Using Multidimensional Prognostic Indices to improve cost-effectiveness of interventions in multimorbid, frail older persons
The MPI_AGE project is a research project co-funded by the European Union through the Health 2007-2013 Programme that has explored ways to reduce unnecessary use of health care resources in older subjects through the design of appropriate, tailored, integrated, multi-professional, planned interventions.

This project opted to use a well-validated diagnostic and prognostic tool, the Multidimensional Prognostic Index (MPI), based on a standard Comprehensive Geriatric Assessment (CGA), and analyzed how it can improve the cost-effectiveness of health interventions in complex older individuals with multimorbidity and polypharmacy.

To do so, a review analysis on the use of predictive rules in clinical and management decision making in older residents in different European regions has been performed to identify reference models to allocate resources and lower costs in healthcare.

Analyses of multi-national databases including information on drug prescriptions and older subjects’ characteristics have identified some setting-specific MPI-profiles in which individual interventions are more cost-effective in terms of improved survival.

The aims of the MPI_AGE project were to:

- identify the most cost-effective health interventions according to the individual prognostic mortality-risk profile;
- improve multi-professional interactions and collaboration in performing integrated care pathways of interventions according to the individual MPI-risk profile;
- develop tailored intervention programs based on the individual MPI-profile of older subjects;
- explore ways to reduce health-related costs, linked to a reduction of hospitalization rates, in-hospital length-of stay, institutionalization rates, and inappropriate and unnecessary prescription drug use.
The MPI_AGE project involves the following centers and organizations in twelve different countries.

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TH E M ULTIDIMENSIONAL PROG NOSTIC INDEX (MPI)

MPI is a prognostic tool based on a standard CGA that has been shown to predict short- and long-term survival in older subjects, as well as other negative health outcomes (hospitalization, nursing home admission, length of hospital stay).

The MPI includes information in 8 domains of CGA as follows:

1. Activities of Daily Living (ADL): 6 items
2. Instrumental Activities of Daily Living (IADL): 8 items
3. Short Portable Mental Status Questionnaire (SPMSQ): 10 items
4. Mini Nutritional Assessment (MNA): 18 items
5. Exton-Smith Scale (ESS): 5 items
6. Cumulative Index Rating Scale – Comorbidity Index (CIRS-CI): 14 items
7. Number of drugs used: 1 item
8. Co-habitation status: 1 item

To obtain the final index of a given individual, a program calculates a MPI score, which ranges from 0 to 1. This calculation can be easily performed by a program that can be downloaded at no cost (www.mpiage.eu) or using an IOS free app (iMPI).

The MPI index predicts mortality – lower values are associated with lower mortality. Usually, results are ranked in three levels:

- 0 to 0.33 – low mortality risk, MPI 1
- 0.34 to 0.66 – moderate mortality risk, MPI 2
- 0.67 to 1 – high mortality risk, MPI 3

Studies have shown that MPI values predict short and long-term mortality in older subjects. The prognostic accuracy of the aggregated MPI is significantly greater than the prognostic accuracy of its individual components considered singularly. Thus, this multidimensional approach can be successfully used in older patients for both clinical and administrative purposes.
A cluster analysis on CGA data was made to identify independent domains and variables of CGA that predicted mortality. Following a step-wise method, other domains of the CGA were progressively included in the model in order to obtain the best combination of different CGA domains for the best prognostic accuracy. Clinical results have confirmed that MPI has a good prognostic effect on short- and long-term mortality, with a close agreement between the estimated and the observed mortality. The MPI has been validated in geriatric complex patients, and also in older patients affected with several acute and chronic diseases such as gastrointestinal bleeding, pneumonia, heart failure, dementia, liver cirrhosis, chronic kidney disease and transient ischemic attack.

The MPI has been validated in hospitalized older people, community-dwelling older (to establish accessibility to nursing homes or homecare services, and healthy older people). Many clinical studies and recent meta-analyses and systematic reviews report that the MPI has high accuracy, excellent calibration, and the highest validity, reliability and feasibility compared to others tools used to identify frail older patients both in clinical practice and in research.

**MPI-SVAMA**

The MPI-SVAMA index is an evolution of the MPI. This version obtains information from SVAMA (Scheda per la Valutazione Multidimensionale delle persone adulte e Anziane), a standardized CGA used in the Veneto Region (Italy) to grant access to health and social care.

The MPI-SVAMA index is calculated from the following nine domains:

1. Age (years)
2. Gender
3. Nursing care: 11 items
4. Exton-Smith scale: 5 items
5. Short Portable Mental Status Questionnaire: 10 items
6. Activities of Daily Living: 6 items
7. Functional mobility (mobility items of Barthel scale): 3 items
8. Social network: 1 item
9. Main medical diagnosis

MPI-SVAMA was built using information from SVAMA of a population of more than 7,800 older people aged ≥ 65 years old living at home, and validated on a separate population of over 4,000 older subjects, using 1-month and 1-year mortality as outcomes. This index can be calculated with the use of a free program (www.mpiage.eu), and also ranges from 0 to 1. However, cut-off points used to rank MPI-SVAMA are different and time dependent.

For short term mortality (1 month):
- 0 to 0.41 – low mortality risk, MPI 1
- 0.42 to 0.53 – moderate mortality risk, MPI 2
- 0.54 to 1 – high mortality risk, MPI 3

For long term mortality (1 year):
- 0 to 0.33 – low mortality risk, MPI 1
- 0.34 to 0.47 – moderate mortality risk, MPI 2
- 0.48 to 1 – high mortality risk, MPI 3
A. Analysis on the use of predictive rules in clinical decision making in community-dwelling older people.

An analysis on the use of predictive rules (MPI) in clinical and management decision-making in community-dwelling older subjects was performed using clinical, functional and administrative data included in large databases from different European regions.

Population-based cohort databases containing data on large populations are potentially an accurate source in predicting multidimensional impairment and frailty in heterogeneous groups of older persons in terms of short- and long-term mortality and other negative health outcomes. This is important for appropriate health care planning. We explored the adaptation of MPI to be used in large databases in order to classify patients to improve decision making.

Multidimensional Prognostic Index in community dwelling older healthy people

The application of MPI in 2,472 older residents in Stockholm (Sweden) included in the Swedish National Study on Aging and Care (SNAC-K) demonstrated a clear and significant association between MPI score and survival time and risk of hospitalization.

Higher MPI risk scores were associated with more days in hospital and with fewer years of survival across a broad and stratified age range (65-74 years, 75-84 years, > 84 years) in this population based setting with a very long-term follow-up (up to 12 years). This is the first study that confirms the prognostic value of MPI in a population-based cohort.

Multidimensional Prognostic Index in community dwelling older people with dementia

Previous studies showed that MPI accurately stratified hospitalized older patients with dementia into groups at varying risk of short- and long-term mortality. Also, MPI was shown to predict the risk of hospitalization in outpatients with cognitive impairment and dementia. Moreover, the MPI has been used as a valid outcome measure in an intervention trial in patients with Alzheimer’s disease.

In MPI_AGE, a cohort of 6,800 community-dwelling older persons with dementia were identified in a database of almost 23,000 community-dwelling older residents in Veneto Region (Italy) who applied to homecare services or nursing home admission. In this population, MPI strongly predicted 3-year mortality. When stratified according to MPI-defined strata, after adjustment for covariables, the use of drugs for dementia (anti-cholinesterase inhibitors and/or memantine) was associated with lower mortality in subjects with MPI-defined low-risk (HR 0.71; 95%CI 0.54-0.92, p<0.01) and moderate-risk (HR 0.61, 95%CI 0.40-0.91, p<0.01), but not in those with high-risk of mortality (HR 1.04, 95%CI 0.52-2.06). These results show that MPI may be useful to make recommendations on treatments in Alzheimer’s disease patients.
B. Use of MPI to improve cost-effectiveness of drug treatments in older people with multimorbidity and polypharmacy.

MPI was used to identify the effectiveness of different drugs across different levels of frailty and dependence in large multinational databases.

Multidimensional Prognostic Index in a general practice database

MPI_AGE explored the usefulness of data included in the THIN database (this database collects information on almost 1,200,000 subjects followed-up by their General Practitioners in the United Kingdom). It was found that multidimensional indicators were not frequently recorded in the THIN database, so a full MPI could not be obtained. However, the accuracy of a model incorporating age, sex, and available functional and cognitive measures was able to predict 1-month and 1-year mortality among community-dwelling older people. The use of such indicators in GP database reflects a newer approach, which may improve mortality prediction among older persons in clinical practice. Expanding the adaptation of MPI or MPI principles to other large databases may be helpful to better classify patients in order to tailor resource use.

Multidimensional Prognostic Index and the care of frail older people: where evidence is lacking

Frail subjects are usually excluded from clinical trials, so clinical guidelines give little insight on how to treat frequent problems in geriatric complex patients. This fact frequently leads to potentially inappropriate under- or over-utilization of drugs and interventions, increasing the risk of adverse drug reactions and reducing the efficiency of use of scarce resources. The use of MPI to better understand risks and benefits of drug treatments in this population was explored in two areas in which evidence is still lacking and the risk-benefit ratios are unclear: the use of statins and anticoagulation therapies in very old, high-risk, frail subjects. First, in the database of almost 23,000 community-dwelling older residents in Veneto Region (Italy), 1,712 subjects with diabetes mellitus (mean age=81.1±7.3 years, males = 43%) were selected. By using the clinical stratification according to the MPI, it was shown that statin treatment was significantly associated with reduced three-year mortality independently of age and multidimensional impairment in this population. A second population of 2,597 patients with coronary artery disease was also analyzed (mean age=84±7.3 years, males = 44.5%), again showing that statin treatment was significantly associated with reduced three-year mortality independently of age and MPI score, although the frailest were less likely to be treated with statins. Put together, these finding are reassuring of the use of statins in old, complex patients that were excluded from trials but are already using such drugs. Finally, a study of 1,827 community-dwelling older persons with atrial fibrillation classified by the MPI in three grades of risk demonstrated a benefit of anticoagulation in terms of lower all-cause mortality over a mean follow-up of 2 years, regardless of poor health and functional conditions. Interaction tests showed that reduction of mortality with anticoagulants was higher in subjects with severe complexity (higher MPI score).

Multidimensional Prognostic Index and invasive procedures

An additional relevant topic in geriatric medicine is the appropriate selection of older patients who can benefit from interventions with invasive therapeutic procedures. To explore the use of MPI in this clinical setting, a prospective observational study was carried out in consecutive patients aged ≥75 years who underwent transcatheter aortic valve implantation (TAVI). MPI was calculated at baseline. A follow-up time of 1-year was performed. Among the 116 patients included (mean age 86.2±4.2 years, mean MPI score 0.39±0.13), mortality rate was significantly different between MPI groups at 6 and 12 months (p=0.04 and p=0.02). Kaplan Meier survival estimates at 1-year stratified by MPI groups were significantly different (HR=2.83, 95% CI 1.38-5.82, p=0.004). The study indicated that CGA-based MPI was an accurate tool to predict prognosis and select older patients for TAVI procedures.
C. Use of MPI to improve resource allocation in older hospitalized persons.

A large multicenter clinical trial was performed to analyze the role of MPI in the identification of hospitalized patients with different characteristics and needs, which were prospectively followed for 1 year.

In the last years, great attention has been given to the proper identification of prognosis to help clinical decision-making to tailor appropriate diagnostic and treatment interventions for frail older patients. It is now well known that adding functional, cognitive, nutritional and social data improves prognostic tools that are only based on an index disease, so multidimensional tools should be useful to better quantify the prognosis of frail older subjects.

However, a large systematic review identified, after searching over 20,000 references, a very small number of validated prognostic indices for mortality that meet the necessary requirements of accuracy and calibration required to be used in a clinical setting, i.e. eight indices for hospitalized older patients, two for those living in nursing homes, and six for community-dwellers. Among the eight indices studied in hospital settings, MPI was the only CGA-based predictive tool. MPI is well-calibrated and has a good discrimination properties and accuracy in predicting mortality both at short-term (1 month) and long-term (1 year). Very recently, a systematic review reported that MPI had the highest validity, reliability and feasibility (i.e. score 14 - maximum value - on the QUADAS system), compared to other tools used to identify frail older patients.

MPI has been used in several multi-center studies in Italy to predict prognosis in hospitalized, frail older individuals. For example, in a prospective multicenter study involving over 2,000 hospitalized older patients in 20 different hospitals, MPI was a significantly more accurate predictor of short- and long-term all-cause mortality than other three frailty indices commonly used in clinical practice including FI-CGA and SOF. Other prospective multicenter studies demonstrated that MPI was an independent predictor of in-hospital mortality and of length of hospital stay in such populations. Moreover, during hospitalization MPI score changed in most of patients (overall, the MPI score improved in 35.3% and worsened in 26.6% of patients, these changes were gender and age-related) and therefore MPI might be used to objectively track and monitor the clinical evolution of acutely ill older patients admitted to the hospital.

The MPI_AGE multicenter trial

Based on these findings, the MPI_AGE project evaluated prospectively 1,148 hospitalized patients recruited in 9 international centers across Europe and Australia (mean age 84.4±8.8 years, females = 61%) and classified them according to the MPI score at admission and at discharge from the hospital. Patients were followed for one year.

Results of this prospective multicenter international study confirmed that MPI at hospital admission significantly predicts in-hospital mortality (MPI-1 HR =1.0 [reference], MPI-2 HR=3.0, 95%CI 1.4-6.7, MPI-3 HR=10.4, 95%CI 4.7-23.2) with good accuracy (area under the curve-AUC=0.76, p<0.001) and MPI at hospital discharge significantly predicts 1-year mortality (MPI-1 HR =1.0 [reference], MPI-2 HR=2.4, 95%CI 1.1-5.4, MPI-3 HR=12.1, 95%CI: 5.2-28.1), again with good accuracy (AUC 0.77). Moreover, MPI class on admission was significantly predictive of length-of-hospital stay (LOS), i.e. MPI 1= 7.9±5.6 days vs MPI 2= 13.5±10.2 days vs MPI 3= 16.5±13.6 days (data adjusted for age, gender, hospital and diagnosis at discharge).
In this population, MPI significantly changed during hospitalization in most of patients, improving in 35% and worsening in 27% of them. Interestingly, an improvement of MPI during hospitalization was associated with a significant reduction in mortality at 1 year (HR=0.65, 95%CI 0.48-0.87, p=0.004). In addition, MPI worsening was significantly associated with a 54% increase in the use of home-services (HR 1.54, 95%CI 1.10-2.15, p=0.01) (data adjusted for MPI at admission, age, gender, hospital, LOS and diagnosis at discharge).

Diagnostic tests used during hospitalization have been classified according to MPI value. Older patients with higher MPI values were more often diagnosed using X-Ray tests (MPI-1 54% vs MPI-2 55% vs MPI-3 61%, p=0.006) and less using ultrasonography (MPI-1 18.5% vs MPI-2 16.6% vs MPI-3 12.8%, p=0.01) or endoscopy (MPI-1 5.0% vs MPI-2 3.5% vs MPI-3 3.7%, p=0.02). No differences were observed in the use of CT, MRI or nuclear medicine diagnostic tests.

During the one-year follow-up period, MPI grade was also significantly associated with the use of home-care services (MPI-1 Odds Ratio 1.0 reference; MPI-2 OR 2.47, 95%CI 1.5-4.0, MPI-3 OR 1.82, 95%CI 1.1-3.0, p=0.002) and with admission to nursing homes (MPI-1 OR 1.0 reference; MPI-2 OR 2.2, 95%CI 1.3-3.8, MPI-3 OR 1.7, 95%CI 0.9-2.9, p=0.002).

Along the one-year follow-up, 606 out of 1,140 patients (53.1%) were re-hospitalized. One-year re-hospitalization was significantly associated with all-cause mortality (HR=1.79, 95%CI 1.42-2.36, p<0.001). Moreover, one-year re-hospitalization was significantly associated with higher MPI grade (MPI-1 Odds Ratio: 1.0 reference; MPI-2 OR 1.69, 95%CI 1.15-2.48, MPI-3 OR 1.60, 95%CI 1.07-2.38), lower age (OR=0.98, 95%CI 0.96-0.99), male gender (OR: 1.29, 95%CI 1.0-1.65) and the hospital center (OR: 0.91, 95%CI 0.86-0.96).
• Health interventions should be adapted to individual needs of older patients, especially for those with high disease burden, high complexity or relevant major physical and mental impairments.

• Individual needs should be objectively assessed by means of validated instruments. These instruments should be multidimensional to capture all aspects that are relevant for each person.

• Objective assessment of needs may avoid discrimination of older people (ageism) in decision-making.

• The Multidimensional Prognostic Index (MPI) has proved to be the best validated assessment instrument in various healthcare settings (community, hospital and nursing homes) and across a wide range of diseases and conditions.

• MPI also identifies problems in several domains that may benefit from specialist comprehensive geriatric care.

• Tailored healthcare interventions have the potential to reduce the inappropriate use of resources (hospitalizations, drugs, diagnostic and other procedures) and to allow well-established treatments and interventions to be used in older people who can benefit from them.

• Tailored healthcare interventions have the potential to reduce inappropriate health-related costs, making health care services more efficient.

• MPI can be adapted for use in population-based (Primary Care) and disease-oriented databases to accurately predict survival and other health outcomes. This can be helpful in order to plan resource deployment and allocation.

• In hospitalized older persons MPI identifies groups at risk for several hospital outcomes (i.e. mortality, length of stay, use of diagnostic tests). Individuals within each risk group may benefit from the adaptation of interventions to his/her prognosis and needs.

• In hospitalized older persons MPI predicts several post-discharge outcomes (one-year mortality, rehospitalisation, admission to a nursing home, use of home-care services).
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