

Early phase studies: Clinical perspective

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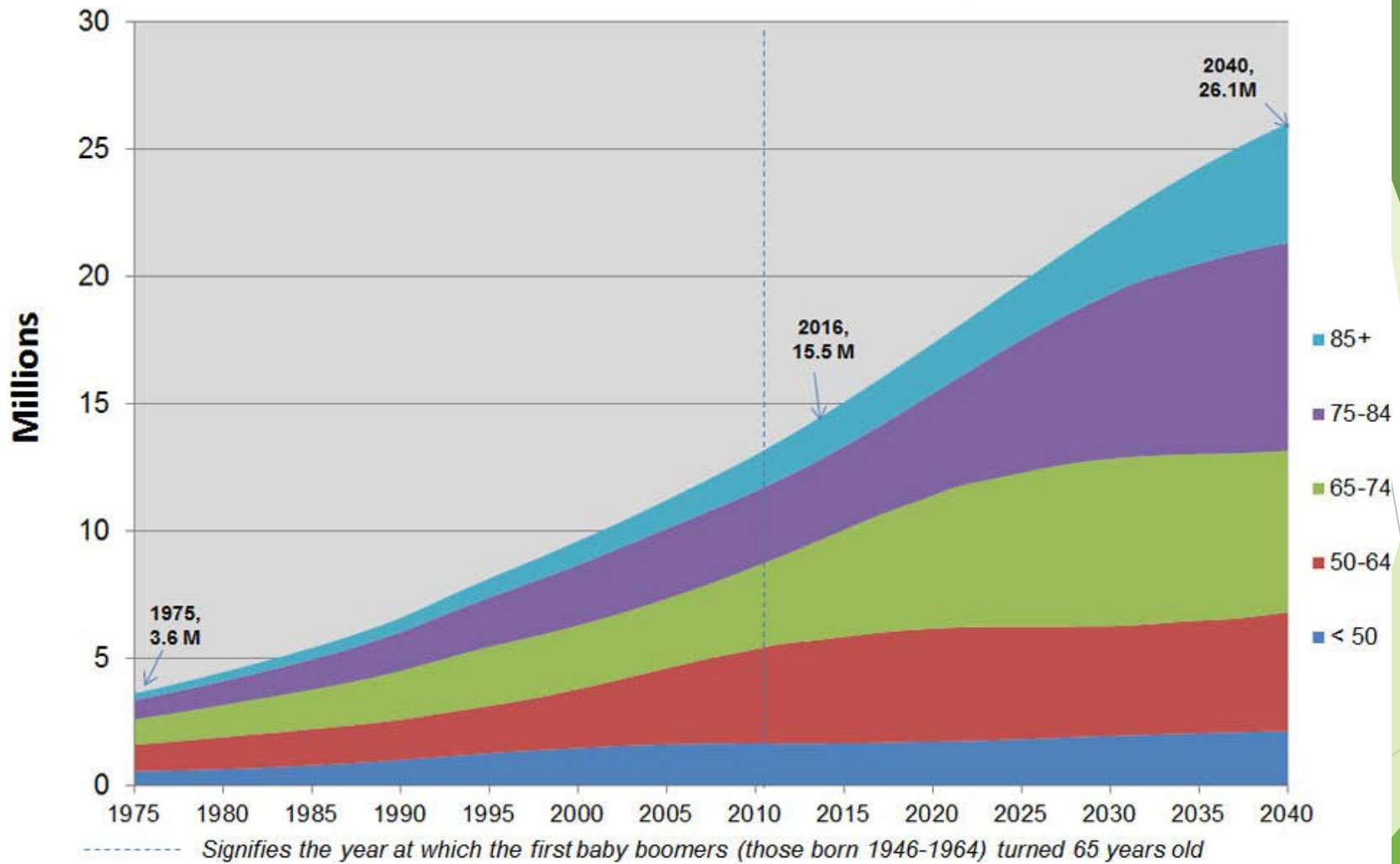
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Disclosures

- ▶ Consultant: Alnylam

Estimated cancer prevalence by age in the US population
from 1975 (216 M) to 2040 (380 M)



CIRS-G

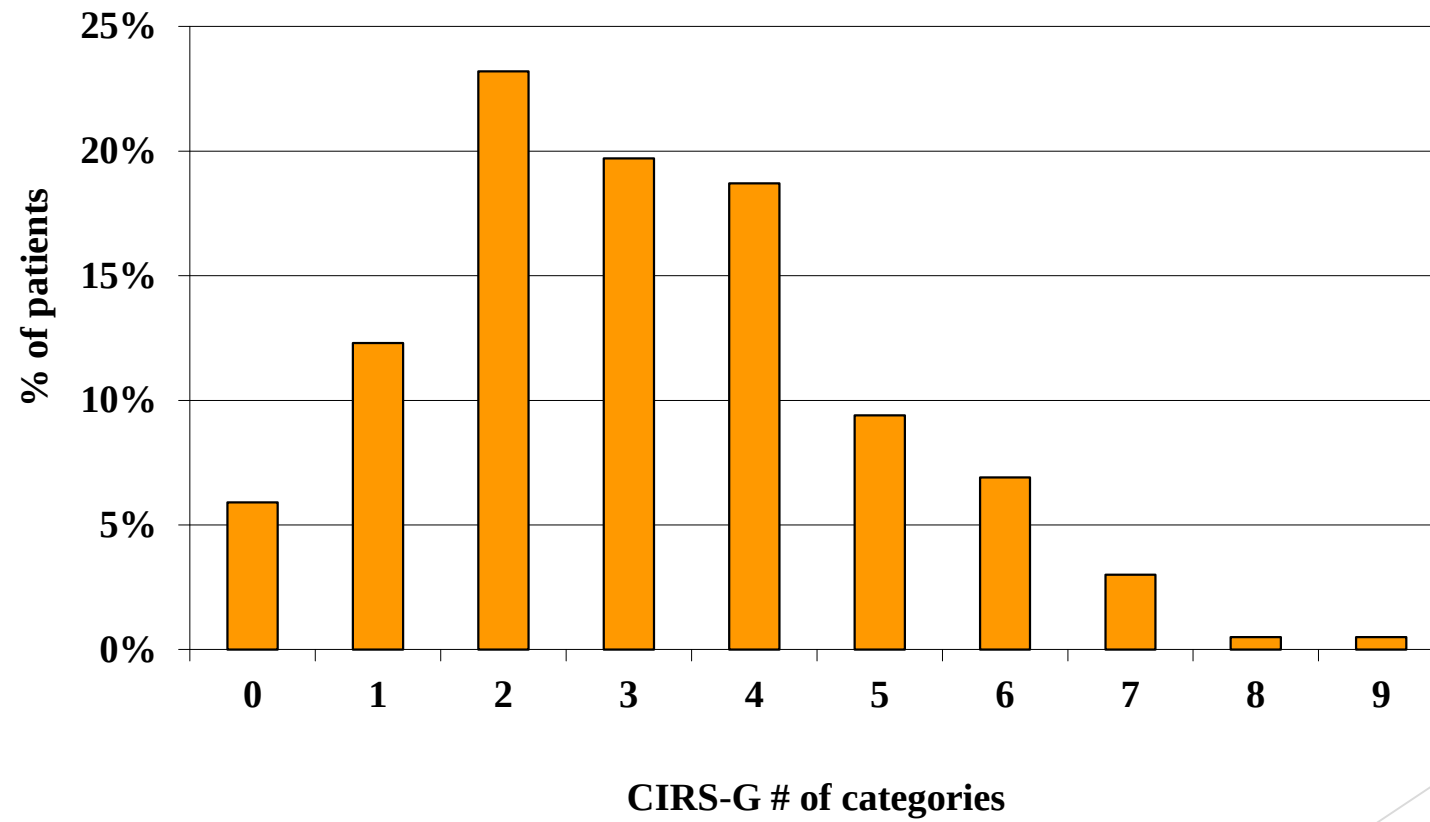
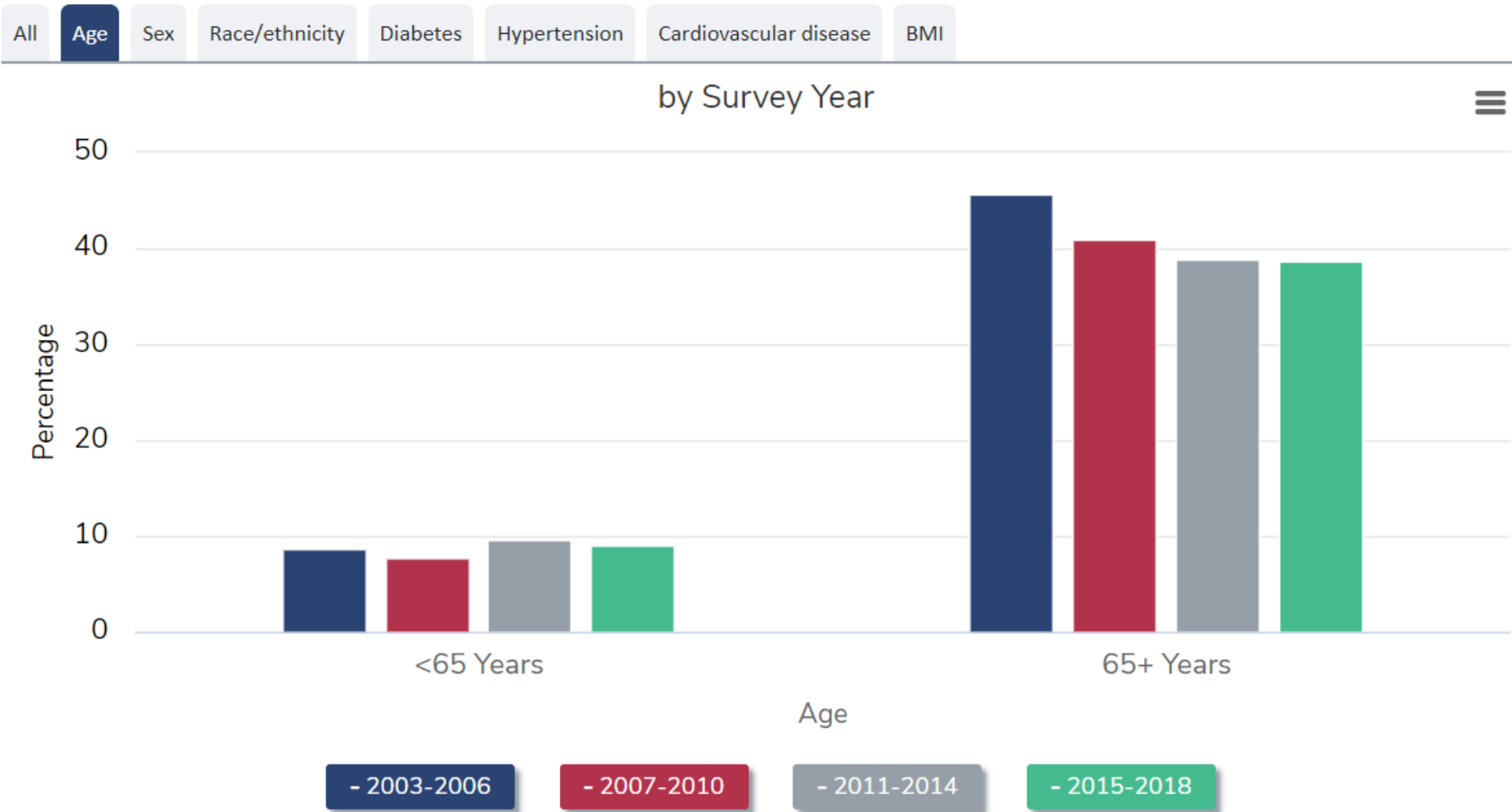


Figure 1.5 Prevalence of CKD in U.S. adults within age, sex, race/ethnicity, & risk factor categories, 2003-2018



And 2/3
oncologic
patients
dependent in
IADL

Data source: National Health and Nutrition Examination Survey (NHANES), 2003-2006, 2007-2010, 2011-2014 and 2015-2018 participants age ≥20 with serum creatinine and urinary ACR. eGFR calculated using the CKD-EPI equation. Abbreviations: ACR, urine albumin/creatinine ratio; BMI, body mass index

Keys to enhance external validity and future study design

- ▶ No matter what type of early phase study design, collect patient data
- ▶ Comorbidity (e.g. CIRS-G)
- ▶ Functional status beyond ECOG PS (e.g. ADL/IADL)
- ▶ Performance test: timed up and go, 4 meters walk
- ▶ Longitudinal ADL/IADL (IADL is the most sensitive to change)
- ▶ PROMs relevant to older patients (e.g. independence)

Information collected at this stage will provide helpful clues for a successful phase III study design

The Progressively Increasing Inclusion Criteria (PIIC) concept:

Indep., no comorb, chemo level 1
6 patients, well tolerated

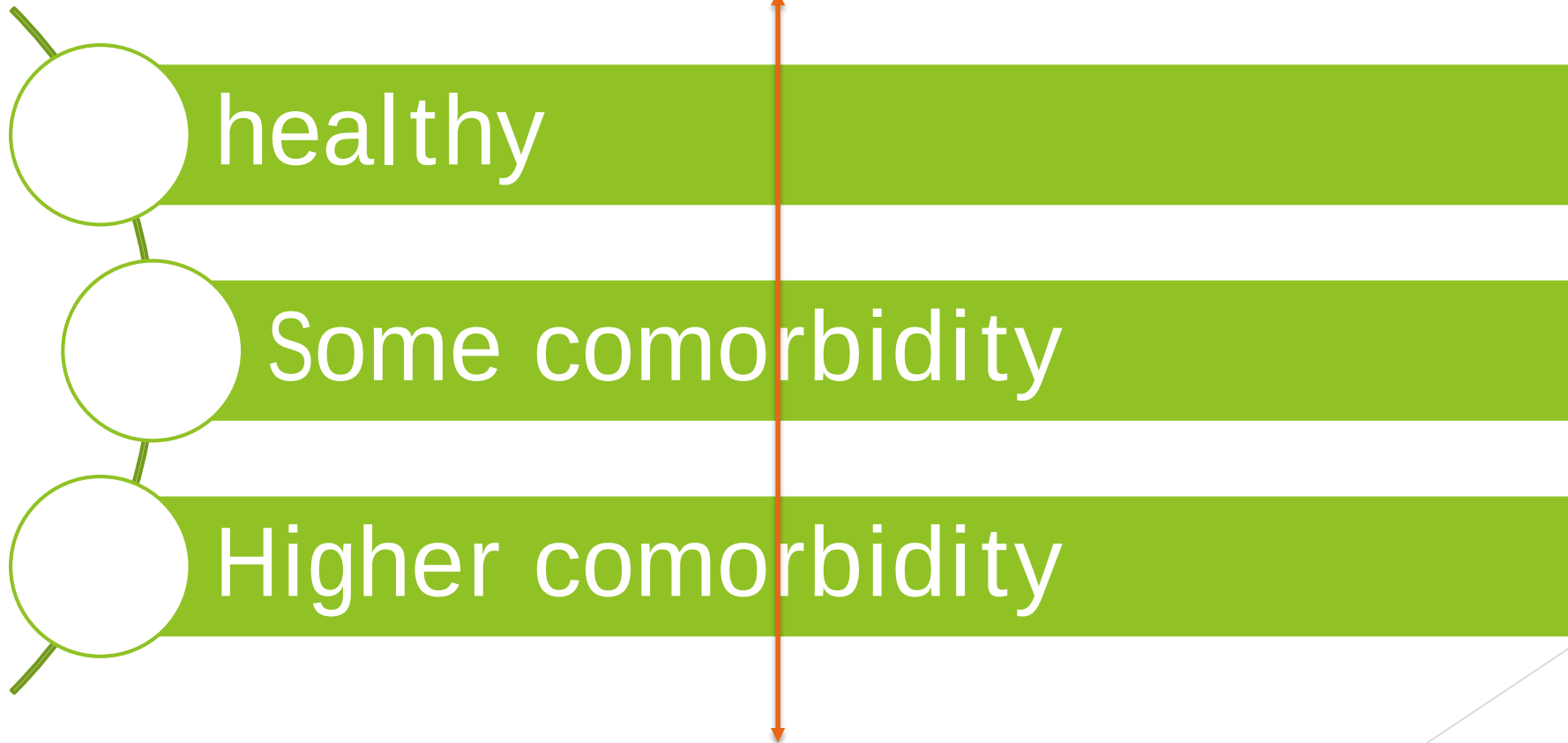
Continue accrual for
Effectiveness end-points

Mild dep or comorbidity, level 1, 2
limit tox, 6 pts level 2, well
tolerated

Moderate dependence or
comorbidity, level 2.....

Stratified design: e.g. phase II

Interim safety analysis



Stratified
effectiveness
analysis

Basket trial

Healthy

Paclitaxel + trastuzumab + new drug

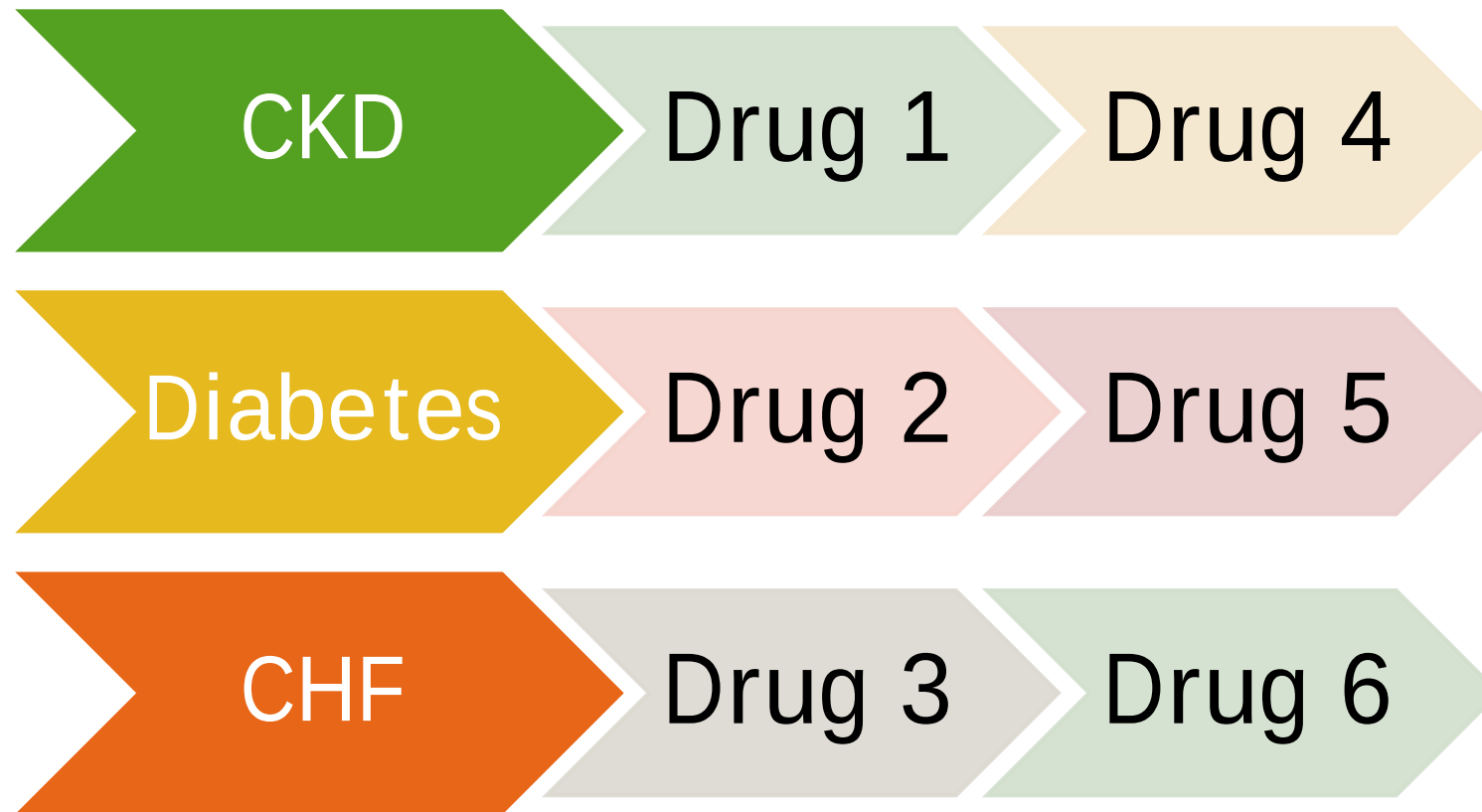
Vulnerable

Cyclophosphamide + trastuzumab + new drug

Frail

Trastuzumab + new drug

Umbrella design: One cancer



Design for patient friendliness

- ▶ Transportation is a big barrier, consider offering help
- ▶ Can some assessments be done remotely?
- ▶ Can local labs be used for simple tests?(e.g. weekly CBC)
- ▶ Try to group assessments
- ▶ Online questionnaires
- ▶ Help for people with poor hearing or vision
- ▶ Everybody wants tissue, but can the tests be done on blood?
- ▶ Leverage wearables

A photograph of a young Black female doctor in a white lab coat with a stethoscope, talking to an elderly white female patient. The doctor is holding a small object in her hand. A speech bubble points from the doctor to the text.

Yes, we have a study for you!