Subsystems contributing to the decline in ability to walk. Bridging the gap between epidemiology and geriatric practice in the In Chianti

Subsystems Contributing to the Decline in Ability to Walk: Bridging the Gap Between Epidemiology and Geriatric Practice in the InCHIANTI Study

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BACKGROUND: Older patients are often referred to geriatricians because of complaints of progressive difficulties in walking. The diagnostic and therapeutic approach to these patients is complex. Multiple physiologic subsystems may influence the ability to walk, and no standard criteria are currently available to establish whether these subsystems are functioning within the normal range. To address this lack of knowledge we conducted the InCHIANTI study.

OBJECTIVE: To identify measures that clinicians can use to understand the causes of walking difficulties in older persons.

DESIGN: A population-based study of persons living in the Chianti geographic area (Tuscany, Italy).

PARTICIPANTS: 1453 persons (age-range 20–102 years; 91.6% of the eligible) selected from city registry of Greve in Chianti and Bagno a Ripoli (Tuscany, Italy), using a multistage sampling method.

MEASUREMENTS: Factors that influence walking ability were classified into six main physiologic subsystems: central nervous system, perceptual system, peripheral nervous system, muscles, bone/joints, and energy production/delivery. Measures of the integrity and functioning of each of these proposed subsystems were identified and administered to all participants.

CONCLUSIONS: Data collected in InCHIANTI will be used to identify the main risk factors that influence loss of the ability to walk in older persons, to define physiologic subsystems that are critical for walking, to select the best measures of their integrity, and to establish critical ranges in these measures that are compatible with "normal" walking ability. The final goal is to translate epidemiological research into a geriatric clinical tool that makes possible more precise diagnosis and more effective treatment in patients with walking dysfunction. J Am Geriatr Soc 48:1618–1625, 2000.

Key words: disability; Physical performance; walking; mobility; prevention; InCHIANTI; aging.

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MOBILITY IS A CRITICAL ASPECT OF FUNCTIONING IN OLDER PEOPLE

Aging is often associated with a decline in physical function that eventually leads to loss of autonomy in daily life activities. In many older persons, such a decline has no explicit connection to a defined medical condition[1] and, often, it does not receive proper medical attention until a late stage.[2,3] Studies have suggested that the appearance of difficulties in walking marks a critical point in this process. In fact, walking is important to maintain independence in daily life activities, to enjoy an adequate level of social interaction[4,5] and to retain good emotional vitality,[6,7] all of which are main determinants of quality of life in old age.[8–10] Even in nondisabled older persons, poor performance in walking is associated with accelerated decline in physical function and elevated risk of been admitted to a nursing home.[11–13]

Many older patients are referred to a geriatric specialist because of the appearance of walking problems. In these patients, the identification of the primary cause of their functional limitation is often difficult, owing to the coexistence of multiple diseases and impairments and because the central nervous system can operate with different motor strategies that fully compensate for minor damages. Furthermore, there is a lack of standard criteria for judging which of the physiologic systems involved in the activity of walking are functioning within normal limits. For example, studies have demonstrated that over a critical threshold, muscle strength is not related to walking performance, suggesting that when muscle strength is above this threshold it is unlikely to be a significant cause of walking disability.[14] However, similar thresholds of functioning have not been described for the other physiologic systems, such as joint passive range of motion or nerve conduction velocity, that play a role in the activity of walking. Thus, the identification of the causes of walking difficulties remains in the domain of the *ars medica*.

The clinical approach to walking problems is intrinsically complex. The activity of walking is so important to life that efficient mobility has probably been a primary target for natural selection throughout human evolution.[15] This has led to physiologic systems that not only are highly redundant but also are capable of functioning and interacting in a number of different ways to accomplish the same task.[16] For example, if a particular muscle cannot be used, its function may be taken over by another muscle or group of muscles, maintaining the same normal gait pattern. As a consequence, walking prob-

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lems become clinically evident only when this large functional reserve is exhausted and even compensatory strategies have failed.[17] This explains why progressive walking difficulties in old age often unfold in the context of frailty, a state characterized by clinical instability and decline in physiologic reserve.[18] In spite of this, recent data suggest that appropriate interventions can substantially improve frailty-related walking ability in older persons[19–22] and, perhaps, counteract the pathophysiologic process that eventually leads to disability.

MULTIPLE FACTORS INFLUENCE GAIT AND ABILITY TO WALK

Multiple risk factors can influence mobility.[23,24] In patients with stroke, hip fracture and other diseases that result in an acute and severe anatomic or functional injury, the causal pathway between the disease and the lack of ability to walk is immediately evident. In these instances, preventing the disease should also prevent walking disability. Furthermore, when disability develops suddenly, as the consequence of an acute medical condition, appropriate rehabilitation techniques usually improve function[25] and, in a large percentage of cases, fully restore walking ability.

In contrast, in older persons who develop walking disability slowly and progressively, the best clinical approach in terms of prevention, diagnosis and treatment remains a matter of speculation. The distinction between acute catastrophic and frailty-associated, progressive limitation in walking has been formally addressed only recently.[3,26] Older age, female gender, diabetes, recent history of acute infection, low muscle strength, poor balance, visual deficit, low cognitive function, and several biomarkers of frailty are all independently associated with poor walking performance.[27,28] Although these findings suggest possible targets for prevention, they are of little help in developing an integrated clinical approach.

Specific diseases produce patterns of gait that can be recognized visually. Criteria for the classification of these patterns have been proposed,[29,30] but only seldom do they apply to older persons who are developing progressive limitation in walking. In fact, comorbidity, coimpairments, and age-associated sub-clinical impairments produce gait patterns that combine aspects that are typical of various diseases but cannot be classified as a pure type.[31] Biomechanical and kinematic measures performed in gait laboratories provide a more promising and global approach to the assessment of walking. Data generated from sophisticated equipment, including force platforms, three-dimensional video recording, and multi-channel electromyography, are fitted to mathematical models. Gait is described in terms of three-dimensional trajectories, velocities and accelerations of the body segments, vectors of force applied to joints and to the ground, and sequences of muscle group contractions. This approach has been found very useful for better understanding gait problems in patients with neurological and orthopedic conditions.[32–35] However, it is still unclear whether gait analysis can provide a synthetic way of abstracting information useful for establishing appropriate treatment of older persons with progressive walking disability. Furthermore, because of the high cost of the equipment and the need for highly skilled personnel, gait laboratories are limited to research institutions.

A CLASSIFICATION MODEL OF THE SUBSYSTEMS THAT DETERMINE WALKING FUNCTION

In the spring of 1997 we decided to focus our research activities on better understanding the causes of walking limitations in older persons. We developed our hypotheses within the framework proposed by the Institute of Medicine,[36] which is a revision of the original ICIDH model of the World Health Organization.[37,38] This model provides definitions for the elements of the dynamic pathway from disease to various functional outcomes:[39] Active pathology refers to biochemical and physiologic abnormalities that are labeled as diseases in medical science; Impairments are dysfunctions and structural abnormalities in specific body systems that can be evaluated through clinical examination, laboratory tests, imaging procedures, and symptoms reports. Factors that affect the ability to walk are in this category; Functional limitations are restrictions in performing fundamental physical and mental actions used in daily life. According to this definition, walking should be included in this category; Disability is experienced difficulty doing activity in any domain of life due to a health or physical problem.

Our purpose was to identify a finite number of impairments that are critical for walking and can be practically measured in a geriatric setting. After a review of the literature, a number of consultations with international experts and extensive discussions, we outlined a reference model in which walking was deconstructed into a simple cascade of events as follows (the elements that were operationalized in our model are in bold): under a motivational clue the **brain** creates a motor program which is transported by **peripheral nerves** and activates **muscles** in a proper sequence. By transforming chemical into physical **energy**, muscles apply forces to the **skeleton**, move the **joints**, and produce forces that, applied to the floor through the feet, stabilize and move forward the body. This activity requires the **circulatory system** to continuously provide nutrients and oxygen to muscles and **visual, proprioceptive** and **vestibular systems** to ensure a continuous feedback.

The basic elements of this model can be classified into six main subsystems: (1) Central nervous system; (2) Peripheral nervous system; (3) Perceptual system, (4) Muscles; (5) Bone and Joints; (6) Energy production and delivery. Ideally, a comprehensive first-line approach to older patients who are experiencing progressive difficulties in walking should include measures for all these subsystems. Even when a precipitating factor that has had a large impact on mobility is easily identified, the potential coexistence of other impairments that contribute to the clinical syndrome is likely and should not be neglected.[40] However, evaluating all subsystems is clinically useful only if the relationship between each factor and walking ability is fully characterized. In fact, because all the subsystems underlying walking ability have a certain amount of functional reserve, small impairments are compatible with normal walking. Only when the magnitude of damage falls below a critical threshold may we assume that the impairment in a specific system contributes to walking difficulties. For example, as already mentioned, clinical and epidemiological studies have shown that above a certain threshold, lower extremity muscle strength is not related to walking speed.[14,41,42] Knowing analogous critical cut points for all six subsystems would help to identify the cause of walking disability in specific patients and to lay out treatment plans

tailored to the underlying impairments. Finding such critical cut points was the main reason why the InCHIANTI study was implemented.

ESTABLISHING THE CAUSES OF DECLINE IN THE ABILITY TO WALK IN AN EPIDEMIOLOGICAL STUDY. THE DESIGN OF INCHIANTI

InCHIANTI (Invecchiare in Chianti, aging in the Chianti area) is a study of the factors contributing to the decline of mobility in late life designed by the Laboratory of Clinical Epidemiology of the Italian National Research Council on Aging, (INRCA, Florence, Italy) in a partnership with the local administrators and the primary care physicians of Greve in Chianti and Bagno a Ripoli, two small towns in the countryside of the Tuscany area where Chianti wine is produced. The data collection started in September 1998 and was completed in March 2000.

The main goals of the InCHIANTI study are: (1) To understand multiple risk factors that influence loss of the ability to walk in older persons; (2) To identify physiologic subsystems that are critical for walking and to develop measures of their integrity that can be administered in a clinical setting; (3) To define critical ranges for tests that evaluate the integrity of the walking subsystems; (4) To translate epidemiological data into clinical tools for the differential diagnosis of the causes of walking disability in older persons.

The Population Sample

InCHIANTI was performed in two sites: Greve in Chianti (11,709 inhabitants; ≥ 65 years: 19.3%; middle of a rural area) and Bagno a Ripoli (Village of Antella, 4704 inhabitants; ≥ 65 years: 20.3%; located outside the urban area of Florence).

In August 1998, 1270 persons aged 65 years or more were selected randomly from the population registry of the two sites. Another 29 subjects were selected randomly from among those who were aged 90 years or older, until at least 30 men and 30 women from this age group were included in the sample. Finally, men and women sampled randomly from the age strata 20–29, 30–39, 40–49, 50–59, and 60–64 years were sequentially invited to participate in the study until at least 30 men and 30 women for each decade from 20 to 59, and 10 men and 10 women aged 60 to 64 had been enrolled. Overall, under the age of 65 years, 69.4% (299/431) of those who were contacted were enrolled in the study. The age and sex distribution of the sample for those persons aged 65 years or more, shown in Table 1, is compared with the reference population and shown separately for the two sites. Of the initial 1299 subjects included in the sample, 17 men and 22 women were not eligible for the study because they had already died or moved away from the area. In those who were eligible, participation rate was very high (overall 91.6%; 1154/1260), tended to increase with age, and, in each age group, was higher for women than for men. There was, however, a drop in participation of the oldest-old (age ≥ 85 years, men: 77.1% women: 78.4%). The percentage of persons who were interviewed but refused to participate in other phases of the study was below 5% for participants younger than 75 years and increased progressively with age up to 19.1% and 21.0%, respectively, in men and women aged 85 years or older.

Overall, of 640 men and 813 women who were interviewed, 577 men and 720 women completed the clinical test session, 588 men and 729 women received a medical examination and functional evaluation on a separate day, and a blood sample was collected from 587 men and 744 women.

Field Data Collection

The INRCA ethical committee ratified the entire study protocol. Shortly after receiving a letter of invitation, a home interview was scheduled by telephone with the potential participant. Subjects who refused the interview were con-

Table 1. Comparison Between the Reference Population and the Initial Sample of the InCHIANTI Study

	Site 1 Greve in Chianti (Total residents = 11.709)				Site 2 Bagno a Ripoli (Antella) (Total residents n = 4.704)			
	Population		Sample		Population		Sample	
	N	%*	133†	%‡	N	%*	N†	%‡
Men								
65–69 yrs	327	2.8	76	23.2	133	2.8	83	62.4
70–74 yrs	329	2.8	86	26.1	119	2.5	72	60.5
75–79 yrs	249	2.1	55	22.1	75	1.6	48	64.0
80–84 yrs	102	0.9	26	25.7	48	1.0	28	58.3
85–89 yrs	100	0.9	21	21.0	35	0.7	23	65.7
90+ yrs	25	0.2	15	60.0	20	0.4	20	100.0
Women								
65–69 yrs	395	3.4	104	26.3	153	3.3	86	56.2
70–74 yrs	368	3.2	83	22.6	130	2.8	85	65.4
75–79 yrs	301	2.6	73	24.3	112	2.4	86	76.8
80–84 yrs	181	1.6	42	23.2	82	1.7	48	58.5
85–89 yrs	179	1.4	41	22.9	64	1.4	45	70.3
90+ yrs	66	0.6	24	36.4	33	0.7	29	87.8

*Percentage of the total reference population, which includes all persons recorded in the town registry office except those whose parents were both non-Italian.
†Those over the age of 90 were oversampled in order to obtain at least 15 men and 15 women in this age group.
‡Percentages of those in the same sex and age group in the reference population.
The subsample of persons <65 years is not reported in this table.

tacted at least four additional times before being considered refusals. Interviews were conducted at the participants' homes by three experienced interviewers. In persons who scored 18 or less on the Mini- Mental State Examination[43] the interview was administered to a proxy. The participants signed an informed participation consent that included permission to consult administrative databases and medical charts and to conduct analyses on samples stored in the biological bank. The interviewer collected information on architectural barriers, household composition and social networks, depressive symptoms,[44] ability to perform daily life activities (with particular focus on walking and including information on time since disability onset, most likely cause, and availability of a caregiver),[45–48] foot problems, falls and fear of falling,[49,50] present and past health-related behaviors, current and past pharmacological treatments,[51] incontinence, quality of sleep,[52] and food intake.[53] The interviewer scheduled two additional appointments and explained the procedure for the 24-hour urine collection, including the food to be avoided (any meat and fish) during the urine collection and over the previous 48 hours.

Within 3 weeks of the home interview, the participant came to the study clinic in the morning, having fasted for at least 8 hours and having just concluded the 24-hour urine collection. A 60-mL blood sample was drawn, stored in cold glass tubes, and delivered within 2 hours to the central laboratory that performed several tests of hematology and clinical chemistry and prepared the samples for the biological bank. These included: 0.3 mL aliquots of plasma and serum and 10 mL aliquots of urine stored at −80°C. Samples of genomic DNA extracted from leukocytes were stored in sterile tubes at 4°C.[54] On the same day, the participants underwent a peripheral quantitative computed tomography (pQCT, Norland Stratec XCT-960 pQCT scanner),[55] a surface electroneurography assessing nerve conduction velocity of the right peroneal nerve,[56] a standard electrocardiogram, an ultrasound color doppler examination of the carotids, vertebral arteries, and veins of the lower limbs, and an assessment of the ankle-brachial index.

Within 2 weeks, the participant returned for a structured medical examination and an objective assessment of physical function performed, respectively, by trained geriatricians and physical therapists. Presence and severity of major medical conditions were ascertained according to standard algorithms[57] that used information on medical history, drug treatments, signs and symptoms, medical documents and hospital discharge records. For participants affected by a disorder of gait, the geriatrician was asked to estimate the most likely cause. The functional examination was aimed at objectively assessing several aspects of physical function, with particular consideration given to muscle strength, joint range of motion, and walking (Table 2). Most performance-based tests had been specifically created for the InCHIANTI study to obtain an ecological assessment of walking ability by incorporating into the walking task several types of interferences that recreate situations that pose environmental challenges, similar to those encountered while walking in daily life.

MEASURES FOR THE SUBSYSTEMS THAT DETERMINE WALKING FUNCTION IN INCHIANTI

In designing InCHIANTI, we operationalized the assessment of the six subsystems that may influence walking ability into measures that are feasible both in a clinical setting and in a large population-based study. Walking ability, the principal outcome of interest, was evaluated combining subjective and objective information. The subjective evaluation started by asking the participant to estimate the maximum distance he/she could walk without stopping. The interviewer provided examples of distances taken from real life: for instance, 150 m was exemplified in Greve as the distance between the municipal building and the local supermarket. Further questions were aimed at assessing: how long the participant usually walked outside home on an average day, according to weather conditions; the degree of difficulty experienced in prolonged walks over uneven (e.g., country roads), slippery (e.g., icy roads), or soft (e.g., sand) surfaces; whether disability in specific activities of daily life was due to mobility problems rather than to other functional limitations.

The objective assessment of walking started with a traditional evaluation of gait velocity over 4 and 7 meters, followed by "provocative" tests including : (1) walking as fast as possible without running; (2) walking fast within the limits of a narrow path (particularly difficult for persons with balance problems who need to maintain a large base of support in order to walk safely); (3) walking with long steps (more energy is required to move the center of gravity up and down over a wider range); (4) overcoming obstacles first with normal illumination and in a semi-dark condition (difficult

Table 2. Assessments Performed in the InCHIANTI Functional Evaluation

Height and weight
Standardized evaluation of balance (60)
Uni- and bi-manual dexterity using the Purdue Pegboard[61]
Objective evaluation of the ability to use stairs
Time to perform 5 chair-stands[12]
Dynamic baropodometric analysis
Performance-based tests of walking*
Walking 4 m and 7 m at usual pace
Walking 4 m and 7 m as fast as possible
Walking 4 m within the limits of a 25 and 15 cm wide path, as fast as possible
Walking 7 m with steps as long as possible
Walking 7 m stepping over 2 obstacles with and without sunglasses
Walking 7 m carrying a large package that does not allow a view of the feet
"Talking while Walking" (7 cm)
Collecting a specific object from the ground during a 7-m walk
Walking 400 m as fast as possible
Walking 60 m as fast as possible while wearing a heavy jacket that increases the weight of the participant by 15%
Anthropometrical measures of the lower extremity
Range of motion of all principal movements of hips, knees, ankles and shoulders[62,63]
Lower extremity muscle power[64]
Muscle strength assessed on 8 muscle groups of the lower extremity and 2 muscle groups of the upper extremity[65]
Grip strength (JAMAR dynamometer, model #BK-7498, Fred Sammons, Inc., Burr Ridge, IL.

*The measure of times in the walking tests was performed using an optoelectronic system connected to a digital chronometer and a printer (Chronoprinter Tag-Heuer CP501, Zingerle Sports Timing, BZ-Italy).

Table 3. Tests Used in InCHIANTI to Evaluate the Degree of Impairment in Each of the Six Subsystems That Influence Walking Performance.

Bone
Trabecular and cortical bone density estimated from pQTC images obtained from right lower leg[55]
Biomarkers of bone metabolism included circulating levels of calcium, bone-specific alkaline phosphatase, Vitamin D, parathyroid hormone and 24-hour urinary excretion of calcium and c-telopeptide of type I collagen.
Participants who reported foot pain while standing or walking evaluated by an expert podiatrist who performed an objective and instrumental examination to establish the causes of such pain and estimate the chances of effective treatment
Spinal mobility evaluated as absolute change in the distance between the spinous processes of the C7 and S1 vertebrae when moving from upright position to maximal trunk flexion, and measuring the distance between C7 and the wall while the person was standing straight with the back touching the wall[66]
Joints
Goniometric measures of the passive range of motion of the hip (abduction, adduction, flexion, extension and external rotation), knee (flexion and extension), ankle (flexion and extension) and shoulder (abduction and elevation)[62,63]
Clinical joint examination
Pain of the lower back, hips and knees and its severity evaluated using standard instruments[67]
Muscle
Lower leg muscle mass, intra-muscular fat and sub-cutaneous fat estimated from pQTC images[43]
Isometric muscle strength using a hand held dynamometer (Nicholas Manual Muscle Tester, Model #BK-5474, Fred Sammons, Inc., Burr Ridge, IL) on 8 muscle groups of the lower extremity (abduction, adduction, flexion and extension of hip; flexion and extension of knee and ankle) and 2 of the upper extremity (abduction and elevation of the shoulder)[65]
Lower extremity explosive muscle power (physical work delivered to the external environment in a unit of time) evaluated using the device proposed by Bassey et. al[64]
Biomarkers of muscle metabolism included circulating levels of myoglobin and creatinine and 24-hour urinary excretion of creatinine and 3-methylhystidine,[68] and the characterization of polymorphisms for myostatin[69,70]
Peripheral nervous system and perceptual system
Nerve conduction velocity evaluated in the right peroneal nerve by standard surface electroneurography[56]
Proprioceptive and vibration sensitivity assessed in the lower extremity by standard methods[71]
Tactile sensitivity assessed using von Frey's monofilaments of pre-defined rigidity[72]
Symptoms attributable to peripheral neuropathy and vestibular dysfunction investigated using specific questionnaires[73]
Near (30 cm) and far (3 m) visual acuity, contrast sensitivity and 3-dimensional perception investigated by standard methods.
Central nervous system
Screening of cognitive impairment performed by the Mini Mental State Examination.[43] Participants who screened positive underwent a comprehensive clinical and neuropsychological assessment to establish the diagnosis of dementia based on the DSM-IIIR criteria[74]
The psychological component of mobility was assessed in term of depressive symptoms and personal mastery by, respectively, the Center for Epidemiological Studies Depression Scale (CES-D) (44) and selected questions from the Hopkins Symptoms Checklist[75]
Ability to maintain balance for ten second in progressively more challenging positions (free position, feet under the anterior iliac spines, feet side by side, semi-tandem, tandem, one leg)[76]
Detailed neurological examination specifically designed to detect even minor signs of neurological impairment such as tremor, pathological reflexes, sub-cortical reflexes, delay in movement initiation, manual dexterity, coordination, ability to perform rhythmic repetitive movements.
Energy production and delivery
Daily intake of various macro and micronutrients assessed by the EPIC questionnaire[53,77]
Circulatory and respiratory function evaluated by standard medical examination
Venous insufficiency and thrombosis evaluated using color-doppler scan
Arterial circulation assessed by measuring ankle-brachial index

for persons with even minor neurological impairments and visual deficits, especially contrast sensitivity); (5) walking carrying a large, light package that obstructs the view of the feet (challenging for persons with impaired proprioception); (6) talking while walking: answering a standard question during walking (the superimposition of a motor and a cognitive task is problematic in persons with even minimal cerebral damage)[58,59]; (7) picking up an object from the floor while walking; (8) walking fast for 400 m (exercise tolerance); (9) walking 60 m while wearing a jacket that increased the weight of the participant by 15%. Finally, the spatial and temporal distribution of weight on the sole while walking was measured with and without shoes using a 1.6-m-long baropodometric mat (ACD Podinamic Sensor, Zeno Buratto Spa. TV, Italy).

A list of the measures that were used to establish the degree of impairment in each of the physiologic subsystems affecting walking ability is shown in Table 3. Balance, a

critical element in walking, is listed under the central nervous system but was difficult to classify under one category as balance problems may result from multiple impairments. Additional information on assessment protocols can be obtained upon request and is accessible on the web site *www.studioinchianti.it.*

BRIDGING THE GAP BETWEEN EPIDEMIOLOGY AND GERIATRIC PRACTICE

InCHIANTI has the potential to shed light on how specific impairments influence the ability to walk in older persons and, in most cases, on what is causing such impairments. The approach is designed to be comprehensive. However, the number of variables needed to fully fit this theoretical model is probably too large to be proposed "as is" for use in geriatric practice. Indeed, the main purpose of InCHIANTI is to establish a minimum set of clinical variables that, in the majority of cases, allow the detection of the underlying causes of walking difficulties and the identification of critical thresholds in these variables that improve their clinical usefulness.

The concept of a clinical threshold is paramount for InCHIANTI and will be a unique contribution of this study to the geriatric field. Thresholds values for blood levels of different cells or chemicals are used every day for the diagnosis of many medical conditions such as diabetes (high glucose), and anemia (low hemoglobin). To a certain extent, InCHIANTI can bring to geriatricians analogous thresholds for the clinical variables that are relevant in the assessment of walking ability, thereby making possible better diagnoses and targeted, more effective treatments. However, threshold values estimated from cross-sectional data should be considered with caution. Walking problems may start from specific impairments, but the resulting reduction of mobility may itself cause additional impairments that complicate the clinical picture. For example, hip arthritis reduces mobility, thereby causing a secondary reduction of muscle strength and mass. Only when longitudinal data are collected will it be possible to sort out the role of specific impairments in the process that leads to walking disability in old age and to estimate functional thresholds that are valid and precise. A longitudinal perspective will also widen the clinical usefulness of the InCHIANTI model. We can hypothesize the existence of ranges of impairments that coexist with normal gait but are predictive of accelerated decline in walking performance. The identification of such "soft" thresholds, indicating preclinical impairments, will be particularly useful for screening candidates for preventive interventions.

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