Supplementary Appendix A Interview Probes

1. Thank you for talking with us today, can you say what is your title in your organization?
2. Can you quickly describe your facility/organization.
3. What EHR system do you use now? How long have you used this system?
4. Do you know the source of drug information that is used by your EHR system? (skip if using Cerner = Multum)
5. Please describe your organization's governance of CDS (Do you foresee any barriers related to approvals and ethics oversight for implementing digital health tools? Who usually approves new CDS?)
    a. For DDIs, do you modify alerts as supplied by vendors? When? How? Is this reviewed by the governance committee?
    b. Who controls the governance priorities within the organization? CMIO? CEO, COO?
    c. Can you provide an example of the successful adoption/ implementation of medication-related CDS? (other non-medication CDS success stories)
       i. What factors do you think made this successful?
       ii. Are there examples of failure to implement CDS? What factors contributed to failure?

    d. In the past when you have implemented new technologies, were there issues related to privacy, security, data integrity, and accuracy? Any ideas on how to mitigate this for future projects like the DDI CDS?
    e. With respect to the implementation of CDS, who is responsible for overseeing implementation of the CDS artifacts, including vendor involvement?
    f. How do clinicians perceive DDI alerts (medication alerts)?
    g. How long do you estimate the process takes for clinician and governance buy-in for CDS?
    h. Are there legal barriers that affect your ability to implement CDS?

6. Can you describe the process of involving stakeholders within your organization?
    a. Are there barriers to engaging stakeholders?
    b. What facilitates stakeholder engagement in your opinion?

7. Please review ddi-cds.org and the associated algorithms. What are your thoughts on implementing the algorithms?
    a. Please comment on whether these appear to be acceptable (codable?, minimally controversial? Are they in line with the values of the organization? belief in the evidence?) based on your past experience?
    b. Prompts: feasible? acceptable? appropriate?
    c. Do you foresee any barriers or facilitators related to the impact to your organization on health outcomes or the patient-clinician encounter within the patient care workflow?

8. Is there a DDI algorithm that would be more valuable or higher priority to you?
9. What resources are available to CDS implementation?
10. What is the organization's capacity to change?
    a. Commitment to CDS implementation from IT, clinical, administration
    b. Technical capabilities affecting CDS implementation
    c. Post-implementation considerations: System updates/version control

11. Are executive leaders supportive of health IT/CDS (a) in general and (b) DDI CDS in particular?
    a. If so, please describe how they are supportive? If not, any thoughts on why they are not supportive
    b. Can you provide insight into how decisions are made to implement CDS in your organization?

12. Can you share with me your organization's general willingness, interest, or motivation to adopt DDI CDS?
    a. Are clinicians integrated into changes in DDI alerts?
    b. Prompts: fit? relevance? Compatibility?

13. Have changes to legislation, policy, and government-mandated financial factors (incentives or penalties) affected the use of CDS?
    a. Do you think policy or financial incentives could influence your organization's decision to use DDI CDS?
    b. Are you concerned about making changes to your system because of regulatory concerns?

14. What concerns do you think your organization will have related to the cost of implementation, maintenance, and support costs?
15. What do you perceive to be the technical barriers to the adoption/implementation of CDS?
    a. What about data standardization, interoperability, or integration?
    b. Have you integrated CDS algorithms not from your EHR vendor? Any SMART on FHIR apps? Third-party software?
    c. Whom do you expect to maintain CDS?

16. Do you measure alert performance? If so, how do you measure the performance of alerts?
    a. Do you examine override rates, rate of alerting?
    b. Do results from alert performance measures affect priorities for technical changes?

17. What challenges exist to train users with CDS, and these algorithms in particular?
18. What advice would you give us with respect to increasing the adoption/implementation of the DDI algorithms?
19. What would successful adoption look like?
20. Are there other comments you would like to provide?

Supplementary Appendix B   Strategies to ensure research rigor

Dimensions[45,46]	Strategies[47]
Credibility	• Coding structure was checked by other researchers (S.G. and V.S.) who are experts in health care research: analyst triangulation • Results were reviewed by experts: expert checking[46] • Peer debriefing after interviews • Researchers' experience in qualitative research[48] • Researchers have extensive experience with interviews in health care[49] • Researchers are knowledgeable on the topic of DDI CDS and implementation science in health care[49]
Transferability	• Purposeful sampling (i.e., snowball sampling)[50] from different backgrounds[51] • Findings were compared with other literature in the field
Dependability	• Multiple rounds of coding[45] • Peer examination[45] • Researcher ensured the accuracy of the transcripts by double-checking[46] • Coding structure and data were checked by other researchers (S.G. and V.S.)[46] • Interviews followed a written protocol[46,52]
Confirmability	• Self-reflections throughout the process[46] via regular meetings • Coding structure, and data were checked by other researchers (S.G. and V.S.)[46]

Abbreviations: CDS, clinical decision support; DDI, drug–drug interaction.

Supplementary Appendix C Barriers Codebook

Supplementary Table S1   Subtheme for hardware and software

Hardware and software	
Maintenance issues	• Difficult to maintain • Lots of maintenance
Technical adoption issues	• Requires lots of effort for setup and accuracy check • Not sure how to implement a new DDI algorithm
Security issues	• Difficult to securely process and share data
Proprietary issues	• Difficult to import algorithms into the current system • Interoperability issue • High dependency on the current system

Abbreviation: DDI, drug–drug interaction.

Supplementary Table S2   Subtheme for clinical content

Clinical content	
Pitfalls of algorithmizing DDI	• The rare delineation between drug interactions • Challenging to categorize levels • Not enough level of evidence • Difficult to find a threshold

Abbreviation: DDI, drug–drug interaction.

Supplementary Table S3   Subtheme for human–computer interaction

Human–computer interface	
Usability issues	● Inability to modify the off-the-shelf drug warnings ● High override rate ● Need more reasons for the dropdowns ● DDI alerts don't provide alternative options ● Overuse of interruptive alerts ● People lack tools to change DDI alerts
Suboptimal DDI CDS user experience	● DDI alert is not helpful, cumbersome, annoying, interruptive, and useless ● DDI alert fatigue

Abbreviations: CDS, clinical decision support; DDI, drug–drug interaction.

Supplementary Table S4   Subtheme for workflow and communication

Workflow and communication	
Insufficient training and education	● No training ● The training program is antiquated, not extensive ● A lot of self-training

Supplementary Table S5   Subtheme for people

People	
Varied DDI alerts exposure among users	● Residents might see them as much more annoying because they're experiencing a lot more often ● Physicians get so many alerts on all of the medicines they order and most of them are useless ● Attendings wanted to see them and believe that they were beneficial ● Clinicians don't complain much about DDI alerts as they only concern immediate and severe alerts with other alerts fired to pharmacists ● Alerts mostly face residents ● Pharmacists like this but no doctor is ever going to read through this kind of thing ● Over alert makes people in the medication and patient safety world happy
Insufficient social capital and capacity	● Pharmacy coordinators are the ones who drive changes but are too occupied ● It's challenging to find clinical people that may have tech interests ● It's challenging to find people who can implement and drive change and actually have time ● It's difficult to find local champions to implement something this complex ● IT team is willing to work on things but has no bandwidth to act on anything ● There is rich data but few people know how to interpret it ● People are interested, but there's a technical and operational inertia

Abbreviation: DDI, drug–drug interaction.

Supplementary Table S6   Subtheme for internal organizational features

Internal organizational features	
Organizational inertia	● Low priority ● Safety events don't usually drive the implementation of DDI algorithms ● Pushback from like risk management ● Limited resource ● Difficult to get through backlogs
Monetary inertia	● Too cost prohibitive ● Difficult to justify cost-benefit
Lengthy governance process	● The DDI algorithm build-review-finalization process is challenging and time-consuming

Abbreviation: DDI, drug–drug interaction.

Supplementary Table S7 Subtheme for external features, rules, and regulations

External features, rules, and regulations	
Legal barriers	● Rarely encountered legal barriers that need a legal team to review ● The legal barrier is minimal ● More conservative with implementation at top litigations areas

Supplementary Table S8 Subtheme for measurement and monitoring

Measurement and monitoring	
Lack of actionable metrics	● Lack of value quality measure ● Lack of systematic process of analyzing alerts and retooling them