HEALTH
UNIVERSITY OF UTAH

CLINICAL DECISION SUPPORT FOR GENOMICS: CLINICAL WORKFLOWS AND INTEROPERABILITY STANDARDS

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WORKFLOWS

- Point-of-care CDS
  - Active
  - On-demand
- Population-based
  - Proactive cohort identification & patient outreach

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RESEARCH ARTICLE Open Access

Integrating clinical decision support systems for pharmacogenomic testing into clinical routine - a scoping review of designs of user-system interactions in recent system development

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Abstract

Background: Pharmacogenomic clinical decision support systems (CDSS) have the potential to help overcome some of the barriers for translating pharmacogenomic knowledge into clinical routine. Before developing a prototype it is crucial for developers to know which pharmacogenomic CDSS features and user-system interactions have yet been developed, implemented and tested in previous pharmacogenomic CDSS efforts and if they have been successfully applied. We address this issue by providing an overview of the designs of user-system interactions of recently developed pharmacogenomic CDSS.

Methods: We searched PubMed for pharmacogenomic CDSS published between January 1, 2012 and November 15, 2016. Thirty-two out of 118 identified articles were summarized and included in the final analysis. We then compared the designs of user-system interactions of the 20 pharmacogenomic CDSS we had identified.

Results: Alerts are the most widespread tools for physician-system interactions, but need to be implemented carefully to prevent alert fatigue and avoid liabilities. Pharmacogenomic test results and override reasons stored in the local EHR might help communicate pharmacogenomic information to other internal care providers. Integrating patients into user-system interactions through patient letters and online portals might be crucial for transferring pharmacogenomic

N=31 studies

Active CDS

- Alerts: n=13
- Inbox: n=9

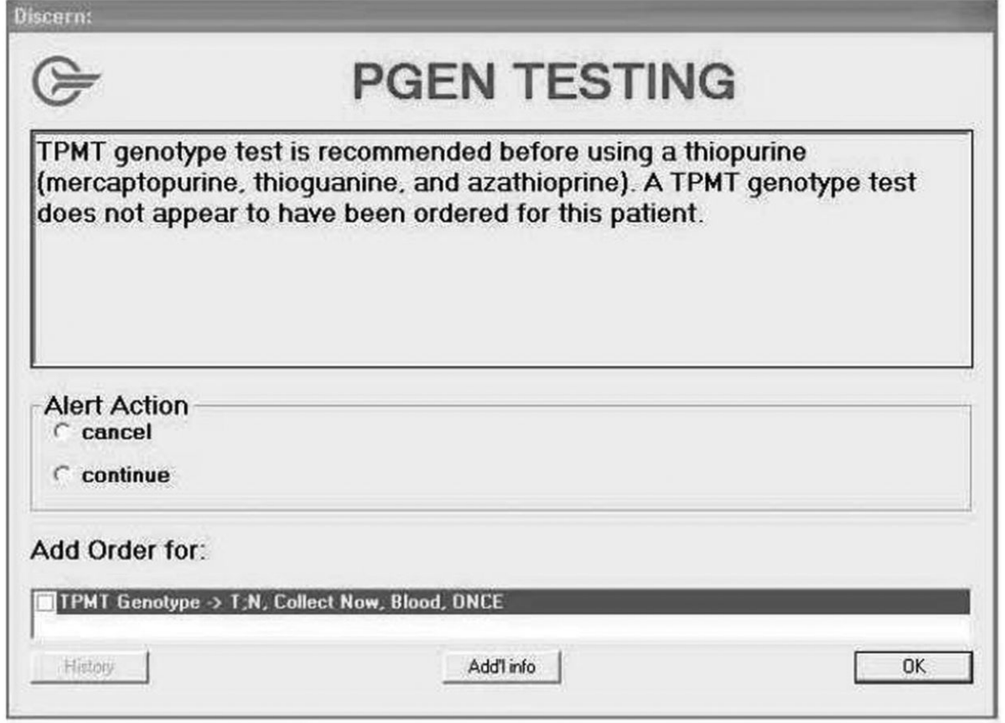
On-demand

- Test reports: n=12
- Problem list: n=4

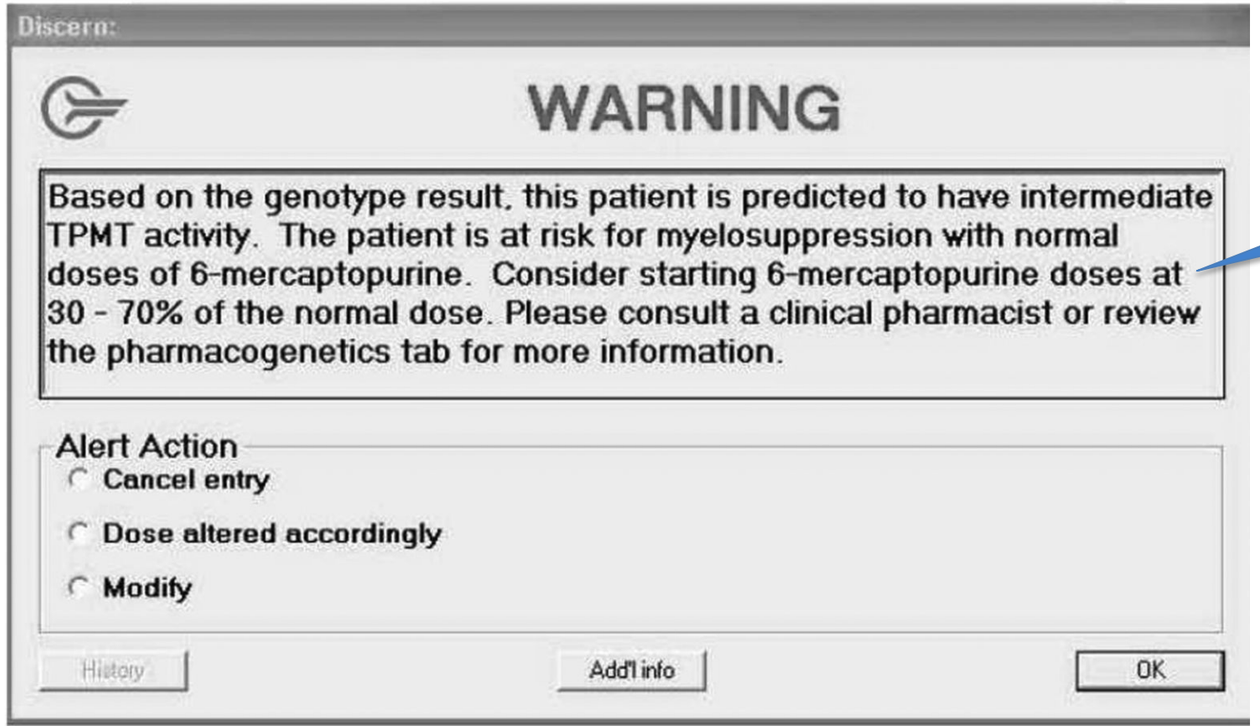
POINT-OF-CARE ALERTS

- Triggered based on user interaction with EHR
- Standards: CDS Hooks

Use case	Trigger	Guidance
Pharmacogenomics (pre-test)	Medication prescribe	Pharmacogenomic test order
Pharmacogenomics (post-test)	Medication prescribe	Treatment recommendation
Family history-based testing	Chart open	Genetic test order / genetic counseling referral
Cancer screening reminders	Chart open	Personalized screening recommendations



Pre-test alert



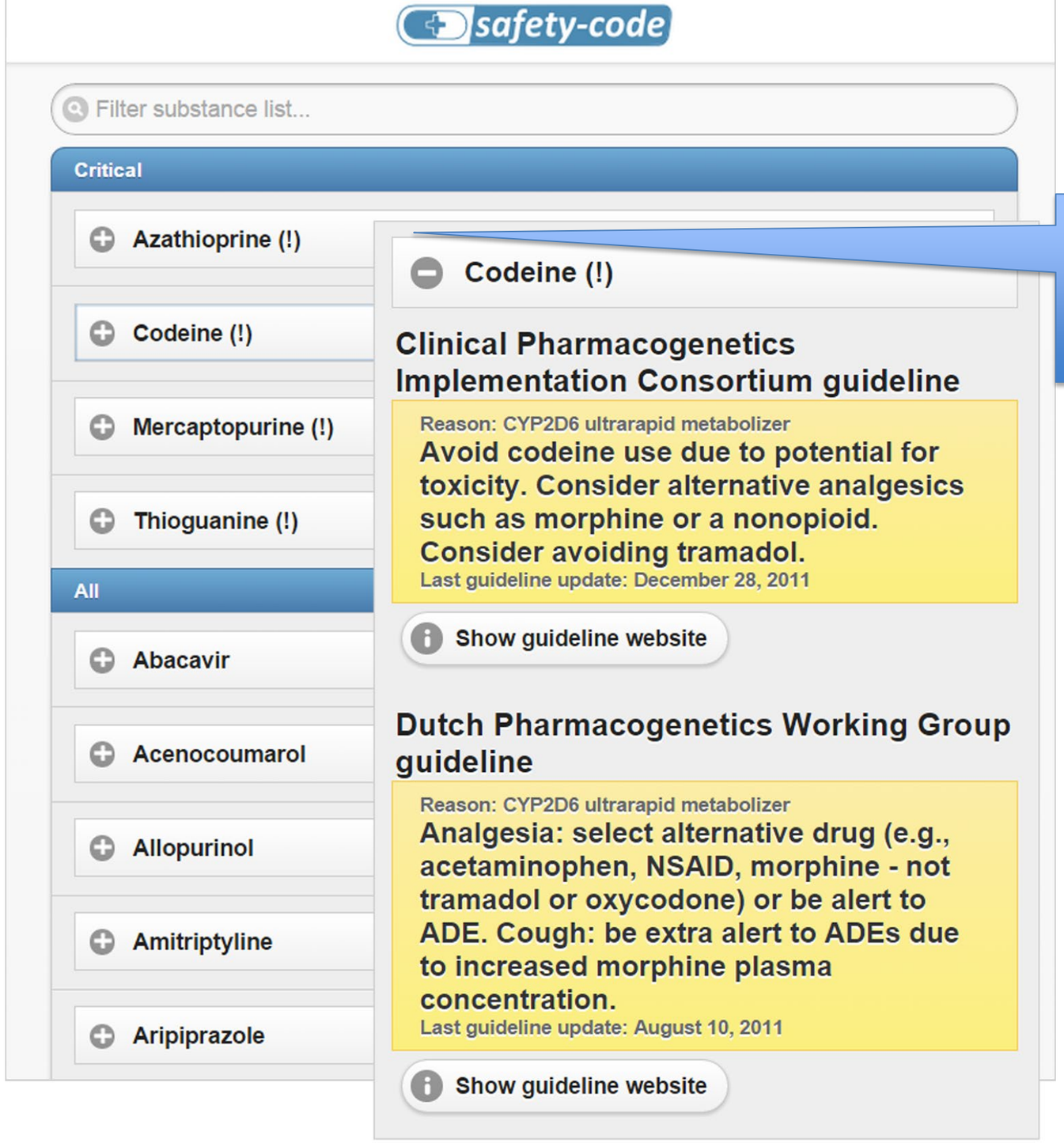
Post-test alert

Bell GC, et al. Development and use of active clinical decision support for preemptive pharmacogenomics. J Am Med Inform Assoc. 2014;21(e1):e93-9. PMID: 23978487.

ON-DEMAND CDS

- Test reports, Infobuttons
- Standards: Infobutton & SMART on FHIR

Use case	Trigger	Guidance
Test interpretation and guidance	• On demand • Suggestion to use app on chart open	Test interpretation and clinical guidance • Links to online resources • App with integrated information display



Critical drugs - CYP2D6 ultrarapid metabolizer

Blagec K, Romagnoli KM, Boyce RD, Samwald M. Examining perceptions of the usefulness and usability of a mobile-based system for pharmacogenomics clinical decision support: a mixed methods study. PeerJ. 2016;4:e1671. PMID: 26925317.

Pharmacokinetics

Clopidogrel must be metabolized into an active metabolite by liver cytochrome P-450 enzymes. The conversion of clopidogrel to its active metabolite requires two sequential oxidative steps. CYP1A2, CYP2B6, CYP2C9, CYP2C19 and CYP3A4/5 are enzymes involved in the metabolism of clopidogrel [Articles:1510701, 11127873, 12485953, 17361128, 19812348]; (for further information see clopidogrel PK pathway). In a competing metabolic reaction, about 85 % of the drug is hydrolyzed to an inactive carboxylic acid derivative by esterases (CES1) [Articles:6943252, 10440420]. ABCB1 is involved in the intestinal absorption of clopidogrel [Articles:17112805, 19106083].

Pharmacodynamics

Clopidogrel binds specifically and irreversibly to the platelet P2RY12 purinergic receptor, inhibiting ADP-mediated platelet activation and aggregation [Articles:11127873, 15199474].

Pharmacogenomics

The CYP2C19*2 (rs4244285) loss of function variant was significantly associated with lower exposure to active metabolite in subjects treated with clopidogrel [Articles:17900275, 19106084]. Furthermore, this variant has been associated with decreased platelet responsiveness to clopidogrel ex vivo [Articles:16772608, 18004210, 19106084] and increased cardiovascular event rates in patients on clopidogrel [Articles:19106083, 19106084, 19108880, 20351750]. Simon et al. showed that patients carrying any two CYP2C19 loss-of-function alleles (*2, *3 (rs4986893), *4 (s28399504) or *5 (rs56337013)) had a higher rate of cardiovascular events than patients who did not have these alleles [Article:19106083]. Similarly, another study reported that carriers of a reduced-function CYP2C19 allele (CYP2C19*2, CYP2C19*3, CYP2C19*4 or CYP2C19*8) had significantly lower levels of clopidogrels active metabolite, diminished platelet inhibition, and a higher

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POPULATION-BASED OUTREACH

- Cohort: identify patients who meet criteria
- Outreach: recommend personalized care
  - Genetic testing / counseling
  - Update test interpretation
  - Changes to clinical management
- Standards: FHIR

SPECIAL SERIES: INFORMATICS TOOLS FOR CANCER RESEARCH AND CARE

Standards-Based Clinical Decision Support Platform to Manage Patients Who Meet Guideline-Based Criteria for Genetic Evaluation of Familial Cancer

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PURPOSE The ubiquitous adoption of electronic health records (EHRs) with family health history (FHH) data provides opportunities for tailoring cancer screening strategies to individuals. We aimed to enable a standards-based clinical decision support (CDS) platform for identifying and managing patients who meet guidelines for genetic evaluation of hereditary cancer.

METHODS The CDS platform (www.opencds.org) was used to implement algorithms based on the 2018 National Comprehensive Cancer Network guidelines for genetic evaluation of hereditary breast/ovarian and colorectal cancer. The platform was designed to be interfaced with different EHR systems via the Health Level Seven International Fast Healthcare Interoperability Resources standard. The platform was integrated with the Epic EHR and evaluated in a pilot study at an academic health care system.

RESULTS The CDS platform was executed against a target population of 143,012 patients; 5,245 (3.7%) met criteria for genetic evaluation based on the FHH recorded in the EHR. In a clinical pilot study, genetic counselors attempted to reach out to 71 of the patients. Of those patients, 25 (35%) scheduled an appointment, 10 (14%) declined, 2 (3%) did not need genetic counseling, 7 (10%) said they would consider it in the future, and 27 (38%) were unreachable. To date, 13 (52%) of the scheduled patients completed visits, and 2 (15%) of those were found to have pathogenic variants in cancer predisposition genes.

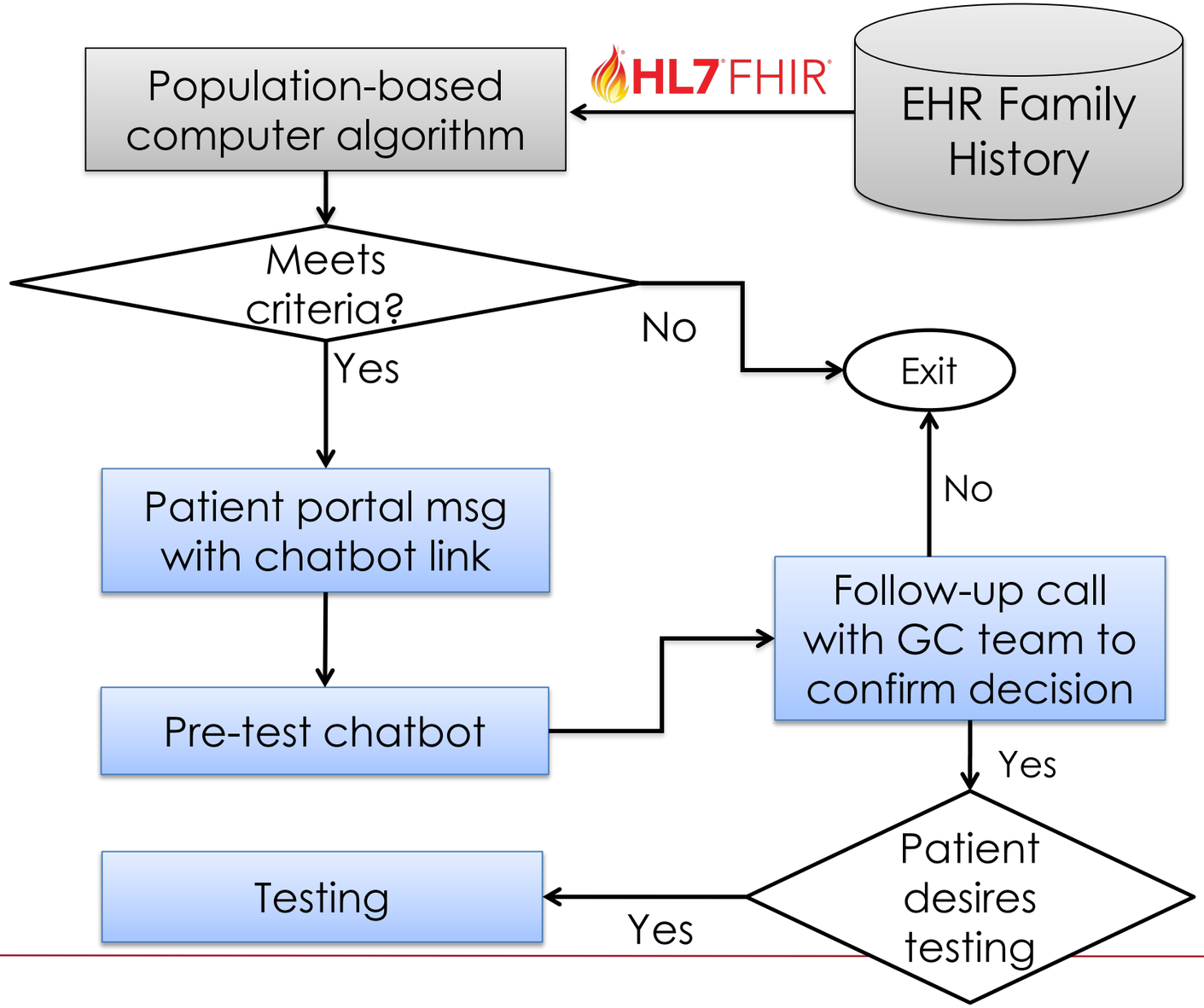
Del Fiol G, Kohlmann W, Bradshaw RL, Weir CR, Flynn M, Hess R, Schiffman JD, Nanjo C, Kawamoto K. Standards-Based Clinical Decision Support Platform to Manage Patients Who Meet Guideline-Based Criteria for Genetic Evaluation of Familial Cancer. JCO Clin Cancer Inform. 2020;4:1-9. PMID: 31951474.

CRITERIA – BREAST CANCER*

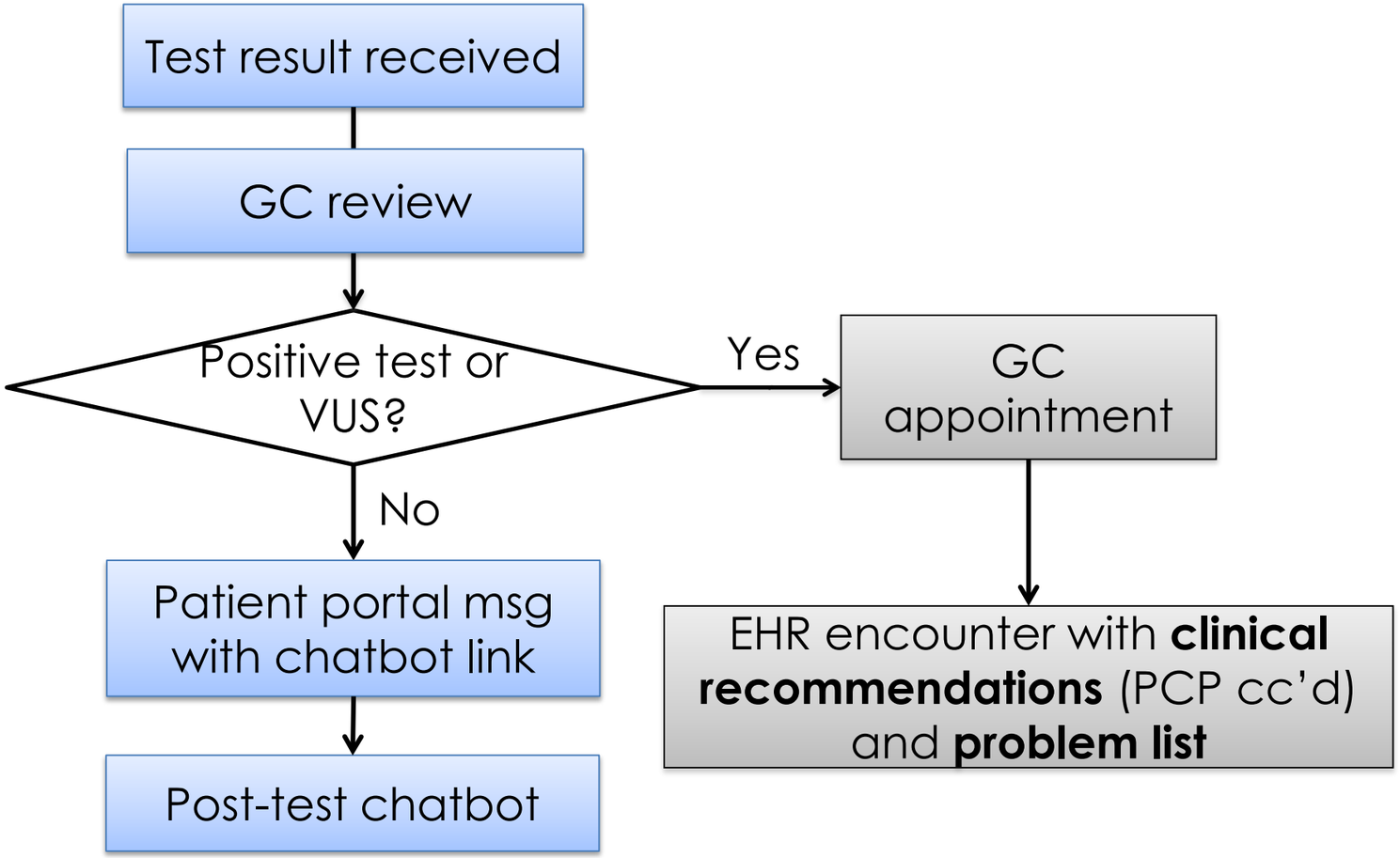
- FHx of BRCA1/2, CHEK2, ATM, PALB2, TP53, PTEN, CDH1, Cowden syndrome, or Li-Fraumeni syndrome
- 1st or 2nd degree relative with breast cancer AND age of onset <= 45
- 1st or 2nd degree relative with ovarian OR pancreatic cancer
- Three or more 1st or 2nd relatives with breast or prostate cancer on same side of family
- Breast cancer in a male 1st or 2nd degree relative
- Ashkenazi Jewish ancestry and any family member with breast, ovarian, prostate, or pancreatic cancer

*Adapted from NCCN guidelines for breast cancer risk reduction

COHORT IDENTIFICATION AND OUTREACH



TEST RESULTS WORKFLOW



SUMMARY

- Prior research: strong emphasis on CDS alerts
- Research gaps
  - Novel workflows
    - Beyond pharmacogenomics
    - Integration with primary care
    - Patient outreach / engagement approaches
  - Leverage emerging standards
    - CDS Hooks / SMART on FHIR
  - Health disparities