Does Multiple Risk Factor Reduction Explain the Reduction in Fall Rate in the Yale FICSIT Trial?

Mary E. Tinetti,[1] Gail McAvay,[2] and Elizabeth Claus[2]

In a recent study of fall prevention in 301 community-living older persons (the Yale FICSIT Trial, 1990–1993), participants in the multifactorial targeted intervention (TI) group experienced significantly fewer falls than participants in the social visit (SV) control group. In the present paper, the authors explore the relation between changes in the studied risk factors and the occurrence of falling. In comparison with SV participants, TI participants showed significantly greater improvements in postural blood pressure change ($p = 0.01$), step length ($p = 0.004$), use of ≥ 4 medications ($p = 0.003$), and unsafe tub and toilet transfers ($p = 0.05$), while change in balance was of borderline significance ($p = 0.08$). Reduction in the occurrence of falling, in turn, was at least marginally associated with improvements in balance, postural blood pressure change, step length, lower extremity strength/range of motion, and transfers. When participants were divided into tertiles based on a composite risk factor change score, a significantly higher percentage of TI participants (42%) than SV participants (22%) were in the greatest risk factor reduction tertile. Among TI participants, there was a progressively lower fall rate per person per year in the tertiles with the least, intermediate, and greatest risk reduction (0.832, 0.624, and 0.260), respectively. A similar but weaker relation between risk factor reduction and fall rate was seen in the SV group. When compared within tertiles, essentially adjusting for the amount of risk factor reduction, the fall rates among TI and SV participants in the greatest risk factor reduction tertile were identical (0.260 falls per person per year), and the rates in the least reduction tertile were similar (0.832 vs. 1.040 falls per person per year); this suggests that risk factor reduction at least partially mediated the treatment effect. These results support the feasibility of implementing and analyzing the effectiveness of a multiple risk factor reduction strategy in the aged. *Am J Epidemiol* 1996;144:389–99.

aged; falls; risk factors

Most controlled clinical trials reported to date (with notable exceptions, such as the Multiple Risk Factor Intervention Trial (1)) have tested single interventions that have been either administered identically to all intervention subjects or adjusted in intensity on the basis of responses to appropriate intermediate measures. A multifactorial risk abatement strategy, however, may be the preferred approach to the prevention or treatment of common geriatric syndromes.

Falling, as with many geriatric syndromes, most often results not from a single disease process but from the accumulated effect of impairment in multiple areas

(2–8). Several studies have shown that the risk of falling increases with the number of impairments possessed (2–4). It is reasonable to postulate that, conversely, risk may be reduced by ameliorating as many of these factors as possible. Indeed, this expectation is further supported by our understanding that individuals maintain their postural stability because of a complex network of sensory, central integrative, and motor systems. The systems contributing to postural stability are redundant, thus allowing the individual to compensate for impairments. Multiple impairments, however, reduce a person's ability to develop compensatory mechanisms (9). A multiple risk factor abatement strategy, by ameliorating several impairments, may restore compensatory ability.

A multiple risk factor abatement approach is additionally appealing because most of the risk factors for falling are chronic impairments that may be amenable to amelioration but not elimination. A multiple risk factor approach which tailors the intervention to each individual's combination of risk impairments may provide a more realistic test of the effectiveness of fall

prevention than an intervention targeted toward a single, standard risk factor implemented regardless of the individual's combination of health problems.

While a multiple risk factor abatement strategy is well justified, there are distinct disadvantages as well. Multicomponent interventions are more complicated to implement clinically and to study than single interventions. A multicomponent intervention is not inherently necessary to reduce the occurrence of a multifactorial process such as falling, since improving an individual's status on even a single contributing factor may be effective. A common argument against a multicomponent intervention is that it is not possible to determine which component or components were responsible for the treatment effect. As health care providers and reimbursers become increasingly concerned about cost-effectiveness in health care, there is an understandable reluctance to recommend expensive treatments that cannot be adequately judged. Certainly, determining the mechanisms of response is an analytic and clinical challenge in multiple risk factor intervention studies, particularly when the risk factors may not be independent (i.e., when change in one risk factor may result in change in another), the interventions (e.g., medication adjustment) may affect more than one risk factor, and participants may receive various combinations of the intervention components (10–12).

Acknowledging these advantages and disadvantages, we recently completed a multiple risk factor abatement intervention trial aimed at reducing the rate of falling among community-living elderly persons (13). Participants in the intervention group experienced a significantly lower rate of falling than participants in the control group during 1 year of follow-up. In the present study, we determined which interventions were effective in reducing levels of the targeted risk factors and which risk factor reductions, individually and in combination, were associated with the lower fall rate. The specific aims were to: 1) determine the difference in the amount of change in individual risk factors between intervention and control group participants (i.e., ascertain the effectiveness of individual interventions); 2) identify the relations between the amount of change in risk factors and the occurrence of falling; and 3) determine which risk factor reductions mediated the treatment effect (i.e., the effectiveness of the multiple risk factor intervention strategy).

MATERIALS AND METHODS

Setting and subjects

The methods of the study, the Yale FICSIT Trial (1990–1993), have been described previously (14) and

are summarized here. Sixteen physicians in the participating health maintenance organization were divided into "high" and "low" subgroups on the basis of two characteristics: the number of their patients at least 70 years of age (>150 vs. ≤150) and the average number of prescriptions written per office visit for elderly patients (≥1 vs. <1). Two physician members of each resulting quartet were assigned randomly to the social visit (SV) group and two were assigned to the targeted intervention (TI) group. Patients were randomly selected until approximately 20 participants had been enrolled from each physician's practice. Participants were assigned to the study group of their physician. Eligibility criteria, in addition to age, included independent ambulation, residence outside of an institution, a score of at least 20 on the Folstein Mini-Mental State Examination (15), no participation in vigorous physical activity, and possession of at least one of the targeted risk factors. Of the 1,950 persons screened, 355 (18 percent) met all of the eligibility criteria. Among eligible participants, 301 (85 percent) agreed to participate; 153 participants were assigned to the TI group and 148 to the SV group. Eligible subjects who refused did not differ from enrolled participants in terms of age, sex, or group assignment.

Assessment

Descriptive data. The baseline assessment was conducted in the participant's home by the study nurse practitioner and physical therapist, both of whom were blinded to group assignment. The nurse practitioner ascertained demographic data, fall history, depressive symptoms (16), self-reported chronic conditions, and self-reported instrumental activities of daily living (17).

Targeted risk factors. The risk factors targeted for intervention were selected on the basis of epidemiologic evidence of an association with falling and the availability of potentially effective interventions that would be feasible in usual clinical practice. The definitions of the risk factors and the criteria for intervention are listed in table 1.

Reassessments. Assessments of the targeted risk factors were repeated for 248 of the 301 participants (82 percent) a median of 4.5 months (range, 3–12 months) after the baseline assessment, usually within 1 month of completing the active intervention or social visit phase. Reasons for missed reassessments included participant refusal (n = 24); an administrative decision, such as the inability to reach the participant after five attempts or an intervening major event such as stroke (n = 21); nursing home placement (n = 3); death (n = 2); and moving away from the area (n = 1). Two individuals whose reassessments were per-

TABLE 1. Risk factors for falls targeted for interventions in the Yale FICSIT* Trial, 1990–1993

Risk factor	Criteria	Intervention
Factors assessed by nurse practitioner		
Postural hypotension	≥20 mmHg drop or drop to ≤90 mmHg when moving from a lying position to standing	•Postural exercises (e.g., ankle pumps) •Elevate head of bed •Medication review and adjustment
Use of sedative-hypnotic medications	Any use of benzodiazepines or other prescription or nonprescription sleeping medications	•Taper off and discontinue medication •Nonpharmacologic treatment of sleeping problems (e.g., sleep restriction)
Use of ≥4 medications	Use of ≥4 medications plus report of any fatigue, dizziness, or fall and use of at least one centrally acting antihypertensive, nitrate diuretic, histamine blocker, or NSAID*	•Medication review and adjustment by primary physician
Tub or toilet transfers	Unsafe during assessment	•Transfer training •Environmental adjustments (e.g., addition of grab bars, raised toilet seat)
Factors assessed by physical therapist		
Gait impairment	Any abnormalities on baseline assessment	•Gait training; use of assistive device •Balance and/or strengthening exercises if indicated
Balance impairment	Any abnormalities on baseline assessment	•Progressive balance exercises; transfer training if indicated
Arm and/or leg strength or range-of-motion impairment	Less than full range of motion against full resistance	•Resistance exercises with tubing, in order of priority: hips > ankles > knee > shoulder > hand > elbow

* FICSIT, Frailty and Injuries Cooperative Studies of Intervention Techniques; NSAID, nonsteroidal anti-inflammatory drug.

formed over 12 months postbaseline were also excluded.

Targeted intervention group

On the basis of baseline assessments, a combination of targeted risk factors was identified for each participant. This information was used to estimate the number of home visits each TI and SV participant would receive, as well as to structure the intervention strategy for the intervention participants. The nurse practitioner and physical therapist used predetermined criteria, shown in table 1, to decide whether participants met the criteria for intervention on each risk factor. As described previously, decision rules, algorithms, and priority lists, incorporated into a procedure manual, were used to select and implement intervention protocols to ensure consistent application of the multicomponent intervention strategy and to avoid overburdening participants (14, 18).

The intervention phase lasted approximately 3 months after the completion of the baseline assessment, but could be extended if participants experienced health problems that interfered temporarily with their ability to exercise. If the new health event resulted in inability to continue the treatment program, the participant was dropped from the intervention but included in all follow-up assessments. A 3-month maintenance phase, during which participants were contacted monthly and encouraged to continue their exercises and other interventions, followed the active intervention phase.

Social visit group

Participants assigned to the SV group received structural life reviews conducted by social work students to control for the time and attention provided to TI participants (19). The number of social work visits was matched to the number of estimated nurse and

therapist visits that would be required for TI participants with comparable risk factors.

Outcomes

The primary study outcome was the occurrence of one or more falls during the 6 months following reassessment. Falls were ascertained by a previously described fall calendar (14). Among the 248 participants with reassessment data, 241 (97 percent) had complete information on falls.

The intermediate outcomes for this study were the changes in the targeted risk factors that occurred between the baseline and reassessment interviews. While the categorization of risk factors as absent versus present was useful for the purpose of identifying participants in need of specific components of the multifactorial intervention, more detailed information on changes in risk factors was desired for the analysis of intermediate outcomes. Continuous measures of the risk factors were constructed for postural blood pressure, balance, and gait. Mean arterial blood pressure change after 2 minutes of standing was used in determining change in postural blood pressure. The balance score used to determine change was based on the amount of time a participant could maintain the following positions: a side-by-side stand; semitandem, tandem, right, and left one-leg stands; and a toe stand. Each position was scored as 0 (unable to perform), 1 (able to perform but not able to maintain for 10 seconds), or 2 (able to perform and to maintain for 10 seconds). Possible balance scores ranged from 0 to 12. Step length, calculated by dividing the distance walked by the number of steps, was used as the parameter to determine gait change, since an increased step length reflects a safer and more efficient gait pattern. Change scores for these three continuous measures were calculated as the reassessment score minus the baseline score.

A second type of change measure was constructed for the risk factors that were either inherently dichotomous or had a highly skewed data distribution. Sedative-hypnotic use, tub and toilet transfers, and the use of ≥ 4 medications were treated as categorical measures. For these risk factors, change was categorized as "improved" if the subject possessed the risk factor at baseline but no longer possessed the risk factor at reassessment. Initially, scores from the individual bilateral muscle and joint groups were aggregated into total upper and lower extremity scores to assess continuous change. Because the upper and lower extremity measures were highly skewed, with most participants attaining the maximum score, we utilized the dichotomous measures of the upper and

lower strength/range-of-motion risk factors to categorize "improvement" as noted above.

Analysis

Descriptive statistics were calculated for baseline characteristics by treatment group. Categorical measures in the two groups were compared using chi-squared tests, while mean values for the continuous variables were compared by t test. Treatment group comparisons of baseline characteristics were conducted first for all study participants ($n = 301$) and then for the subset of participants who had completed reassessments within 12 months of the baseline interview ($n = 248$).

The impact of the intervention on observed change in the continuous risk factor measures was examined using analysis of covariance, with baseline score and time of reassessment (3–4, 5–6, or 7–12 months) included as the independent variables. The intervention's effect on improvements in the categorical risk factors was determined using a Mantel-Haenszel chi-squared test, with strata defined by time of reassessment.

We constructed a residual change score for each continuous risk factor that was independent of the baseline level, by regressing each observed change score on the baseline measure and utilizing the residuals from these regressions as a second measure of change (20). These residual change scores were used in all analyses examining the correlations between changes in risk factors and the effect of the changes on falling. Pearson correlation coefficients were calculated for continuous variables and chi-squared tests were conducted for discrete variables in order to determine whether changes in the individual risk factors were significantly associated with each other.

The relations between changes in individual risk factors and falling were examined using logistic regression models applied to the repeated observations on falls (21, 22). For these analyses, the period between the baseline and reassessment interviews was used to assess the changes in risk factors, whereas the 6-month period following the reassessment interview was used to determine fall rates. Each individual week during the 6-month fall follow-up period was included as a separate observation for each participant. The outcome was defined as fall versus no fall for each week, allowing us to incorporate multiple falls in the analysis. To account for the correlation among repeated falls, we utilized sample survey regression methods that allow for robust estimation of standard errors for clustered data (21, 22). Specifically, the individual participant was defined as the cluster and the standard errors for the regression coefficients were

computed using Taylor series linearization methods with the SUDAAN software package (23). Incidence rate ratios were estimated from the adjusted odds ratios calculated in the logistic regression analyses. The initial models, constructed to examine the association between risk factor change and falling for each of the risk factors separately, were adjusted for age (<76 years vs. ≥76 years). Interactions between age and each of the risk factor changes were also tested. Other measures considered but not included in these models because of a lack of statistical significance were sex, education, the baseline level of each risk factor, and hospitalizations during the 6-month fall follow-up period.

A final set of analyses addressed the question of whether the total combination of changes in risk factors mediated the observed effect of the targeted intervention on fall rates. A multivariate model that included age was constructed using a stepwise selection procedure among the risk factor changes, with significance levels of 0.25 for entry into the model and 0.15 for staying in the model. Since the purpose of this analysis was to examine the potential mediators of treatment effect, only risk factor changes that differed by treatment group were included in this model. A composite change-in-risk-factor score was then constructed using the coefficients from this pooled logistic model (see table 4). Specifically, this composite score

was calculated by using the logistic regression coefficients to "weight" the relative importance of each individual risk factor change. This score reflects the "best" combination of changes in risk factors in terms of ordering study participants according to their risk of falling. Tertiles for this composite change-in-risk-factor score were determined from the combined data distribution for the two groups. The percentage of participants and the fall rate within each of these tertile groupings was then calculated for each treatment group.

RESULTS

Baseline characteristics of the TI and SV participants are shown in table 2 for all 301 participants, as well as for the 248 participants who completed reassessments. In the study sample as a whole, the participants who were not reassessed differed from the rest of the sample only in terms of mean age (76.6 years (standard deviation (SD) 4.5) vs. 78.2 years (SD 5.4)) and the percentage who used sedative-hypnotic medications at baseline (30 percent vs. 16 percent). The TI and SV groups were well-matched on most characteristics, although the TI group had higher mean Folstein Mini-Mental State and balance scores and a greater stride length than the SV group. A lower percentage of TI participants than of SV participants had a lower-

TABLE 2. Baseline characteristics of the Yale FICSIT† Trial participants, by treatment group, 1990–1993

| | Targeted Intervention group | | | | | | Social visit group | | | | | |
| | All participants | | | Participants in analysis | | | All participants | | | Participants in analysis | | |
Characteristic	No.	Mean or %	SD†	No.	Mean or %	SD	No.	Mean or %	SD	No.	Mean or %	SD
Age (years)	153	78.3	5.3	129	78.3	5.3	148	77.5	5.3	119	78.0	5.5
Female sex (%)	153	69		129	72		148	69		119	66	
Fall during year prior to study (%)	153	41		129	43		148	44		119	44	
Mini-Mental State Examination‡	153	27.2*	2.1	129	27.2**	2.1	144	26.5	2.3	116	26.5	2.4
At least two chronic conditions (%)	153	76		129	77		148	70		119	71	
No. of instrumental activities of daily living participant can do without help‡	153	7.4	2.0	129	7.4	2.0	148	7.1	2.2	119	7.1	2.2
Postural blood pressure change (mmHg)‡	153	−1.5	9.3	129	−1.6	9.5	147	−1.2	11.0	118	−0.2	10.2
Balance score‡	152	7.7	2.5	128	7.7	2.5	140	7.3	2.6	114	7.1	2.5
Step length (cm)‡	151	33.1*	7.3	127	33.2**	6.8	145	31.4	8.4	116	31.2	8.1
Upper extremity strength/range-of-motion impairment (%)	153	29		129	32		148	37		119	36	
Lower extremity strength/range-of-motion impairment (%)	153	37*		129	36**		148	51		119	54	
Use of sedative-hypnotic medications (%)	153	19		129	20		148	18		119	12	
Use of ≥4 medications (%)	153	43		129	42		148	41		119	37	
Unsafe tub/toilet transfers (%)	152	65		128	67		147	64		118	66	
No. of risk factors meeting criteria for intervention	153	3.6	1.7	129	3.7	1.7	148	3.9	1.7	119	3.7	1.6

* p ≤ 0.05 (targeted intervention group vs. social visit group) for all participants.
** p ≤ 0.05 (targeted intervention group vs. social visit group) for participants in analysis.
† SD, standard deviation; FICSIT, Frailty and Injuries Cooperative Studies of Intervention Techniques.
‡ See "Materials and Methods" for definition.

extremity impairment (37 percent vs. 51 percent). TI and SV participants had identical numbers of risk factors meeting the criteria for intervention (3.7 factors (SD 1.7) vs. 3.7 factors (SD 1.6).

Changes in risk factor levels by treatment group

The baseline and change scores for postural blood pressure change, balance score, and stride length, the three continuous risk factor variables, are given in table 3, as are the percentages of participants who improved in each group with regard to the five categorical factors (sedative-hypnotic use, use of ≥ 4 prescription medications, unsafe tub or toilet transfers, and lower and upper extremity impairment). Results are given first for all reassessed participants and then for the subgroup of participants who met the criteria for intervention presented in table 1 for each of the targeted risk factors. Also included in table 3 are the numbers of TI participants meeting the criteria who received the intervention. As can be seen, the majority of persons with postural hypotension, use of ≥ 4 medications, and impairments of balance, gait, transfer,

TABLE 3. Baseline values and changes in the targeted risk factors among Yale FICSIT* Trial participants, 1990-1993

Risk factor†	Targeted intervention group					Social visit group					p-value‡
	Total no.§	Baseline		Change‖		Total no.	Baseline		Change‖		
		Mean	SD*	Mean	SD		Mean	SD	Mean	SD	
Continuous variables											
Postural blood pressure change (mmHg)											
All subjects	126	−1.6	9.6	+1.1	8.2	117	+0.2	9.5	−1.5	7.7	0.01
Criteria for intervention	56 (55)¶	−7.2	9.6	+5.5	7.6	40	−4.1	6.3	−0.4	10.4	0.003
Timed balance (score)											
All subjects	124	7.9	2.4	+3.2	2.1	108	7.2	2.4	−0.2	2.0	0.08
Criteria for intervention	73 (69)	7.5	2.3	+0.4	2.2	66	6.8	2.4	−0.3	2.1	0.09
Step length (cm)											
All subjects	126	33.3	6.7	+3.4	6.6	113	31.5	7.9	+1.0	5.7	0.004
Criteria for intervention	76 (70)	31.8	6.8	+3.1	5.7	78	30.1	8.1	+0.9	5.8	0.03

	Number and percentage of participants who improved#						
	Total no.	No.	%	Total no.	No.	%	
Categorical variables							
Sedative-hypnotic use							
All subjects	129	12	9	119	6	5	0.12
Criteria for intervention	26 (19)	12	46	14	6	43	0.74
Use of ≥4 medications							
All subjects	129	20	16	119	6	5	0.003
Criteria for intervention	54 (44)	20	37	44	27	14	0.003
Tub/toilet transfers							
All subjects	128	44	34	117	27	23	0.05
Criteria for intervention	86 (69)	44	51	77	27	35	0.05
Lower extremity strength/ range of motion							
All subjects	129	16	12	119	22	18	0.21
Criteria for intervention	47 (30)	16	34	64	22	34	0.83
Upper extremity strength/ range of motion							
All subjects	129	12	9	119	8	7	0.38
Criteria for intervention	41 (18)	12	29	43	8	19	0.27

* FICSIT, Frailty and Injuries Cooperative Studies of Intervention Techniques; SD, standard deviation.

† Refer to table 1 and "Materials and Methods" for definitions. Results are reported first for all participants and then for the subset who met the criteria for intervention as defined in table 1.

‡ p value for the treatment effect from analysis of covariance (continuous variables) or the Mantel-Haenszel chi-squared test (categorical variables).

§ Totals vary because of missing data.

‖ Reassessment value minus baseline value, adjusted for baseline value and reassessment time (3–4, 5–6, or 7–12 months).

¶ Numbers in parentheses, number of participants with the risk factor who received the intervention.

Participants who possessed the risk factor at baseline but no longer did at reassessment were categorized as improved.

and a lower extremity received an intervention. The factor with the smallest percentage of persons receiving an intervention was upper extremity impairment—the risk factor given the lowest priority.

The TI group showed significantly greater improvements in postural blood pressure change, stride length, use of ≥ 4 medications, and unsafe transfers, while change in balance score was of borderline significance. No difference was seen between TI and SV participants for changes in the use of sedatives-hypnotics or upper or lower extremity impairments.

Pearson correlation coefficients were computed and chi-squared tests were conducted to determine whether changes in individual risk factors were significantly associated with one another. Change in stride length and improved tub and toilet transfers ($r = 0.30$, $p = 0.0001$), change in balance and improved lower extremity impairment ($r = 0.15$, $p = 0.02$), improved tub and toilet transfers and sedative use ($\chi^2 = 5.18$, $p = 0.02$), change in postural blood pressure and lower extremity impairment ($r = -0.12$, $p = 0.06$), and use of sedatives-hypnotics and ≥ 4 medications ($\chi^2 = 2.9$, $p = 0.09$) were the changes at least marginally associated with each other. These correlations between risk factor changes were not significantly different in the two groups of participants.

While the correlation between a decrease in medications and postural blood pressure change was not significant, we examined this relation further, because medication adjustment was a major component of the intervention for postural blood pressure. Among the 53 TI participants who were using at least four medications at baseline and were reassessed, the 20 who exhibited a decrease to less than four medications showed a mean improvement in postural blood pressure change of +2.9 (SD 8.8) mmHg, compared with a mean increase of only +0.9 (SD 7.1) mmHg for the 33 participants who did not decline in their number of medications. No such relation between a decrease in medications and improvement in postural blood pressure change was noted in the SV group.

Relations between changes in individual and combined risk factors and falling

Our first model explored the treatment effect associated with assignment to the TI group, adjusting for age. The adjusted incidence rate ratio for the TI group versus the SV group was 0.61 (95 percent confidence interval (CI) 0.38–0.96), indicating a 39 percent reduction in falling associated with the targeted intervention.

We next examined whether reduction in any individual risk factor was associated with a reduction in fall rate using individual logistic models. As table 4 indicates, balance, stride length, improved lower ex-

TABLE 4. Results of logistic regression analyses for the relation between changes in individual risk factors and rates of falls among Yale FICSIT* Trial participants (n = 222), 1990–1993

Risk factor	Individual models†		Multivariate model‡	
	IRR*,§	95% CI*	IRR§	95% CI
Change in balance score‖	0.89	0.80–1.00	0.89	0.80–0.99
Change in blood pressure (mmHg)	0.98	0.95–1.01	0.98	0.95–1.01
Change in stride length (cm)¶				
Age <76 years	0.91	0.85–0.98	0.91	0.84–0.98
Age ≥76 years	1.00	0.96–1.04	1.00	0.96–1.04
Improvement in lower extremity strength/range of motion (yes/no)	0.50	0.23–1.08		
Improvement in no. of prescription medications used (yes/no)	0.92	0.44–1.91		
Improvement in tub/toilet transfers (yes/no)¶				
Age <76 years	0.32	0.10–1.11		
Age ≥76 years	1.20	0.68–2.10		
Improvement in sedative-hypnotic use (yes/no)	1.04	0.45–2.40		
Improvement in upper extremity strength/range of motion (yes/no)	1.37	0.66–2.87		

* FICSIT, Frailty and Injuries Cooperative Studies of Intervention Techniques; IRR, incidence rate ratio; CI, confidence interval.

† Models were adjusted for age only.

‡ Model was adjusted for age (<76 years vs. ≥76 years) and the other risk factors listed in the table.

§ Estimated by the odds ratio.

‖ See "Materials and Methods" for definition.

¶ Interaction between risk factor and age.

tremity strength/range of motion, and transfer improvements were the risk factor changes at least marginally associated with fall rate. Significant interactions, however, were found between age and both change in stride length and improved transfers. For participants under 76 years of age, an increase in stride length was significantly associated with a reduced risk of falling, while improved transfers were of borderline significance.

To determine which combinations of risk factor reductions were independently associated with a reduction in fall rate, changes in the individual risk factors that differed by treatment group (i.e., balance, postural blood pressure, stride length, transfers, and medications) were entered into a stepwise logistic regression model with age (table 4). The adjusted incidence rate ratios for changes in balance, postural blood pressure, and stride length (for subjects under 76 years of age)—the factors of at least borderline significance—were 0.89 (95 percent CI 0.80–0.99), 0.98 (95 percent CI 0.95–1.01), and 0.91 (95 percent CI 0.84–0.98), respectively. Thus, a 1-point improvement in balance score, for example, was associated with an 11 percent decrease in fall rate, independent of changes in the other factors in the model, while a 1-mmHg increase in postural blood pressure was associated with a 2 percent decrease and a 1-cm increase in stride length was associated with a 9 percent decrease. Improvement in transfers, which did not remain in the final model, was, however, correlated with change in stride length ($r = 0.30$, $p < 0.0001$).

Does risk factor reduction mediate the treatment effect of the TI strategy?

We next explored whether, and to what extent, risk factor reduction mediated the significant treatment effect seen with the TI strategy. Changes in balance, postural blood pressure change, and age × gait (stride length), the three risk factors which showed at least a

marginal treatment effect and were associated independently with falling, were included in this analysis. A composite change-in-risk-factor score was constructed using the coefficients from the final logistic regression model shown in table 4. Participants were divided into tertiles based on the combined distribution of this composite risk factor change score in the two groups.

The relation between combined risk factor reduction and the fall rate is displayed in table 5 by treatment group. First, as expected, a significantly higher percentage of TI participants than of SV participants (42 percent vs. 22 percent) were in the greatest combined risk factor reduction score tertile, again demonstrating that there was greater risk factor improvement in the TI group than in the SV group. Second, among the TI participants, there was a progressively lower fall rate in the tertiles with the least, intermediate, and greatest risk reduction (0.832, 0.624, and 0.260 falls per person per year), respectively. A similar but weaker relation between risk factor reduction and fall rate was seen in the SV group. Third, when compared within tertiles as shown in table 5—essentially adjusting for the amount of risk factor reduction—the fall rates among TI and SV participants in the greatest risk factor reduction tertile were identical (0.260 falls per person year), and the rates in the least reduction tertile were similar (0.832 vs. 1.040). This suggests that risk factor reduction at least partially mediated the treatment effect. Among persons in the intermediate reduction tertiles, however, assignment to the TI group was still associated with a lower fall rate than inclusion in the SV group (0.624 vs. 1.040).

DISCUSSION

As we previously reported (13), our multiple risk factor reduction strategy resulted in a significant reduction in fall rates among community-living elderly

TABLE 5. Combined risk factor reduction score tertiles, by treatment group and fall rates, in Yale FICSIT† Trial participants, 1990–1993

Combined risk factor reduction score tertile‡	Targeted intervention group		Fall rate per person		Social visit group		Fall rate per person	
	No.	%*	Weekly	Yearly	No.	%*	Weekly	Yearly
Greatest reduction	50	42	0.005	0.260	23	22	0.005	0.260
Intermediate reduction	34	29	0.012	0.624	40	39	0.020	1.040
Least reduction	34	29	0.016	0.832	41	39	0.020	1.040
Overall	118	100	0.010	0.520	104	100	0.017	0.884

* $p < 0.01$ (Mantel-Haenszel chi-squared test for trend) for risk factor reduction score tertile by treatment group.

† FICSIT, Frailty and Injuries Cooperative Studies of Intervention Techniques.

‡ Based on a composite change-in-combined-risk-factor score constructed using the coefficients from the final logistic regression model shown in table 4. Tertiles were based on the combined distribution for the two groups.

persons. In the present analyses, we found that our intervention strategy resulted in a reduced presence or severity of at least five of the eight targeted risk factors, and that the reductions in several of these risk factors were, in turn, associated with a reduction in the occurrence of falling. We also found that, while changes in several of the risk factors were correlated with each other, reductions in three risk factors were at least marginally associated with reduction in the rate of falling, independent of the effect of the other risk factor changes. Furthermore, the reduction in the fall rate was strongly associated with the extent of combined risk factor reduction. Finally, the treatment effect (i.e., assignment to the TI group vs. the SV group) was negligible among the one third of participants showing the greatest combined risk factor reduction. This combination of findings suggests that multiple risk factor reduction did indeed result in a marked reduction in the occurrence of falls, and that much, although probably not all, of the risk factor reduction resulted from our targeted, multifactorial intervention strategy.

Significant improvements were seen in balance, postural blood pressure, gait, tub and toilet transfers, and use of ≥ 4 medications. These were the risk factors that had the highest prevalence and the largest percentage of participants with the risk factor who received an intervention, because of our priority rules among the risk factors. While a decrease in medications to less than four was not directly associated with a reduction in the rate of falling, this decrease was moderately associated with an improvement in postural blood pressure change among participants in the TI group, suggesting that medication reduction was an important mechanism for ameliorating postural hypotension.

There was no evidence of improvement in the TI group compared with the SV group in upper or lower extremity impairment or sedative-hypnotic use. These were the risk factors with the lowest baseline prevalence in the study population. Possible explanations for the observed lack of effect for upper and lower extremity impairments include 1) some persons with the impairment not receiving an intervention because of the priority decision rules, 2) an insufficiently intense exercise regimen, or, alternatively, 3) the use of a measure of impairment that was insensitive to change. Given the evidence from other clinical trials that intensive training does increase strength in elderly persons, further work in this area is important (24). Losses to follow-up probably contributed to our inability to detect an effect for sedative-hypnotic use. It was the only risk factor that was significantly more frequent among participants excluded from analysis

because of lack of reassessment than among participants included in analysis (30 percent vs. 16 percent; $p < 0.05$). Furthermore, a higher percentage of SV participants using sedative-hypnotics at baseline were lost to follow-up than TI subjects (48 percent vs. 10 percent). Unfortunately, because of these losses, the effect of stopping sedative-hypnotic use on falling could not be adequately assessed in this study.

While our findings suggest that multiple risk factor reduction was an important mechanism of treatment effect, assignment to the TI group remained somewhat associated with a reduction in fall rate among the two thirds of participants who experienced the intermediate or least reduction in overall risk score. This finding suggests that additional factors besides the three whose reductions were measured in our composite reduction score influenced the occurrence of falls. One possible explanation is suggested by the correlations seen among changes in several of the risk factors. It is possible that improvement in certain risk factors influenced other risk factors (e.g., that medication adjustment influenced postural blood pressure or that gait training affected transfers) and these effects were not measured in our risk factor reduction score. Adherence to the study protocol is known to affect treatment response. Since there was no measure of adherence in the SV group, we could not directly assess the effect of adherence in this study. The TI strategy may have affected the occurrence of falls in a manner other than directly through risk factor improvement. One possibility is increased confidence, with resultant improvement in the performance of mobility tasks. This possibility is supported by our previous finding of greater improvement in ratings of confidence in performing activities of daily living without falling in the TI group versus the SV group (13). Finally, we intervened only in risk factors that were present at the time of the baseline assessment. Since this was an elderly population, some participants probably developed risk factors after the baseline assessment and, conversely, some participants who possessed risk factors at baseline improved over time for reasons other than our intervention. This possibility is supported by another finding in our study—namely, the relation between combined risk factor reduction score and fall rate seen in the SV group as well as in the TI group.

Several of our methods require comment. TI and SV participants were well-matched at baseline; any differences were controlled for in the analyses and did not appear to affect results. As we noted previously, a slightly higher percentage of SV participants than TI participants were lost to follow-up. With the exception of sedative-hypnotic use, however, the distribution of baseline characteristics and targeted risk factors did

not differ in the subset included in the present analyses compared with the total study sample. Both small numbers and measures that were insensitive to change could have impeded our ability to adequately detect the relation between changes in the targeted risk factors and the occurrence of falling. We used continuous measures rather than dichotomous measures whenever feasible to enhance sensitivity, and looked for trends rather than rigid statistical levels of significance. Ideally, we would liked to have had sufficient power to analyze all of the intermediate and process measures as well as the primary study outcome. Unfortunately, because of the limited resources available, this option was not feasible. Given these limitations, however, we were able to detect significant differences in several of the risk factors. Thus, if anything, we probably underestimated the effectiveness of our intervention strategy.

The results of this study have important methodological and clinical implications. Methodologically, through a series of analyses, we produced a chain of evidence supporting the effectiveness of the multiple risk factor abatement strategy and determining which risk factor reductions contributed most effectively to the observed reduction in fall rates. Investigators have been reluctant to embark on multifactorial interventions, even though this approach might be considered the most clinically relevant and sensible, because of the widely accepted premise that it is not possible to determine which components of a multifactorial strategy contributed to any observed treatment effect. While the analytic strategies used in the present study are not the only approach to investigating multifactorial interventions, and while there are limitations to our approach, results suggest that it may be possible to discern the individual effects of a multifactorial intervention.

The primary clinical implication of our results is that a multiple risk factor abatement strategy tailored to an individual's combination of risk factors is not only feasible but is likely to be more effective in reducing the rate of falls than an intervention targeted toward a single risk factor. In considering implementation of our multiple risk factor intervention strategy, evidence is strongest for including interventions targeting postural blood pressure change, balance and transfers, and gait. Furthermore, given the relation between the reduction in number of medications and the improvement in postural blood pressure drop, medication review and adjustment should probably be included as well.

Given their inherently multifactorial and variable etiology, the results of our study have great importance for other geriatric syndromes and, indeed, many chronic health conditions in elderly persons. While they are more complicated to design, implement, and analyze, this study suggests that it is feasible, and indeed appropriate, to tailor intervention protocols to individuals rather than (as has been the more usual practice) tailor individuals to a standardized protocol.

REFERENCES

1. Multiple Risk Factor Intervention Trial Research Group. Multiple Risk Factor Intervention Trial: risk factor changes and mortality results. JAMA 1982;248:1465–77.
2. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med 1988;319:1701–7.
3. Nevitt MC, Cummings SR, Kidd S, et al. Risk factors for recurrent nonsyncopal falls: a prospective study. JAMA 1989; 261:2663–8.
4. Robbins AS, Rubenstein LZ, Josephson KR, et al. Predictors of falls among elderly people: results of two population-based studies. Arch Intern Med 1989;149:1628–33.
5. O'Loughlin JL, Robitaille Y, Boivin J-F, et al. Incidence of and risk factors for falls and injurious falls among the community-dwelling elderly. Am J Epidemiol 1993;137: 342–54.
6. Blake AJ, Morgan K, Bendall MJ, et al. Falls by elderly people at home: prevalence and associated factors. Age Ageing 1988;17:365–72.
7. Campbell AJ, Borrie MJ, Spears GF. Risk factors for falls in a community-based prospective study of people 70 years and older. J Gerontol 1989;44:M112–17.
8. Alexander NB. Postural control in older adults. J Am Geriatr Soc 1994;42:93–108.
9. Tinetti ME, Inouye SK, Gill TM, et al. Shared risk factors for falls, incontinence, and functional dependence: unifying the approach to geriatric syndromes. JAMA 1995;273:1348–53.
10. Multiple Risk Factor Intervention Trial Research Group. Statistical design considerations in the NHLI Multiple Risk Factor Intervention Trial (MRFIT). J Chronic Dis 1977;30: 261–75.
11. Judd CM, Kenny DA. Process analysis estimating mediation in treatment evaluations. Eval Rev 1981;5:602–19.
12. Mulrow CD, Pugh J. Making sense of complex interventions. (Editorial). J Gen Intern Med 1995;10:111–12.
13. Tinetti ME, Baker DI, McAvay G, et al. A multifactorial intervention to reduce the risk of falling among elderly people living in the community. N Engl J Med 1994;331:821–7.
14. Tinetti ME, Baker DI, Garrett PA, et al. Yale FICSIT: risk factor abatement strategy for fall prevention. J Am Geriatr Soc 1993;41:315–20.
15. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98.

16. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.
17. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179–86.
18. Koch M, Gottschalk M, Baker DI, et al. An impairment and disability assessment and treatment protocol for community-living elderly persons. Phys Ther 1994;74:286–98.
19. Merriam SB. The structure of simple reminiscence. Gerontologist 1989;29:761–7.
20. Rosner B. The analysis of longitudinal data in epidemiologic

studies. J Chronic Dis 1979;32:163–73.
21. Lavange LM, Keyes LL, Koch GG, et al. Application of sample survey methods for modelling ratios to incidence densities. Stat Med 1994;13:343–55.
22. Graubard BI, Korn EL. Regression analysis with clustered data. Stat Med 1994;13:509–22.
23. Shah BV, Barnwell BG, Bieler GS. SUDAAN user's manual: software for analysis of correlated data. Release 6.40. Research Triangle Park, NC: Research Triangle Institute, 1995.
24. Fiatarone MA, O'Neill EF, Ryan ND, et al. Exercise training and nutritional supplementation for physical frailty in very elderly people. N Engl J Med 1994;330:1769–75.