Comprehensive Geriatric Assessment for Elderly Patients

Jee Hyun Kim, M.D., Ph.D.

**Seoul National University College of Medicine**

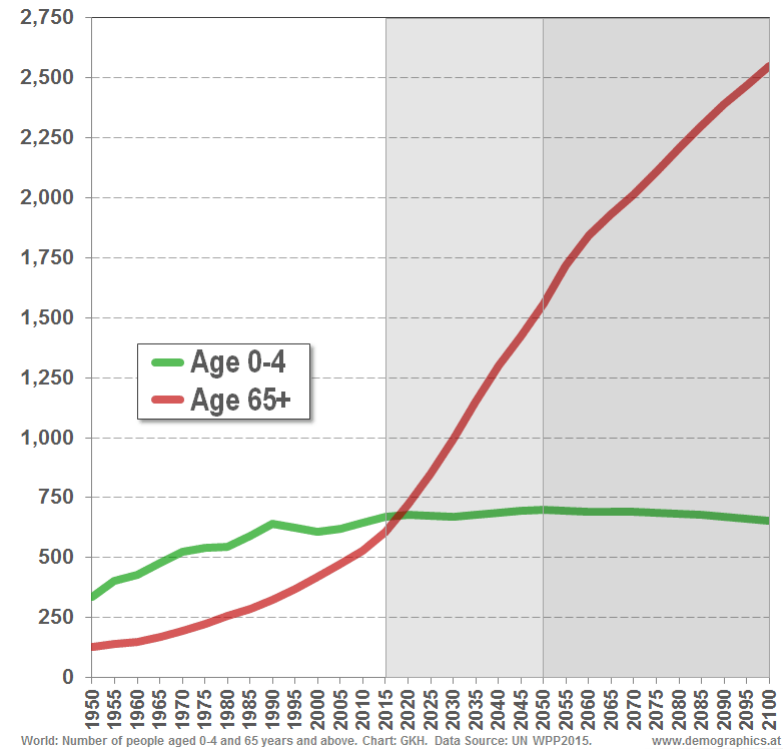**Seoul National University Bundang Hospital**

Contents

- Introduction on aging
  - Why do we need different approaches for older patients
- Geriatric assessment
  - Domains of GA
  - Clinical uses of GA in cancer
  - Screening tools
  - Application in oncology clinic
- Summary

World population is aging

Median age by major regions

Legend:
- World
- Africa
- Asia
- Europe
- Lat. America / Caribbean
- Northern America
- Oceania
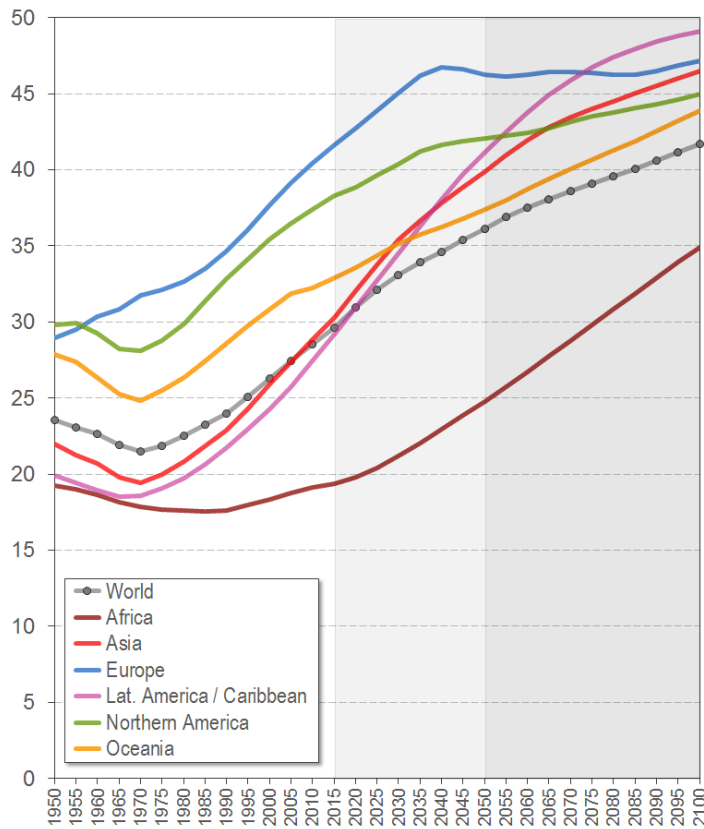
World: population aged 0-4 and 65+
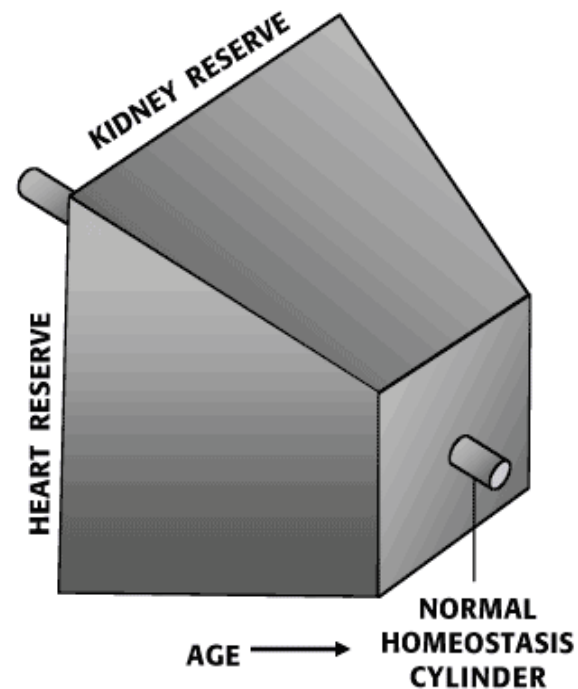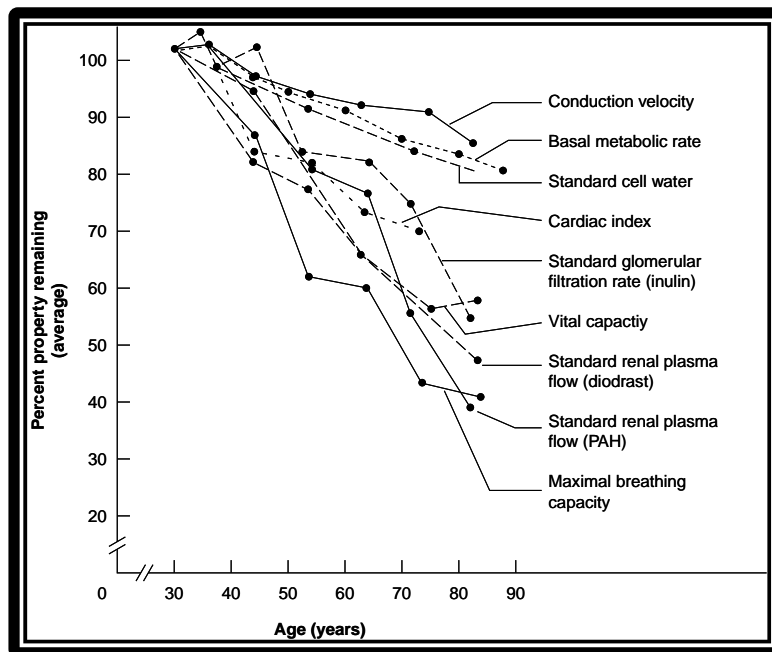

- Age 0-4
- Age 65+
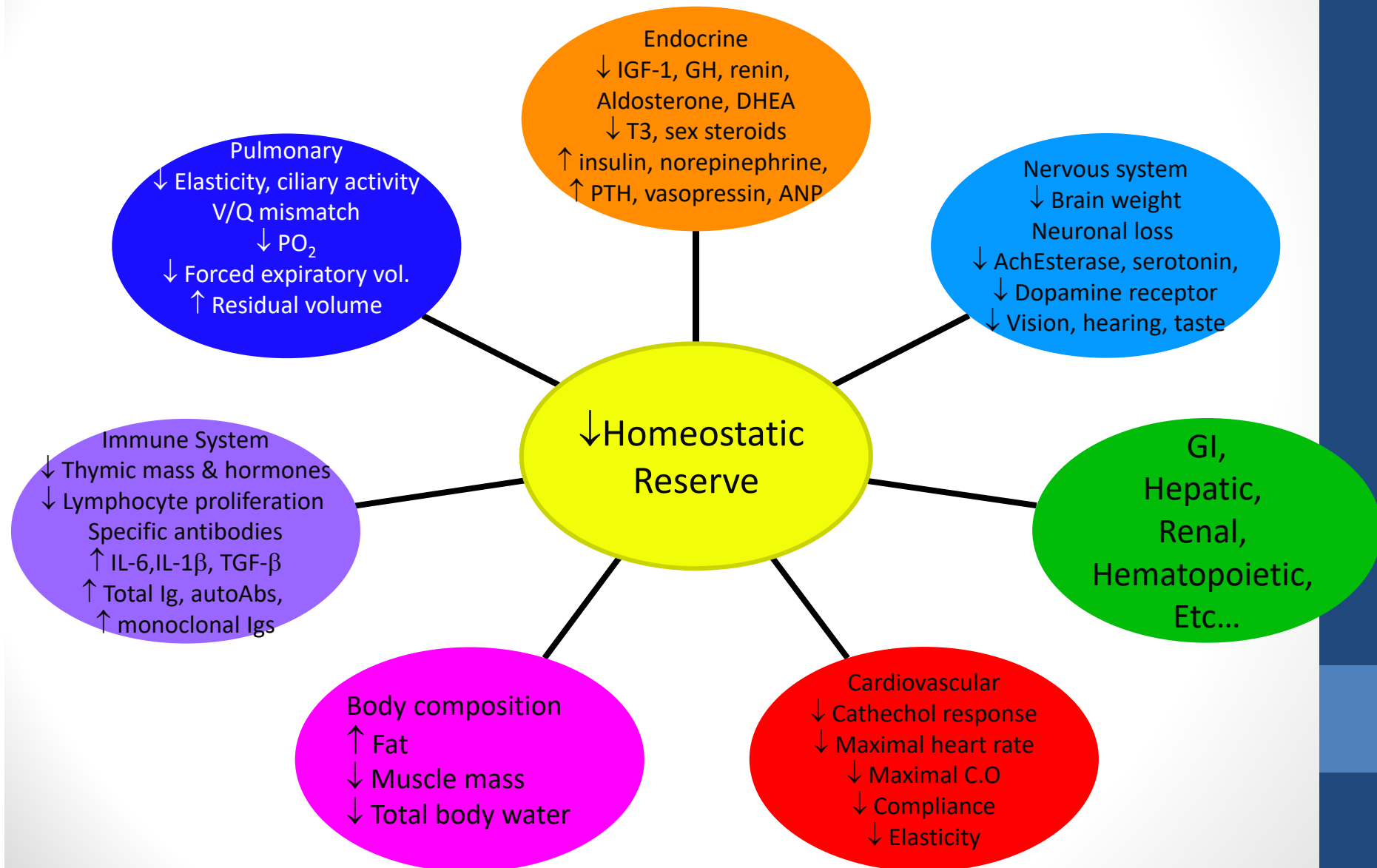
World: Number of people aged 0-4 and 65 years and above. Chart: GKH. Data Source: UN WPP2015. www.demographics.at

United Nations, World Population Prospects 2015

Aging = (homeostenosis)

- Progressive decline of stress tolerance due to restriction in the functional reserve of multiple organ systems.

Physiology of aging

What's different about older patients

- Disease presentation: atypical
  - Vague, atypical symptom
  - Change in eating/sleeping/toileting habit, fever may represent development of new illness
- Decreased physiologic reserve → develop symptoms at an earlier stage of their disease
  - Heart failure by mild hyperthyroidism, urinary retention by mild BPH
  - Drug side effects can occur at low dose
- Multiple pathology, polypharmacy
- Non-medical factors influence course of disease

Vulnerability of frail older patients

Functional abilities

Minor illness (eg, urinary tract infection)

Independent
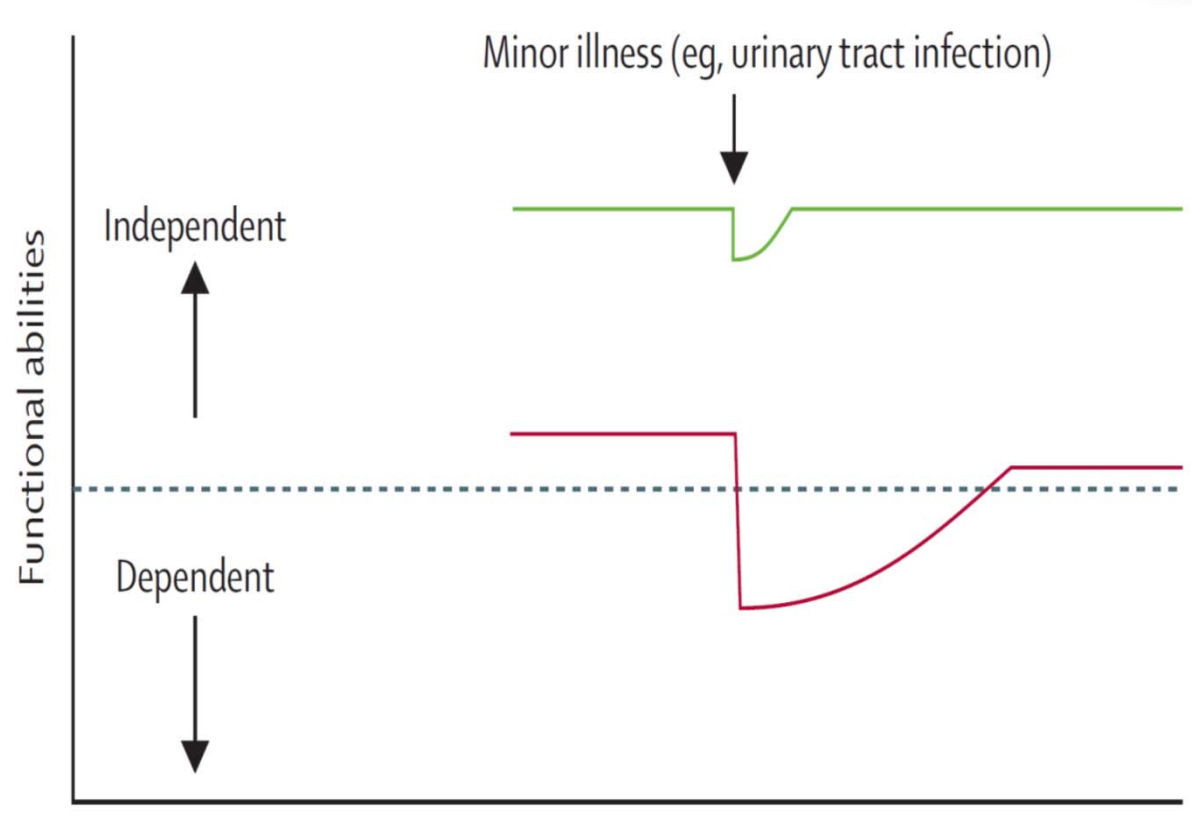
Dependent

Where is the patient? – determine phase of aging (biological age)

Fit	Vulnerable	Frail	Predeath

Little limitation in activity
Independent

Severe limitations with no significant recovery of functional reserve

Frailty phenotype by Cardiovascular Health Study
- Unintentional weight loss
  (10 pounds = 4.5kg, or 5% of body weight loss/year)
- Self-reported exhaustion
- Weakness (grip strength in the lowest 20%)
- Slow gait speed
- Low physical activity

Frailty $\geq$ 3, pre-frail: 1-2, non-fit

Fried LP, et al. J Gerontol A Biol Sci Med Sci 2001

Geriatric assessment

- Multi-dimensional, interdisciplinary evaluation tool used primarily by geriatricians to evaluate elderly patients' functional and global health status
  - Focused on defining the "physiologic age" of the patient identifying those at greatest risk of hospitalization and functional decline
  - Identify and manage age-related problems

Domains of GA

- Comorbidity
- Functional status
- Physical performance
- Nutritional status
- Polypharmacy

- Social support
- Cognition
- Psychological status

- CCI, CIRS-G
- ADL, IADL
- Timed Up and Go, grip strength
- BMI, MNA, unintentional wt loss
- Use of inappropriate medications (Beers criteria), No of medications
- Medical outcomes survey
- MMSE, MCA, BOMC, Mini-Cog
- GDS, Hospitalized Anxiety and Depression Scale, Distress thermometer

Functional Status

- Activities of daily living (ADLs)
  - Bathing
  - Dressing
  - Toileting
  - Transferring
  - Continence
  - Feeding

<u>Basic self-care skills required to maintain independence in the home</u>

Assistance with ADLs

- Predictive of
  - Prolonged hospital stay
  - Worsening of function in the hospital
  - Greater home care use
  - Nursing home placement
  - Death

  - Assistance in ≥ 1 ADL : average life expectancy of < 3 yrs

Narain et al. JAGS 1988, Mor et al, Am J Public Health, 1994

Functional Status

- Instrumental activity of daily living (IADLs)
  - Ability to use telephone
  - Shopping
  - Food preparation
  - Housekeeping
  - Laundry
  - Mode of transportation
  - Ability to take own medications
  - Ability to handle finances

<u>Higher order of function required to maintain independence in the community</u>

Needs for functional assistance → future institutionalization and mortality

Follow up (1990)

Baseline: functional status (1984)

N=7527 Age 70+	Odds Ratio	
	Risk of institutionalization (95% CI)	Risk of Mortality (95% CI)
IADL assistance	6.7 (4.6-9.6)	6.6 (5.1-8.6)
ADL assistance (moderate)	9.8 (6.8-14.0)	8.6 (6.6-11.0)
ADL assistance (severe)	17.0 (9.1-32.0)	30.0 (18.0-

Mor et al, Am J Public Health, 1994

Assistance with IADLs

- Better baseline IADL (p=0.04) significantly associated with better survival

Maione P et al, J Clin Oncol 2005;23:6865-72

Comorbidity

Number of comorbidities

Age	Number
55-64	2.9
65-74	3.6
>75	4.2
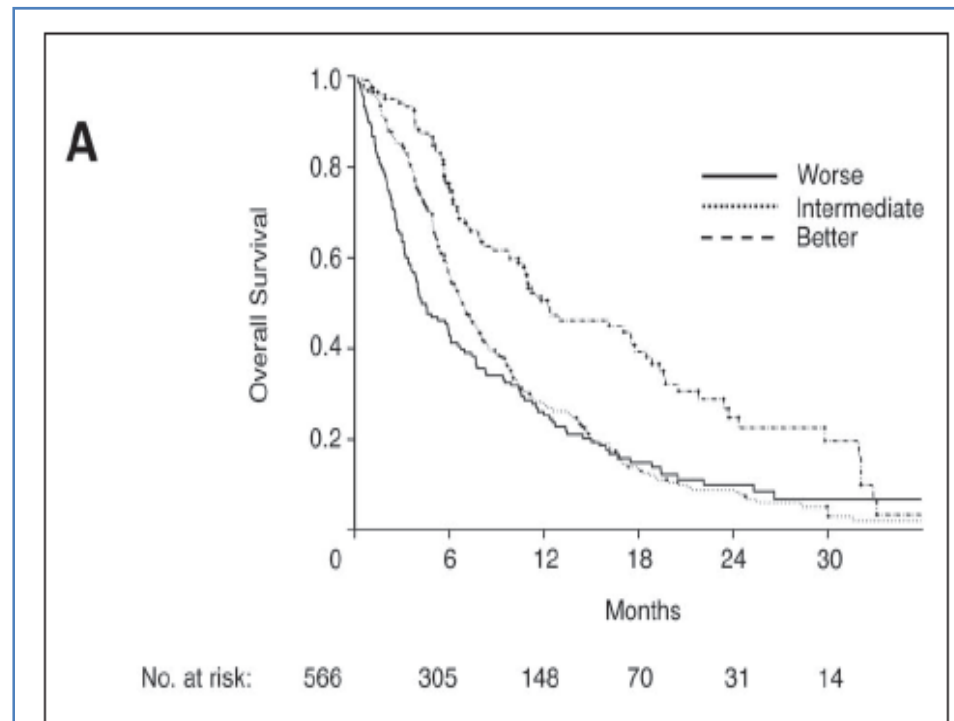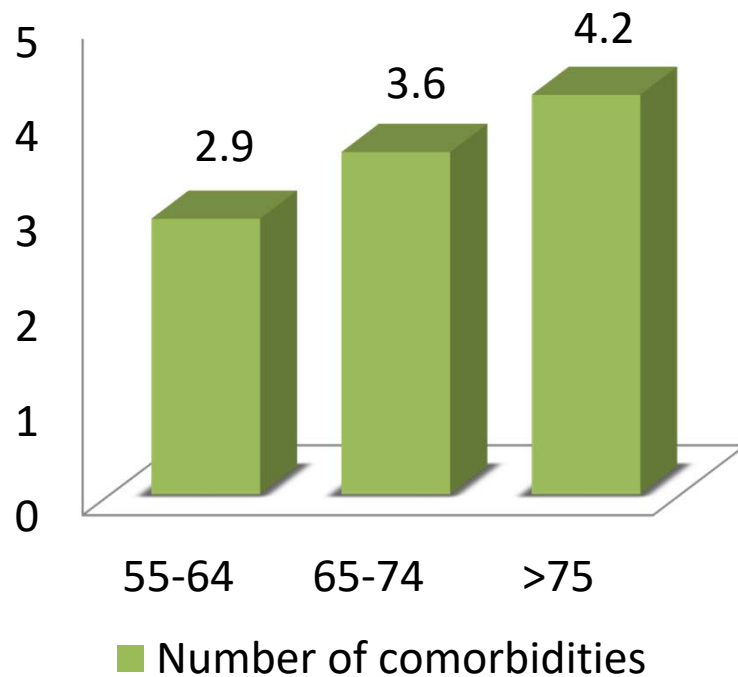
- Concurrent, independent health condition
- Increases with age
- Increase all cause mortality
  - ≥ 3 comorbidities associated with lower survival in cancer patients
- Increase the risk of complications
- Modify cancer behavior
- Mask symptoms with subsequent delays in cancer diagnosis
- Cancer treatment may worsen comorbidities or increase the frequency of drug interactions

Yancik et al, Cancer 1997

Effect of comorbidity on survival in early breast cancer

	Number of comorbid illnesses			
	0	1	2	≥ 3
No. of patients	483	288	124	41
Mean age (y)	60	65	69	70
Breast cancer/other	4.1	1.7	0.8	0.3

Satariano WA et al. Ann Intern Med 1994;120:104-110

Table 3. Cause of Death According to Age Group*

	Age, y				Total
	55-64	65-74	75-84	≥85	
Breast cancer	48 (75.0)	33 (58.9)	38 (44.7)	16 (27.6)	135 (51.3)
Other cancer	4 (6.2)	6 (10.7)	9 (10.6)	3 (5.2)	22 (8.4)
Heart disease	4 (6.2)	4 (7.1)	18 (21.2)	19 (32.8)	45 (17.1)
Cerebrovascular disease	0	1 (1.8)	4 (4.7)	8 (13.8)	13 (4.9)
Digestive system	1 (1.6)	1 (1.8)	3 (3.5)	4 (6.9)	9 (3.4)
Alzheimer disease/dementia	1 (1.6)	0	4 (4.7)	2 (3.4)	7 (2.7)
Pneumonia	0	0	2 (2.4)	3 (5.2)	5 (1.9)
COPD/other respiratory	1 (1.6)	2 (3.6)	1 (1.2)	1 (1.7)	5 (1.9)
Other	5 (7.8)	4 (7.1)	2 (2.4)	2 (3.4)	13 (4.9)
Unknown	0	5 (8.9)	4 (4.7)	0	9 (3.4)
Total No. of Deaths	64	56	85	58	263
Total No. of Patients	622	624	427	127	1800

Yancik R et al, JAMA 2001;285:885-92

Cognitive function

- By age 85, 37% of all people have some sign of Alzheimer's disease

- Evaluate <u>before</u> starting treatment!
  - Ability to follow complex directions
  - Ability to take medications on schedule
  - Ability to recognize toxicity and seek help
  - Family member to help

- Mini-mental status exam (MMSE), Montreal Cognitive Assessment (MoCA), Mini-Cog

Polypharmacy

- Age-related changes in PK and PD
  - Absorption: Change in gastric motility and bowel transit time
  - Distribution
    - Decrease in lean body mass & total body water ($\downarrow$ Volume of distribution of water soluble drugs, with higher blood levels)
    - Increase in body fat ($\uparrow$Vd of fat soluble drugs with increased half life)
    - Decrease in serum binding proteins, albumin (elevation of free-drug level even with the decreased total drug concentration)
  - Metabolism
    - Reduced liver mass & hepatic blood flow; reduced enzyme activity of P450 system
  - Elimination
    - Reduced renal blood flow and renal mass- decreased elimination
- Multiple comorbidities and multiple medications

Polypharmacy

- PIMs (Potentially Inappropriate Medications)
  - Consensus guideline known as Beers criteria (1995, updated in 2015) : drug lists particularly problematic for older patients
  - Examples of PIMs: 1st generation antihistamines, ticlopidine, peripheral alpha-1 blockers, digoxin, nifedipine, amitriptyline, nortriptyline, paroxetine, benzodiazepines, megestrol, PPIs (> 8 weeks unless for high risk patients), etc
- Prevalence of polypharmacy and PIM in older patients with newly diagnosed cancer: 80% & 41%
  - Lead to adverse drug events and increased morbidity
- Adherence also am important factor in the success or failure of treatment

AGS 2015 Beers Criteria Update Expert panel. J Am Geriatr Soc 2015

Clinical uses of CGA in cancer

- Uncover multiple geriatric problems not detected by routine history & physical examination, lead to targeted interventions, follow up on symptoms

- Predicts outcome
  - Survival
  - Postoperative complications
  - Chemotherapy-related toxicity

- Select appropriate treatment
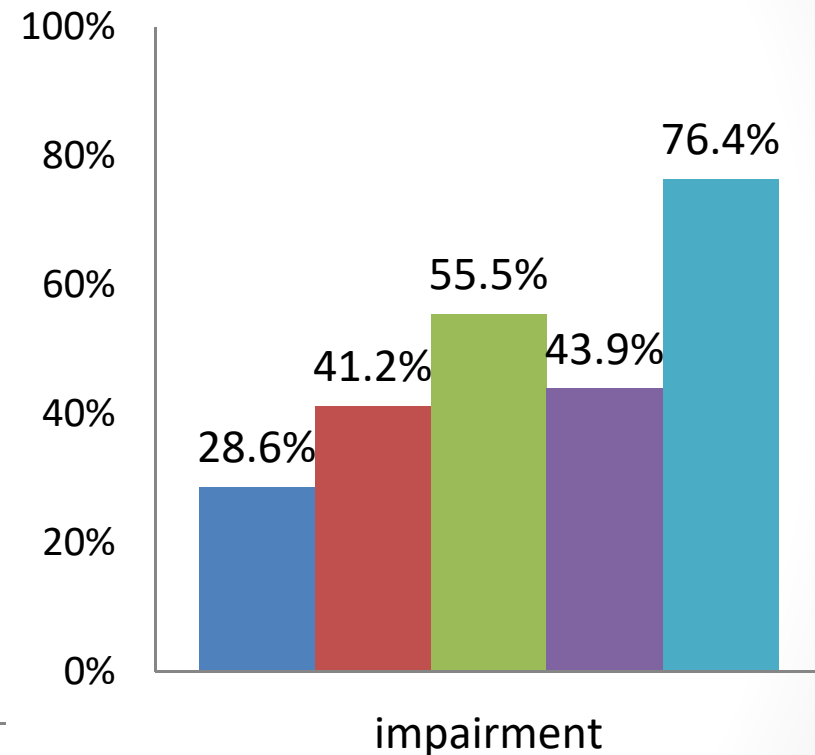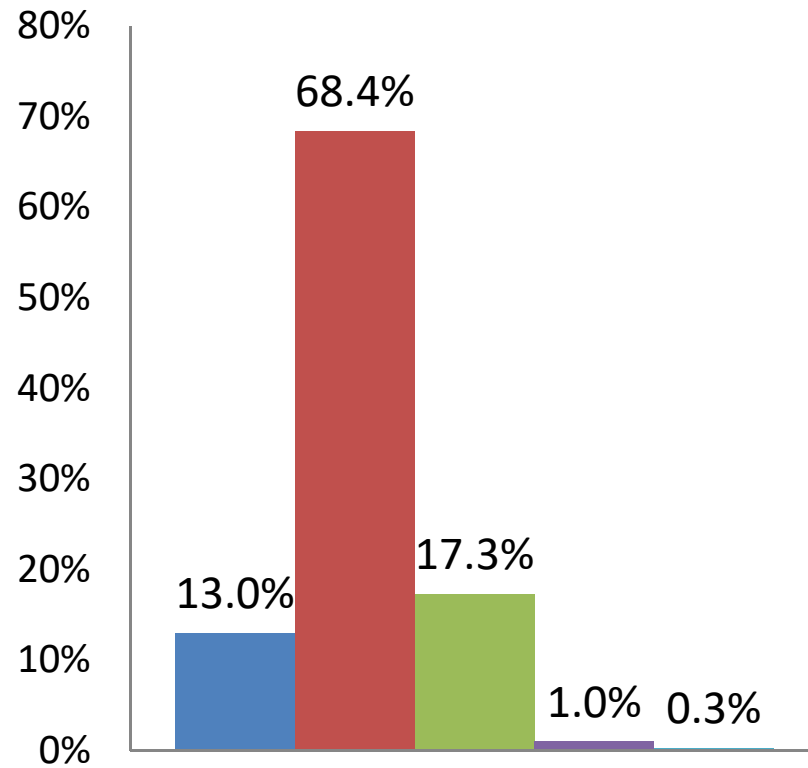 - May affect cancer treatment in more than 50% of older patients

Uncover multiple problems of elderly

- In 203 elderly patients with cancer..
  - Moderate correlation of ECOG PS with ADL (ρ =0.51) and IADL (ρ = 0.61).

ECOG PS		ADL		IADL	
Score	% pts	Dependence level	% Pts	Dependence level	% Pts
0	30.5	Independent	78.8	Independent (>27)	43.8
1	52.7	Partial	19.2	Mild/moderate (14-27)	48.3
2	11.8	complete	2.0	Major (<14)	7.9
3	4.9				

Extermann et al, J Clin Oncol 1998;16:1582-7
Repetto L et al, J Clin Oncol 2002;20:494-50210

Prospective multicenter cohort undergoing 1st line palliative chemotherapy, KCSG PC 13-09
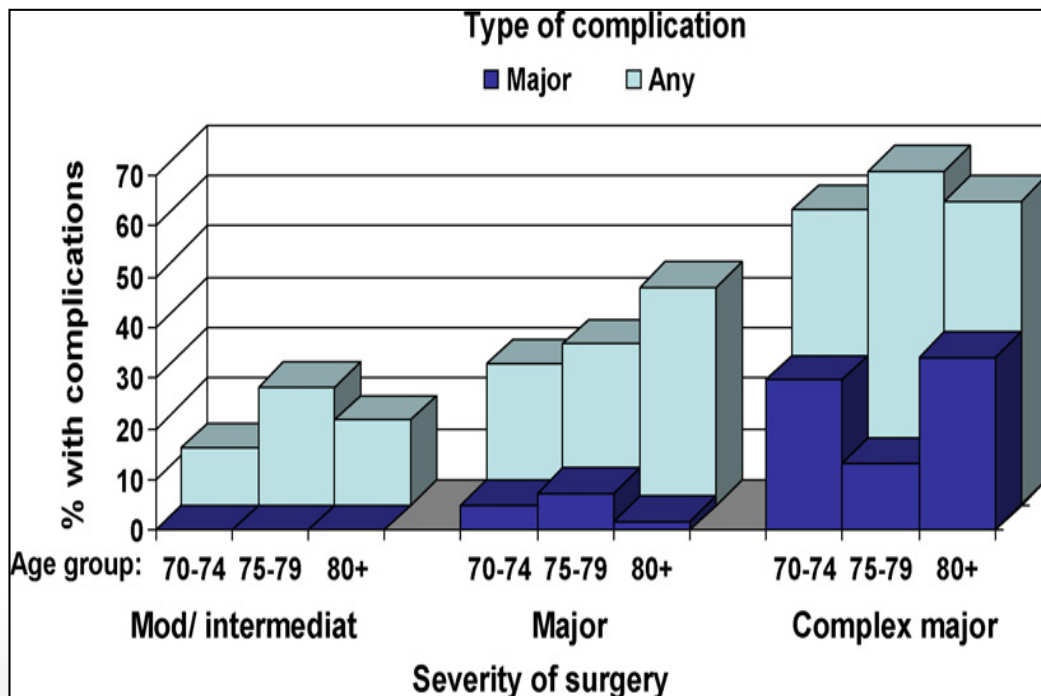

ECOG PS: 0: 13.0%, 1: 68.4%, 2: 17.3%, 3: 1.0%, 4: 0.3%

Legend: 0, 1, 2, 3, 4

impairment: ADL: 28.6%, IADL: 41.2%, MMSE: 55.5%, S-GDS: 43.9%, MNA: 76.4%

Legend: ADL, IADL, MMSE, S-GDS, MNA

(n=300, median age 75)

Prediction of post-surgical complication

- Preoperative Assessment of Cancer in the Elderly in 460 elderly receiving elective surgery (≥ 70)
  - CGA, assessment of fatigue (BFI), PS, ASA score

37.8% had at least one complication within 30 days after surgery
- Breast cancer (18.9%)
- GI cancer (59.9%)
- GU cancer (52.1%)
Complications were;
Wound infection (19.8%)
Respiratory morbidity (10.6%)
Nutritional problem (7.7%)
Cardiac failure (5.5%)

Audisio R, et al. CROH, 2008

Association between components of PACE with surgical complications

- 30-day morbidity (any and major complications)

  - Moderate-severe fatigue (RR=1.46, 95% CI=1/18-2.13)

  - Dependent IADL (RR=1.36, 95% CI=1.04-2.05)

  - Abnormal PS (RR=1.64, 95% CI=1.07-2.52)

  - Abnormal ASA (RR=1.96, 95% CI = 1.09-3.53)

- Hospital stay

Component of PACE	RR	95% CI
MMS abnormal (<24)	1.18	076-1.86
ADL dependent (>0)	2.01	1.37-2.93
IADL dependent (<8)	1.58	1.11-2.24
GDS depressed (>4)	1.30	0.91-1.85
BFI mod/severe fatigue (>3)	1.29	0.90-1.84
ASA abnormal (≥2)	0.85	0.60-1.20
PS abnormal (>1)	1.64	1.06-2.56
Satariano's index (1)	1.23	0.85-1.78
Satariano's index (2+)	1.36	0.70-2.65

Audisio R, et al. CROH, 2008

Original Investigation | SURGICAL CARE OF THE AGING POPULATION

Multidimensional Frailty Score for the Prediction of Postoperative Mortality Risk

Sun-wook Kim, MD; Ho-Seong Han, MD, PhD; Hee-won Jung, MD; Kwang-il Kim, MD, PhD; Dae Wook Hwang, MD, PhD; Sung-Bum Kang, MD, PhD; Cheol-Ho Kim, MD, PhD

- ## 275 patients (≥ 65yrs)

- ## Outcome
  - ### 1-year all-cause mortality rate, Postop complications, Hospital stay, Nursing facility
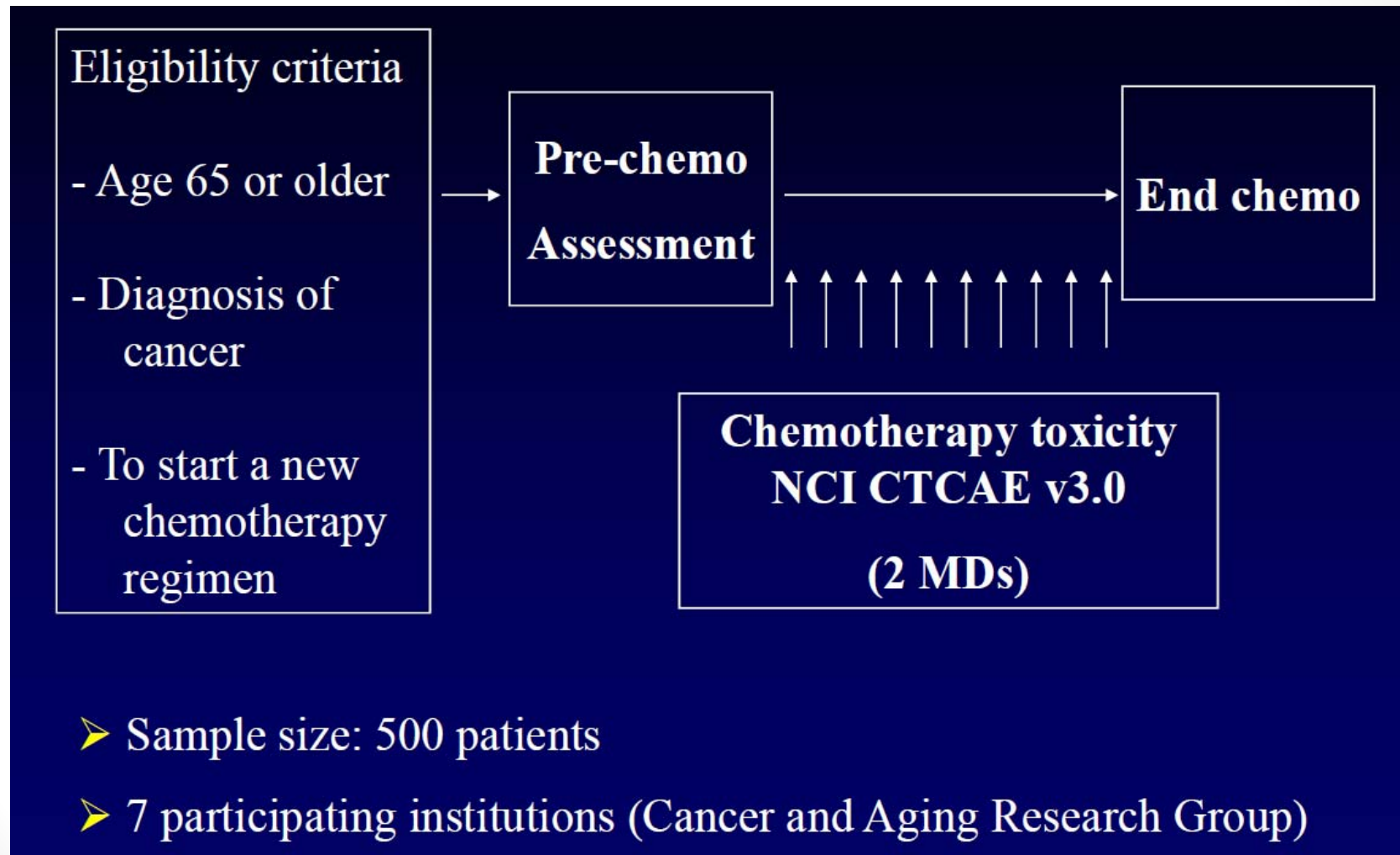
Table 2. Composition of Multidimensional Frailty Score

Item	Score 0	Score 1	Score 2
Malignant disease	Benign disease	Malignant disease	NA
Charlson Comorbidity Index	0	1-2	>2
Albumin, g/dL	>3.9	3.5-3.9	<3.5
ADLs (modified Barthel Index)	Independent	Partially dependent	Fully dependent
IADLs (Lawton and Brody Index)	Independent	Dependent	NA
Dementia (MMSE-KC)	Normal	Mild cognitive impairment	Dementia
Risk of delirium (Nu-DESC)	0-1	≥2	NA
MNA	Normal	Risk of malnutrition	Malnutrition
Midarm circumference, cm	>27.0	24.6-27.0	<24.6

Figure 3. Number of Patients and 1-Year All-Cause Mortality Rate by Multidimensional Frailty Score
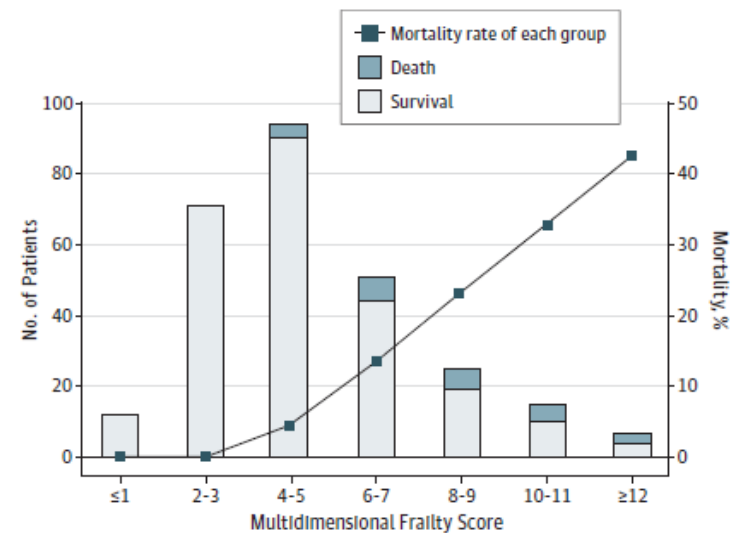
Bars represent numbers of patients (and deaths); black line, mortality rate. As scores increase, the occurrence of the primary outcome (death) increased, and the slope for mortality rates suddenly became steep for patients with scores of 5 or above.

Kim SW, Kim KI et al. JAMA Surg 2014

Prediction of chemotherapy toxicity

- Eligibility criteria

  - Age 65 or older

  - Diagnosis of cancer

  - To start a new chemotherapy regimen

Pre-chemo Assessment

End chemo

Chemotherapy toxicity NCI CTCAE v3.0 (2 MDs)

➤ Sample size: 500 patients

➤ 7 participating institutions (Cancer and Aging Research Group)

Hurria et al. JCO 2011

Prediction of chemotherapy tolerance - risk prediction model incorporating CGA

Risk factors for Gr 3-5 toxicity	OR (95% CI)	Score
Age ≥ 72 vs < 72	1.85 (1.22-2.82)	2
GI/GU cancer v other	2.13 (1.39-3.24)	2
Standard dose vs upfront dose reduction	2.13 (1.29-3.52)	2
Polychemotherapy vs monochemotherapy	1.69 (1.08-2.65)	2
Hb (M < 11, F < 10)	2.31 (1.15-4.64)	3
Ccr < 34	2.46 (1.11-5.44)	3
1 or more falls /6 m	2.47 (1.43-4.27)	3
Hearing impairment	1.67 (1.04-2.69)	2
Limited in walking 1 block	1.71 (1.02-2.86)	2
Assistance with medication intake	1.50 (0.66-3.38)	1
Decreased social activity	1.36 (0.90-2.06)	1
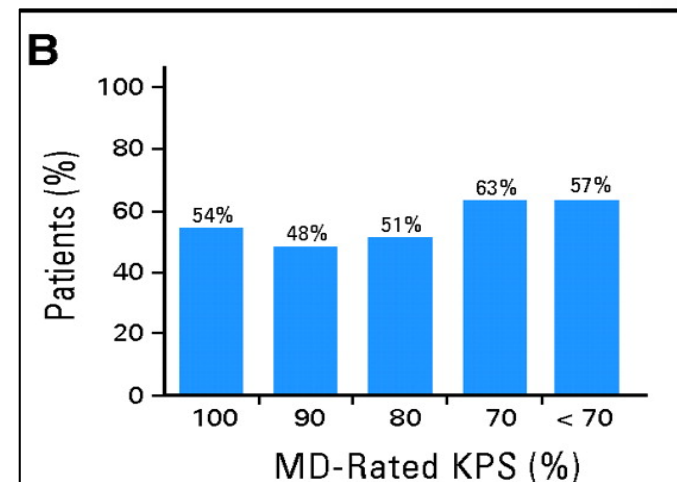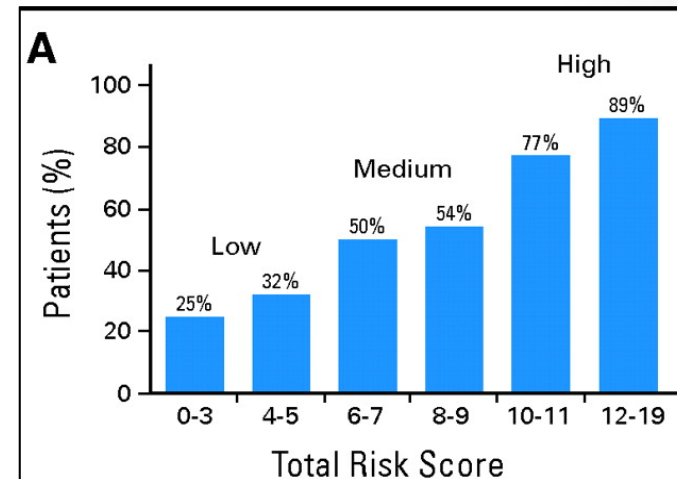
Hurria et al, JCO 2011

Prediction of chemotherapy toxicity : CARG & CRASH score

CARG study
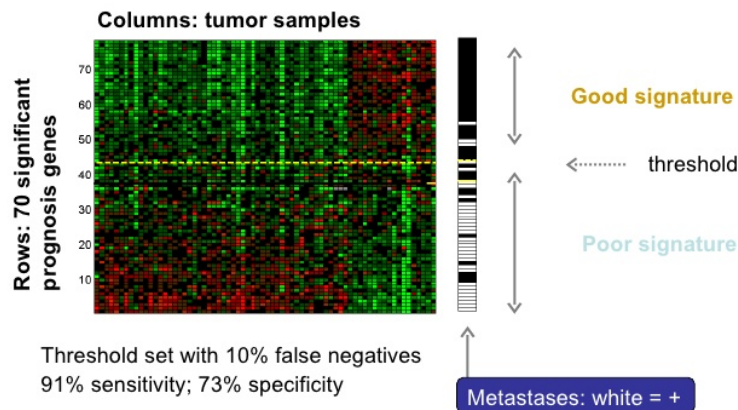Age ≥ 73
GI or GU cancer
Standard dose
Polychemotherapy
Fall within past 6 months
Assistance in IADL
Decreased social activity

CRASH -heme
IADL score
Serum LDH
Diastolic BP
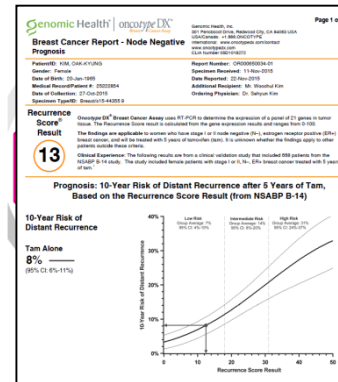Serum albumin

CRASH non-heme
ECOG PS
Hemoglobin
CCr
Albumin
MMSE
MNA
Comorbidity

Columns: tumor samples

Good signature

←--------- threshold

Poor signature

Rows: 70 significant prognosis genes

Threshold set with 10% false negatives
91% sensitivity; 73% specificity

Metastases: white = +

BCI Predictive

Reports the individualized likelihood of benefit from extended endocrine therapy[4]

- Quantitative molecular assessment of estrogen signaling pathways
- Genes: HoxB13/IL17BR (H/I)
- Binary result (HIGH/LOW)

Genomic Health | oncotype DX
Breast Cancer Report - Node Negative Prognosis

Recurrence Score Result
13

Prognosis: 10-Year Risk of Distant Recurrence after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-14)

10-Year Risk of Distant Recurrence

Tam Alone
8%
(95% CI: 6%-11%)

BCI Prognostic

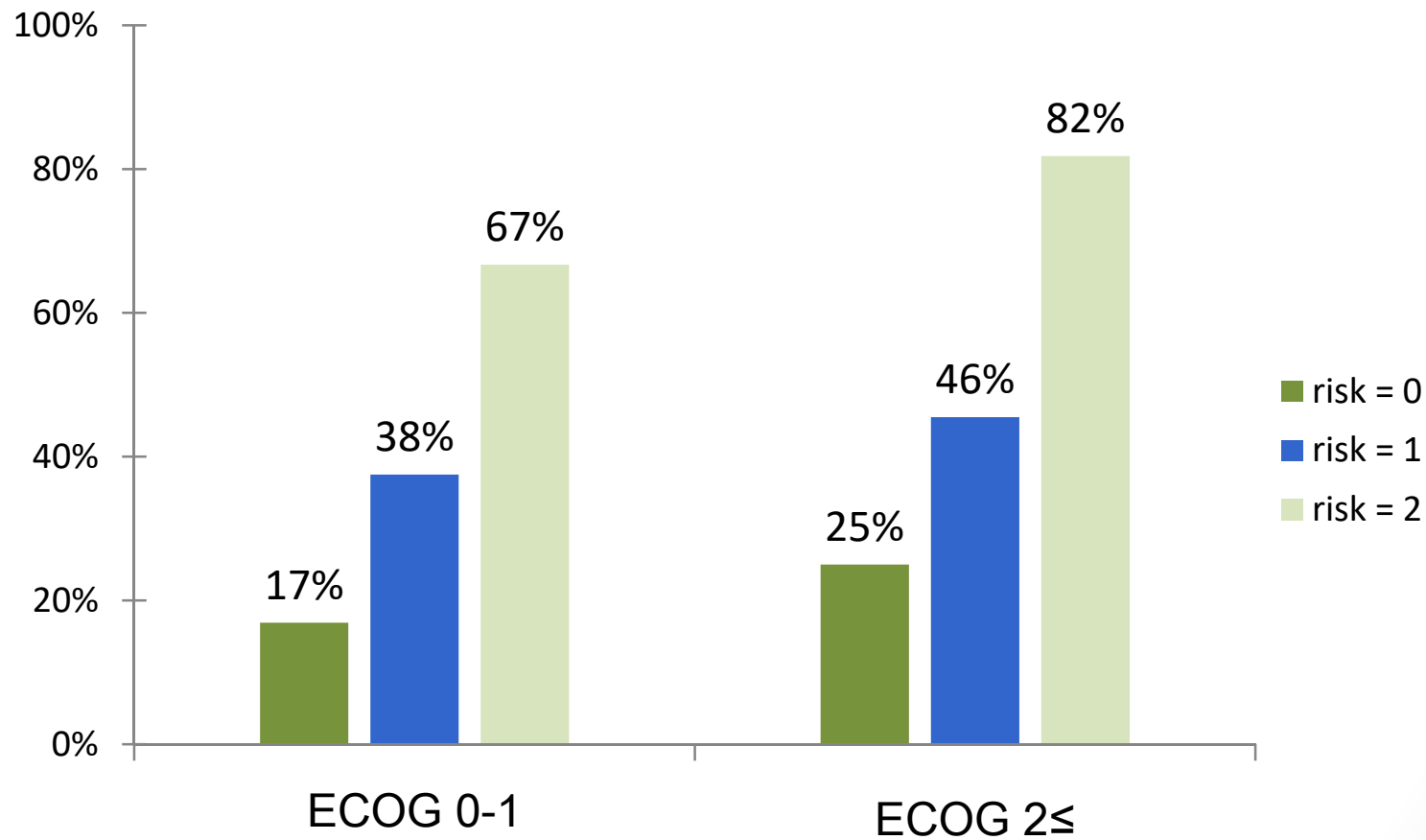Reports the individualized risk of late distant recurrence of breast cancer (Years 5 - 10)[2, 3, *]

- Algorithmic combination of Molecular Grade Index (MGI: proliferation) and HoxB13/IL17BR: estrogen signaling pathway
- Genes: BUB1B, CENPA, NEK2, RACGAP1, RRM2, H/I
- Numerical result reported on a continuous curve (delineated by HIGH/LOW risk categories)

Hurria et al, JCO 2011, Extermann et al Cancer 2011

Risk factor of stopping further treatment after 1st line chemotherapy, SNUBH (n =98, aged ≥ 65)
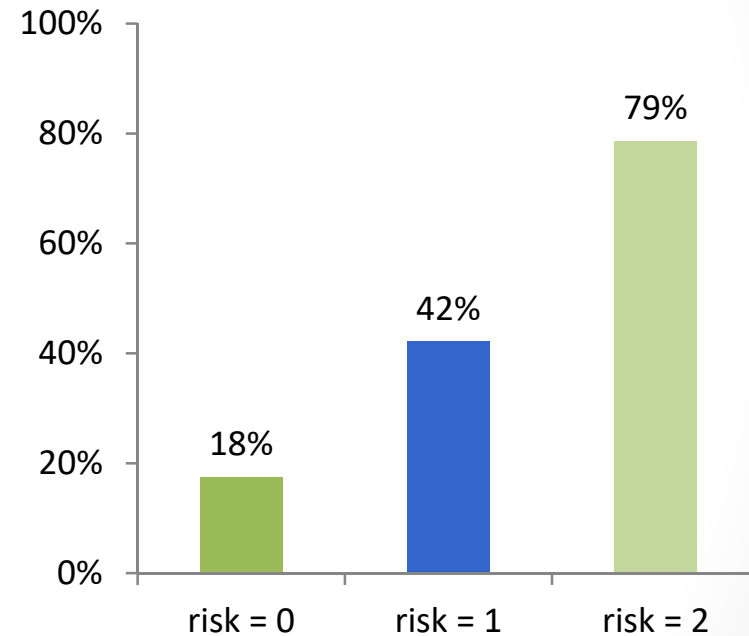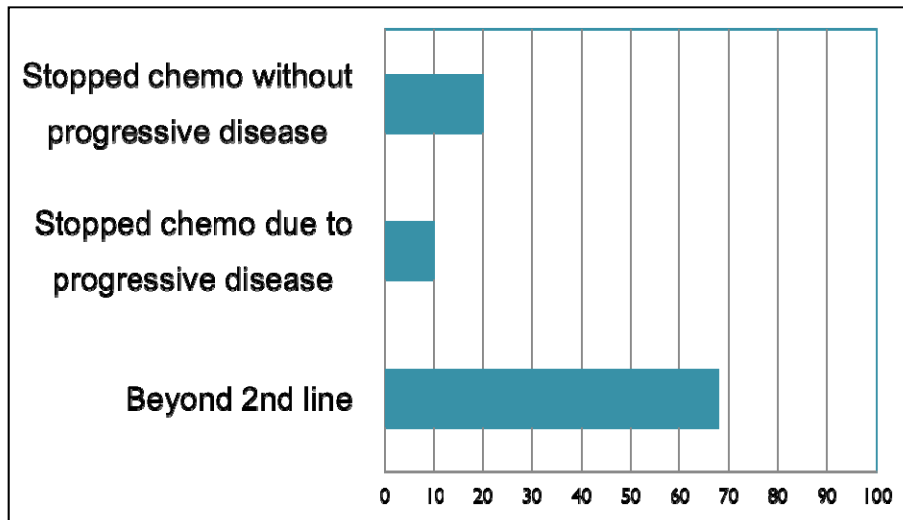
	OR	95% CI	P
MNA			
Non-malnutrition	1.00	-	-
Malnutrition (<17)	5.03	1.50-16.87	0.009
IADL			
Independent	1.00	-	-
Dependent	3.06	1.03-9.12	0.045

Kim JW, Kim JH, et al. Support Care Cancer 2013

The frequency of stopping further treatment according to number of risk factors (malnutrition, dependent IADL)

ELCAPA study – can CGA change treatment plan?

Patients 70 years or older with newly diagnosed cancer
(N = 656)

Treatment proposed by the oncologist:
initial cancer treatment plan
(n = 656)

Referred to geriatrician
Comprehensive Geriatric Assessment
(n = 392)

Undefined initial cancer treatment plan
(n = 17)

Multidisciplinary meeting: decision about the cancer treatment plan: final cancer treatment plan
(n = 375)

No change in the initial cancer treatment plan
(n = 297)

Change in the initial cancer treatment plan
(n = 78)

Change in therapy

Intensification 10%

Delay Tx to allow geriatric management 9%

Decrease in cancer treatment intensity 80.8%

Caillet P et al. JCO 2011;29:3636-3642

GA in oncology clinics

- US NCCN guideline & SIOG recommended some form of GA to help cancer specialists determine the best treatment for their older patients
- Several barriers to GA
  - Time consuming
  - Lack of trained staff
  - Lack of consensus / standardization of GA
  - Poor financial rewarding by health insurance
  - Not necessary in all elderly patients with cancer
  - Can geriatric assessment interventions lead to survival benefit in cancer patients?
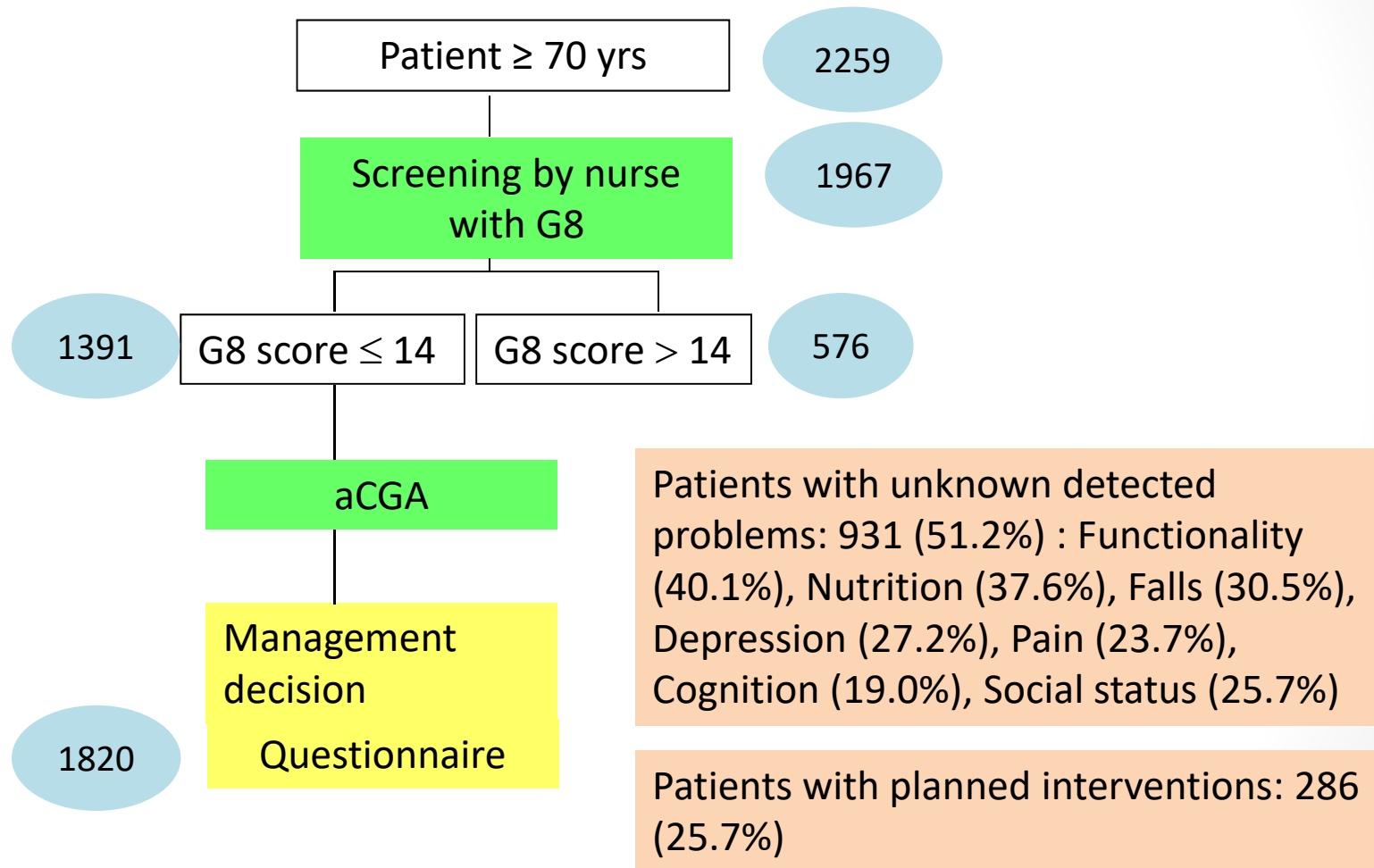
Screening tools

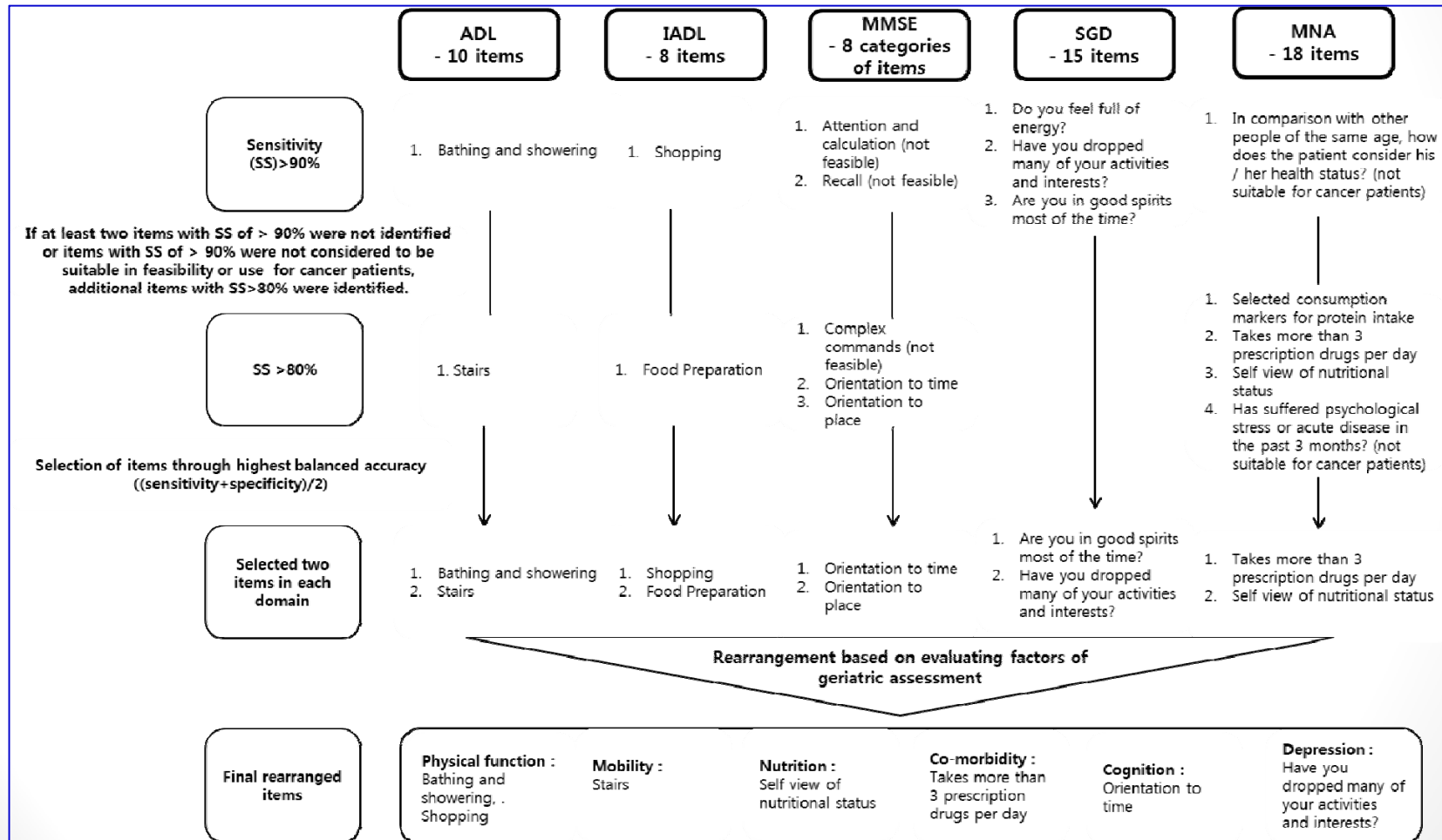| Tool	Developed for	Items	Abnormal	Time (min)
G8	Oncology pts	8	≤ 14	5
VES-13	General older pop	13	≥ 3	5
fTRST	Older pts at ED	5	≥ 2	2
GFI	General older pop	15	≥ 4	NR
SOF	General older pop	3	≥ 2	NR
Karnofsky PS	Oncology pts	1	≤ 80	1
ECOG PS	Oncology pts	1	≥ 1	1
Fried	General older population	5	≥ 3	NR
Barber	General older population	9	≥ 1	NR
ISAR	Older pts at ED	6	≥ 3	NR
OGS	Oncology pts	10	≥ 1	NR
aCGA	Oncology pts	15	≥ 1	5
Gerhematolim	Hematology pts	27	NR	NR
SAOP2	Oncology pts	15	≥ 1	NR
PPT	General older population	7	≤ 20	5
Handgrip	General older population	NA	NA	NA

G8 (geriatric 8), VES-13(vulnerable elders' survey-13), fTRST (Flemish version of the Triage Risk Screening Tool), GFI (groningen frailty index), SOF (study of osteoporotic fractures), ISAR (Identification of Seniors at Risk), OGS (Onco Geriatric screening tool), aCGA (abbreviated CGA), SAOP (Senior Adult Oncology Program), PPT (Physical Performance Testing), ED (emergency department)

Systematic geriatric screening and assessment study

Patient ≥ 70 yrs — 2259

Screening by nurse with G8 — 1967

1391 — G8 score ≤ 14 | G8 score > 14 — 576

aCGA

Management decision

Questionnaire — 1820

Patients with unknown detected problems: 931 (51.2%) : Functionality (40.1%), Nutrition (37.6%), Falls (30.5%), Depression (27.2%), Pain (23.7%), Cognition (19.0%), Social status (25.7%)

Patients with planned interventions: 286 (25.7%)

Kenis C, et al. Ann Oncol 2013

Development of Screening tool : KG-7 Geriatric Assessment cohort (n=1284)

*Kim JW and Kim JH, et al. Plos One 2015*

KG-7 (KCSG Geriatric Score-7)

1. Can you take a shower or bath without help?

2. Can you ascend the stairs without help?

3. Can you take care of all shopping needs independently?

4. How is the self-view of your nutritional status?

5. Do you take more than 3 prescription drugs per day?

6. What year, month and day is this?

7. Have you dropped many of your activities and interests?

Total points (   )/7 points

Kim JW and Kim JH, et al. Plos One 2015

Validation of KG-7 in retrospective (n=99) & prospective cohort (n=300)
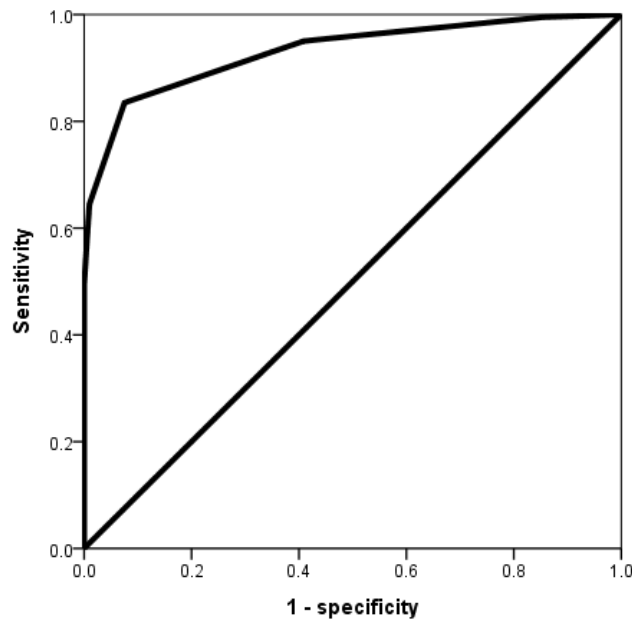
AUC 0.930, (95% confidence interval, 0.916-0.945), p<0.001,

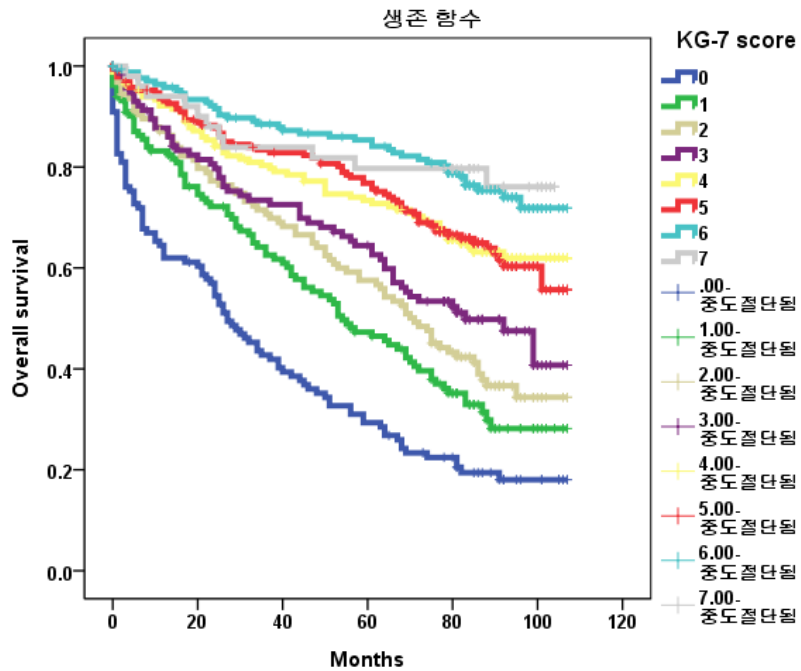- The cut-off value was decided at ≤ 5 points, with AUC 0.930

Sensitivity	Specificity	PPV	NPV
95.0%	59.2%	85.3%	82.6%

- In the retrospective validation cohort, the AUC was 0.82 (95% CI 0.73−0.90)

Sensitivity	Specificity	PPV	NPV
89.5%	48.6%	77.3%	75.0%

- Prospective validation cohort (n=300) – ASCO 2017

Kim JW and Kim JH, et al. Plos One 2015

Overall Survival according to KG-7, development cohort

P<0.001
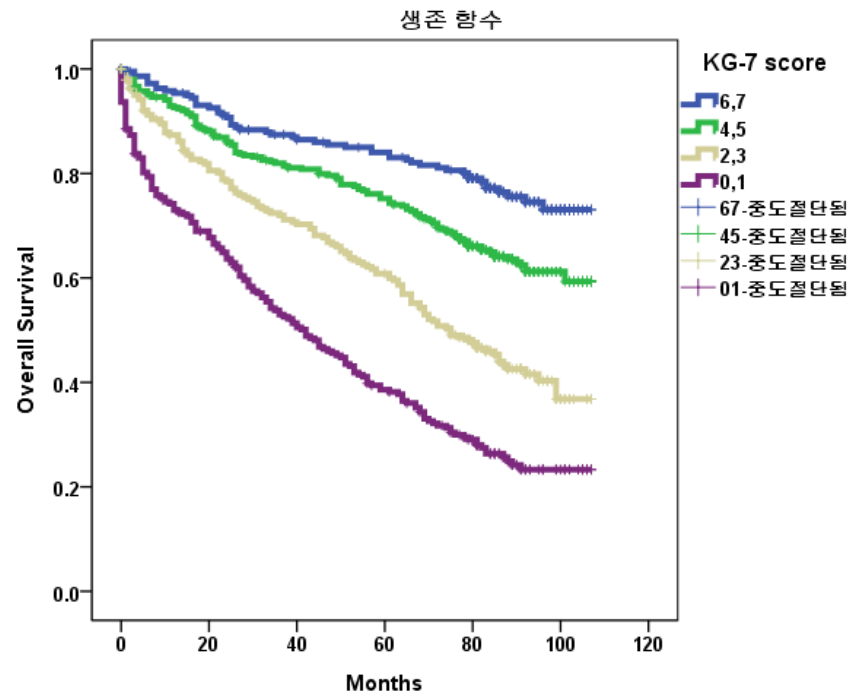
P<0.001

Prospective validation study /biomarker substudy – ASCO 2017

Take home message

- Cancer is disease of aging
- Older patients have
  - Decreased organ function and stress tolerance
  - Competing cause of mortality (comorbidity)
  - Different tolerance to treatment
- Comprehensive geriatric assessment
  - Predicts survival, post-treatment complication
  - Uncover health problems of elderly, leading to intervention
  - Change in treatment selection
- Consideration of geriatric factors is essential in treatment decision : GA and focused intervention

Acknowledgement

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Oncology Working Party

Seoul National University Bundang Hospital
Geriatric Oncology Team