Institutes of Health (NIH NCCAM 1-R01-AT-1428). The University of Wisconsin School of Medicine and Public Health and the University of Wisconsin Department of Family Medicine have also invested substantially in this trial, particularly in the support of Drs Rakel, Barrett, and Craig. Support for Dr Barrett’s conception of the original trial came from a K-23 career development grant from NIH NCCAM and a career development grant from the Robert Wood Johnson Foundation Generalist Physician Scholars Program. The second author is supported by predoctoral training grant T32 HS000083 from the Agency for Healthcare Research and Quality (AHRQ).

This study was presented (“Practitioner Empathy and the Common Cold”) by the second author at the Wisconsin Research and Education Network (WREN) meeting on November 1, 2007, in Wisconsin Dells, Wis.

Special thanks to Charlene Luchterhand in helping prepare the manuscript and coinvestigators Lucille Marchand, David Rabago, Randy Brown, Jo Sheder, Raandi Schmidt, Gay Thomas, and Shari Barlow. Thanks also to Steward Mercer for reviewing the manuscript. Lastly, we appreciate the hundreds of trial participants who graciously gave of their time, energy, and good will to support medical research during a time of illness..

Corresponding Author: Address correspondence to Dr Rakel, University of Wisconsin, Department of Family Medicine, 777 S. Mills, Madison, WI 53715. 608-265-8421. Fax: 608-263-5813. drakel@fammed.wisc.edu.

REFERENCES

- Covington H. Caring presence. Delineation of a concept for holistic nursing. *J Holist Nurs* 2003;21(3):301-17.
- Beach MC, Inui T. Relationship-centered Care Research Network. Relationship-centered care. A constructive reframing. *J Gen Intern Med* 2006;21 Suppl 1:S3-S8.
- Borrell-Carrio F, Suchman AL, Epstein RM. The biopsychosocial model 25 years later: principles, practice, and scientific inquiry. *Ann Fam Med* 2004;2(6):576-82.
- Di Blasi Z, Harkness E, Ernst E, Georgiou A, Kleijnen J. Influence of context effects on health outcomes: a systematic review. *Lancet* 2001;357(9258):757-62.
- Mercer SW, Reynolds WJ. Empathy and quality of care. *Br J Gen Pract* 2002;52 Suppl:S9-S12.
- Engel GL. The need for a new medical model: a challenge for biomedicine. *Science* 1977;196(4286):129-36.
- Novack DH. Realizing Engel’s vision: psychosomatic medicine and the education of physician-healers. *Psychosom Med* 2003;65(6):925-30.
- Kim SS, Kaplowitz S, Johnston MV. The effects of physician empathy on patient satisfaction and compliance. *Eval Health Prof* 2004;27(3):237-51.
- Bikker AP, Mercer SW, Reilly D. A pilot prospective study on the consultation and relational empathy, patient enablement, and health changes over 12 months in patients going to the Glasgow Homoeopathic Hospital. *J Altern Complement Med* 2005;11(4):591-600.
- Price S, Mercer SW, MacPherson H. Practitioner empathy, patient enablement, and health outcomes: a prospective study of acupuncture patients. *Patient Educ Couns* 2006;63(1-2):239-45.
- Barrett B, Muller D, Rakel D, Rabago D, Marchand L, Scheder JC. Placebo, meaning, and health. *Perspect Biol Med* 2006;49(2):178-98.
- Barrett B, Rakel D, Chewning B, et al. Rationale and methods for a trial assessing placebo, echinacea, and doctor-patient interaction in the common cold. *Explore (NY)* 2007;3(6):561-72.
- Mercer SW, Maxwell M, Heaney D, Watt GC. The consultation and relational empathy (CARE) measure: development and preliminary validation and reliability of an empathy-based consultation process measure. *Fam Pract* 2004;21(6):699-705.
- Mercer SW, McConnachie A, Maxwell M, Heaney D, Watt GC. Relevance and practical use of the consultation and relational empathy (CARE) measure in general practice. *Fam Pract* 2005;22(3):328-34.
- Barrett B, Brown R, Mundt M, et al. The Wisconsin Upper Respiratory Symptom Survey is responsive, reliable, and valid. *J Clin Epidemiol* 2005;58(6):609-17.
- Barrett B, Locken K, Maberry R, et al. The Wisconsin Upper Respiratory Symptom Survey (WURSS): a new research instrument for assessing the common cold. *J Fam Pract* 2002;51(3):265.
- Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the life orientation test. *J Pers Soc Psychol* 1994;67(6):1063-78.
- Cohen S, Williamson G. Perceived stress in a probability sample of the United States. In: Spacapan S, Oskamp S, eds. *The Social Psychology of Health*. Newbury Park, Calif: Sage Publications, 1988:31-67.
- Ware JE, Kosinski M, Dewey JE, Gandek B, eds. *How to score and interpret single-item health status measures: a manual for users of the SF-8 Health Survey*. Lincoln, RI: Quality Metric, 2001.
- Schunemann HJ, Griffith L, Jaeschke R, Goldstein R, Stubbings D, Guyatt GH. Evaluation of the minimal important difference for the feeling thermometer and the St. George’s respiratory questionnaire in patients with chronic airflow obstruction. *J Clin Epidemiol* 2003;56(12):1170-6.
- Hsueh Y. The Hawthorne experiments and the introduction of Jean Piaget in American industrial psychology, 1929–1932. *Hist Psychol* 2002;5(2):163-89.
- Starfield B, Wray C, Hess K, Gross R, Birk PS, D’Lugoff BC. The influence of patient-practitioner agreement on outcome of care. *Am J Public Health* 1981;71(2):127-31.
- Stewart M, Brown JB, Boon H, Galajda J, Meredith L, Sangster M. Evidence on patient-doctor communication. *Cancer Prev Control* 1999;3(1):25-30.
- Suchman AL, Markakis K, Beckman HB, Frankel R. A model of empathic communication in the medical interview. *JAMA* 1997;277(8):678-82.
- Thomas KB. The consultation and the therapeutic illusion. *Br Med J* 1978;1(6123):1327-8.
- Roter DL, Hall JA, Merisca R, Nordstrom B, Cretin D, Svarstad B. Effectiveness of interventions to improve patient compliance: a meta-analysis. *Med Care* 1998;36(8):1138-61.
- Roter DL, Hall JA. Doctors talking with patients: patients talking with doctors: improving communication in medical visits. Westport, Conn: Auburn House, 1992.
- Flood AB, Lorence DP, Ding J, McPherson K, Black NA. The role of expectations in patients’ reports of post-operative outcomes and improvement following therapy. *Med Care* 1993;31(11):1043-56.
- Little P, Everitt H, Williamson I, et al. Observational study of effect of patient centredness and positive approach on outcomes of general practice consultations. *BMJ* 2001;323(7318):908-11.
- Mondloch MV, Cole DC, Frank JW. Does how you do depend on how you think you’ll do? A systematic review of the evidence for a relation between patients’ recovery expectations and health outcomes. *CMAJ* 2001;165(2):174-9.
- Petrie KJ, Weinman J, Sharpe N, Buckley J. Role of patients’ view of their illness in predicting return to work and functioning after myocardial infarction: longitudinal study. *BMJ* 1996;312(7040):1191-4.
- Ryff CD. Positive mental health. In: Blechman EA, Brownell KD, eds. *Behavioral medicine and women: a comprehensive handbook*. New York: Guilford Publications, Inc, 1998:183-8.

33. Savage R, Armstrong D. Effect of a general practitioner's consulting style on patients' satisfaction: a controlled study. *BMJ* 1990;301(6758):968-70.
34. Roter DL, Hall JA. Patient-provider communication. In: Glanz K, Lewis FM, Rimer BK, eds. *Health behavior and health education: theory, research and practice*. San Francisco: Jossey-Bass, A Wiley Company, 1997:206-26.
35. Evans RG, Barer ML, Marmor TR. Why are some people healthy and others not? The determinants of health of populations. Hawthorne, NY: Aldine de Gruyter, 1994.
36. Marmot MG. Social differentials in health within and between populations. *Daedalus: Journal of the American Academy of Arts and Sciences* 1994;123:197-216.
37. McKnight JL. Health and empowerment. *Can J Public Health* 1985;76 (Suppl 1):37-8.
38. Singer B, Ryff CD. Hierarchies of life histories and associated health risks. *Ann N Y Acad Sci* 1999;896:96-115.
39. Guadagnoli E, Ward P. Patient participation in decision-making. *Soc Sci Med* 1998;47(3):329-39.
40. Suchman AL, Matthews DA. What makes the patient-doctor relationship therapeutic? Exploring the connexional dimension of medical care. *Ann Intern Med* 1988;108(1):125-30.
41. Matthews DA, Suchman AL, Branch WT Jr. Making "connexions:" enhancing the therapeutic potential of patient-clinician relationships. *Ann Intern Med* 1993;118(12):973-7.
42. Scheier MF, Carver CS. Optimism, coping, and health: assessment and implications of generalized outcome expectancies. *Health Psychol* 1985;4(3):219-47.
43. Tsay JY, Chen IW, Maxon HR, Heminger L. A statistical method for determining normal ranges from laboratory data including values below the minimum detectable value. *Clin Chem* 1979;25(12):2011-14.
44. Klemens C, Rasp G, Jund F, et al. Mediators and cytokines in allergic and viral-triggered rhinitis. *Allergy Asthma Proc* 2007;28(4):434-41.
45. Stoll D. Inflammatory acute rhinosinusitis. *Presse Med* 2001;30(39-40 Pt 2):33-40.
46. Barrett B, Brown R, Voland R, Maberry R, Turner R. Relations among questionnaire and laboratory measures of rhinovirus infection. *Eur Respir J* 2006;28(2):358-63.
47. Cohen S. Keynote presentation at the Eighth International Congress of Behavioral Medicine. The Pittsburgh Common Cold Studies: psychosocial predictors of susceptibility to respiratory infectious illness. *Int J Behav Med* 2005;12(3):123-31.
48. Irwin MR, Miller AH. Depressive disorders and immunity: 20 years of progress and discovery. *Brain Behav Immun* 2007;21(4):374-83.
49. Coe CL, Laudenslager ML. Psychosocial influences on immunity, including effects on immune maturation and senescence. *Brain Behav Immun* 2007;21(8):1000-8.
50. Patick AK. Rhinovirus chemotherapy. *Antiviral Res* 2006;71(2-3):391-6.
51. Hayden FG, Herrington DT, Coats TL, et al. Efficacy and safety of oral pleconaril for treatment of colds due to picornaviruses in adults: results of two double-blind, randomized, placebo-controlled trials. *Clin Infect Dis* 2003;36(12):1523-32.