Appendix 3: Scoping Review Articles

1. Bindman AB. Learning healthcare systems: a perspective from the US. Public health research & practice. 2019;29(3). https://doi.org/10.17061/phrp2931920

2. Brannon E, Wang T, Lapedis J, et al. Towards a Learning Health System to Reduce Emergency Department Visits at a Population Level. AMIA Annu Symp Proc. 2018;2018:295-304.

3. Flott K, Nelson D, Moorcroft T, et al. Enhancing Safety Culture Through Improved Incident Reporting: A Case Study In Translational Research. Health Aff (Millwood). 2018;37(11):1797-804. doi:10.1377/hlthaff.2018.0706

4. Gardner W. Policy Capacity in the Learning Healthcare System Comment on "Health Reform Requires Policy Capacity". International journal of health policy and management. 2015;4(12):841-3. https://doi.org/10.15171/ijhpm.2015.147

5. Holm S, Ploug T. Big Data and Health Research—The Governance Challenges in a Mixed Data Economy. Journal of bioethical inquiry. 2017;14(4):515-25. https://doi.org/10.1007/s11673-017-9810-0

6. Lessard L, Michalowski W, Fung-Kee-Fung M, Jones L, Grudniewicz A. Architectural frameworks: defining the structures for implementing learning health systems. Implementation science : IS. 2017;12(1):78-. https://doi.org/10.1186/s13012-017-0607-7

7. Marsolo K. In Search of a Data-in-Once, Electronic Health Record-Linked, Multicenter Registry-- How Far We Have Come and How Far We Still Have to Go. eGEMs (Generating Evidence & Methods to improve patient outcomes). 2013;1(1):1003-. https://doi.org/10.13063/2327-9214.1003

8. Mathews S, Golden S, Demski R, Pronovost P, Ishii L. Advancing health care quality and safety through action learning. Leadership in health services (2007). 2017;30(2):148-58. https://doi.org/10.1108/lhs-10-2016-0051

9. Morain SR, Majumder MA, McGuire AL. Learning Health System - Moving from Ethical Frameworks to Practical Implementation. J Law Med Ethics. 2019;47(3):454-8. https://doi.org/10.1177/1073110519876180

10. Sadler E, Porat T, Marshall I, et al. Shaping innovations in long-term care for stroke survivors with multimorbidity through stakeholder engagement. PloS one. 2017;12(5):e0177102-e. https://doi.org/10.1371/journal.pone.0177102

11. Teare GF, Keller M, Hall D. Bringing Together Research and Quality Improvement: The Saskatchewan Approach. Healthc Q. 2018;21(Sp):56-60. https://doi.org/10.12927/hcq.2018.25637

12. Van Royen P, Rees CE, Groenewegen P. Patient-centred interprofessional collaboration in primary care: challenges for clinical, educational and health services research. An EGPRN keynote paper. The European journal of general practice. 2014;20(4):327-32. https://doi.org/10.3109/13814788.2014.908462

13. Wulff A, Marschollek M. Learning Healthcare Systems in Pediatrics: Cross-Institutional and Data-Driven Decision-Support for Intensive Care Environments (CADDIE). Stud Health Technol Inform. 2018;251:109-12.

14. Cahan A, Cimino JJ. A Learning Health Care System Using Computer-Aided Diagnosis. Journal of medical Internet research. 2017;19(3):e54-e. https://doi.org/10.2196/jmir.6663

15. Deeny SR, Steventon A. Making sense of the shadows: priorities for creating a learning healthcare system based on routinely collected data. BMJ quality & safety. 2015;24(8):505-15. https://doi.org/10.1136/bmjqs-2015-004278

16. Gaveikaite V, Filos D, Schonenberg H, van der Heijden R, Maglaveras N, Chouvarda I. Learning Healthcare Systems: Scaling-Up Integrated Care Programs. Studies in health technology and informatics. 2018;247:825-9.

17. Gonzalo JD, Thompson BM, Haidet P, Mann K, Wolpaw DR. A Constructive Reframing of Student Roles and Systems Learning in Medical Education Using a Communities of Practice Lens. Academic medicine. 2017;92(12):1687-94. https://doi.org/10.1097/acm.0000000000001778

18. Jagsi R, Griffith KA, Jones RD, et al. Effect of Public Deliberation on Patient Attitudes Regarding Consent and Data Use in a Learning Health Care System for Oncology. Journal of clinical oncology. 2019;37(34):3203-11. https://doi.org/10.1200/jco.19.01693

19. Kim KK, Sankar P, Wilson MD, Haynes SC. Factors affecting willingness to share electronic health data among California consumers. BMC medical ethics. 2017;18(1):25. https://doi.org/10.1186/s12910-017-0185-x

20. Lee DJ, Ding J, Guzzo TJ. Improving Operating Room Efficiency. Current urology reports. 2019;20(6):1-8. https://doi.org/10.1007/s11934-019-0895-3

21. Budrionis A, Bellika JG. J Biomed Inform. The Learning Healthcare System: Where are we now? A systematic review. 2016;64:87-92. https://doi.org/10.1016/j.jbi.2016.09.018

22. Etheredge LM. A Rapid-Learning Health System. Health Affairs. 2007;26(2): w107-w18. https://doi.org/10.1377/hlthaff.26.2.w107

23. Forrest CB, Chesley FD, Tregear ML, Mistry KB. Development of the Learning Health System Researcher Core Competencies. Health services research. 2018;53(4):2615-32. https://doi.org/10.1111/1475-6773.12751

24. Fore D, Goldenhar LM, Margolis PA, Seid M. Using goal-directed design to create a novel system for improving chronic illness care. JMIR research protocols. 2013;2(2): e43. https://doi.org/10.2196/resprot.2749

25. Kumar S, Hanss T, Johnson L, et al. Leveraging Contextual Inquiry Methods to Empower Patients in a Learning Health System. 2015. p. 3141-7. https://doi.org/10.1109/HICSS.2015.379

26. Galvin HK, Petersen C, Subbian V, Solomonides A. Patients as Agents in Behavioral Health Research and Service Provision: Recommendations to Support the Learning Health System. Applied Clinical Informatics. 2019;10(5):841-8. https://doi.org/10.1055/s-0039-1700536

27. Cipriano PF. The importance of knowledge-based technology. Nursing administration quarterly. 2012;36(2):136-46. https://doi.org/10.1097/NAQ.0b013e31824a004c

28. Greenberg-Worisek AJ, Shippee ND, Schaffhausen C, et al. The Learning Health System Competency Appraisal Inventory (LHS-CAI): A novel tool for assessing LHS-focused education needs. Learning Health Systems. 2020. https://doi.org/10.1002/lrh2.10218

29. Hsu ER, Klemm JD, Kerlavage AR, Kusnezov D, Kibbe WA. Cancer Moonshot Data and Technology Team: Enabling a National Learning Healthcare System for Cancer to Unleash the Power of Data. Clinical pharmacology and therapeutics. 2017;101(5):613-5. https://doi.org/10.1002/cpt.636

30. Krumholz HM. Big data and new knowledge in medicine: the thinking, training, and tools needed for a learning health system. Health affairs Web exclusive. 2014;33(7):1163-70. https://doi.org/10.1377/hlthaff.2014.0053

31. Irimu G, Ogero M, Mbevi G, et al. Approaching quality improvement at scale: a learning health system approach in Kenya. Arch Dis Child. 2018;103(11):1013-9. https://doi.org/10.1136/archdischild-2017-314348

32. Lannon CM, Peterson LE. Pediatric collaborative improvement networks: background and overview. Pediatrics (Evanston). 2013;131 Suppl 4(Supplement): S189-S95. https://doi.org/10.1542/peds.2012-3786E

33. McLachlan S, Dube K, Johnson O, et al. A framework for analysing learning health systems: Are we removing the most impactful barriers? Learning Health Systems. 2019;3(4). https://doi.org/10.1002/lrh2.10189

34. Newhouse RP. Nursing's Role in Engineering a Learning Healthcare System. The Journal of nursing administration. 2009;39(6):260-2. https://doi.org/10.1097/NNA.0b013e3181a7293e

3

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

35. Satterfield K, Rubin JC, Yang D, Friedman CP. Understanding the roles of three academic communities in a prospective learning health ecosystem for diagnostic excellence. Learning Health Systems. 2020;4(1). https://doi.org/10.1002/lrh2.10204

36. Scobie S, Castle-Clarke S. Implementing learning health systems in the UK NHS: Policy actions to improve collaboration and transparency and support innovation and better use of analytics. Learning Health Systems. 2020;4(1). https://doi.org/10.1002/lrh2.10209

37. Liu VX, Morehouse JW, Baker JM, Greene JD, Kipnis P, Escobar GJ. Data that drive: Closing the loop in the learning hospital system. Journal of hospital medicine. 2016;11(S1): S11-S7. https://doi.org/10.1002/jhm.2651

38. Reid RJ. Embedding Research in the Learning Health System. HealthcarePapers (Toronto). 2016;16(SP):30-5. https://doi.org/10.12927/hcpap.2016.24724

39. Christensen V, Floyd N, Anderson J. It Would've Been Nice if They Interpreted the Data a Little Bit. It Didn't Really Say Much, and It Didn't Really Help Us.": A Qualitative Study of VA Health System Evidence Needs. Medical Care. 2019;57: S228-S32. https://doi.org/10.1097/MLR.0000000000001171

40. Kilbourne AM, Goodrich DE, Miake-Lye I, Braganza MZ, Bowersox NW. Quality Enhancement Research Initiative Implementation Roadmap: Toward Sustainability of Evidence-based Practices in a Learning Health System. Medical Care. 2019;57: S286-S93. https://doi.org/10.1097/MLR.0000000000001144

41. Hemingway H, Asselbergs FW, Danesh J, et al. Big data from electronic health records for early and late translational cardiovascular research: Challenges and potential. European heart journal. 2018;39(16):1481-95. https://doi.org/10.1093/eurheartj/ehx487

42. Harper E. Can big data transform electronic health records into learning health systems? Studies in health technology and informatics. 2014; 201:470-5.

43. Felkey BG, Fox BI. Are you Practicing in a Learning Health System? Hospital pharmacy (Philadelphia). 2017;52(1):82-4. https://doi.org/10.1310/hpj5201-82

44. McNutt TR, Benedict SH, Low DA, et al. Using Big Data Analytics to Advance Precision Radiation Oncology. International journal of radiation oncology, biology, physics. 2018;101(2):285-91. https://doi.org/10.1016/j.ijrobp.2018.02.028

45. Finkelstein J, Zhang F, Levitin SA, Cappelli D. Using big data to promote precision oral health in the context of a learning healthcare system. Journal of Public Health Dentistry. 2020;80(S1): S43-S58. https://doi.org/10.1111/jphd.12354

46. Peng DM, Rosenthal DN, Zafar F, Smyth L, VanderPluym CJ, Lorts A. Collaboration and new data in ACTION: a learning health care system to improve pediatric heart failure

4

and ventricular assist device outcomes. Transl Pediatr. 2019;8(4):349-55. https://doi.org/10.21037/tp.2019.07.12

47. Kaboli PJ, Miake-Lye IM, Ruser C, et al. Sequelae of an Evidence-based Approach to Management for Access to Care in the Veterans Health Administration. Medical Care. 2019;57: S213-S20. https://doi.org/10.1097/MLR.0000000000001177

48. Joda T, Waltimo T, Probst-Hensch N, Pauli-Magnus C, Zitzmann NU. Health Data in Dentistry: An Attempt to Master the Digital Challenge. Public Health Genomics. 2019;22(1-2):1-7. https://doi.org/10.1159/000501643

49. Friedman CP, Rubin JC, Sullivan KJ. Toward an Information Infrastructure for Global Health Improvement. Yearbook of medical informatics. 2017;26(1):16-23. https://doi.org/10.15265/IY-2017-004

50. English M, Irimu G, Agweyu A, et al. Building Learning Health Systems to Accelerate Research and Improve Outcomes of Clinical Care in Low- and Middle-Income Countries. PLoS medicine. 2016;13(4): e1001991-e. https://doi.org/10.1371/journal.pmed.1001991

51. Elnahal SM, Clancy CM, Shulkin DJ. A Framework for Disseminating Clinical Best Practices in the VA Health System. JAMA: the journal of the American Medical Association. 2017;317(3):255-6. https://doi.org/10.1001/jama.2016.18764

52. Williams MS, Buchanan AH, Davis FD, et al. Patient-Centered Precision Health in A Learning Health Care System: Geisinger's Genomic Medicine Experience. Health affairs Web exclusive. 2018;37(5):757-64. https://doi.org/10.1377/hlthaff.2017.1557

53. Ovretveit J, Nelson E, James B. Building a learning health system using clinical registers: a non-technical introduction. Journal of health organization and management. 2016;30(7):1105-18. https://doi.org/10.1108/JHOM-06-2016-0110

54. Reams C, Edwards R, Powell M. State Synergies and Disease Surveillance: Creating an Electronic Health Data Communication Model for Cancer Reporting and Comparative Effectiveness Research in Kentucky. eGEMs (Generating Evidence & Methods to improve patient outcomes). 2014;2(2):1064. https://doi.org/10.13063/2327-9214.1064

55. Lai J, Klag M, Shikako-Thomas K. Designing a program evaluation for a medical-dental service for adults with autism and intellectual disabilities using the RE-AIM framework. Learning Health Systems. 2019;3(3). https://doi.org/10.1002/lrh2.10192

56. Delaney BC, Peterson KA, Speedie S, Taweel AP, Arvanitis TN, Hobbs FDR. Envisioning a Learning Health Care System: The Electronic Primary Care Research Network, A Case Study. Annals of family medicine. 2012;10(1):54-9. https://doi.org/10.1370/afm.1313

57. Lovestone S. The European medical information framework: A novel ecosystem for sharing healthcare data across Europe. Learn Health Syst. 2020;4(2): e10214. https://doi.org/10.1002/lrh2.10214

58. Friedman C, Rigby M. Conceptualising and creating a global learning health system. International journal of medical informatics (Shannon, Ireland). 2012;82(4): e63-e71. https://doi.org/10.1016/j.ijmedinf.2012.05.010

59. Braunstein ML, Detmer D. Interoperable informatics for health enterprise transformation. Journal of Enterprise Transformation. 2016;6(3-4):110-9. https://doi.org/10.1080/19488289.2016.1254692

60. Tabano DC, Cole E, Holve E, Davidson AJ. Distributed Data Networks That Support Public Health Information Needs. Journal of public health management and practice. 2017;23(6):674-83. https://doi.org/10.1097/PHH.0000000000000614

61. Colicchio TK, Del Fiol G, Cimino JJ. Health information technology as a learning health system: Call for a national monitoring system. Learning Health Systems. 2020;4(1). https://doi.org/10.1002/lrh2.10207

62. Woody SK, Burdick D, Lapp H, Huang ES. Application programming interfaces for knowledge transfer and generation in the life sciences and healthcare. NPJ Digit Med. 2020; 3:24. https://doi.org/10.1038/s41746-020-0235-5

63. Harrison MI, Shortell SM. Multi-level analysis of the learning health system: Integrating contributions from research on organizations and implementation. Learning Health Systems. 2020. https://doi.org/10.1002/lrh2.10226

64. Davis FD, Williams MS, Stametz RA. Geisinger's effort to realize its potential as a learning health system: A progress report. Learning Health Systems. 2020. https://doi.org/10.1002/lrh2.10221

65. Yang UC, Hsiao TH, Lin CH, Lee WJ, Lee YS, Fann YC. Integrative LHS for precision medicine research: A shared NIH and Taiwan CIMS experience. Learning Health Systems. 2019;3(1). https://doi.org/10.1002/lrh2.10071

66. Fiuzat M, Califf RM. The US Food and Drug Administration and the Future of Cardiovascular Medicine. JAMA cardiology. 2016;1(8):950-2. https://doi.org/10.1001/jamacardio.2016.2580

67. Friedman CP, Wong AK, Blumenthal D. Achieving a nationwide learning health system. Science translational medicine. 2010;2(57):57cm29-57cm29. https://doi.org/10.1126/scitranslmed.3001456

68. Lu CY, Williams MS, Ginsburg GS, Toh S, Brown JS, Khoury MJ. A proposed approach to accelerate evidence generation for genomic-based technologies in the context of a

learning health system. Genetics in medicine. 2018;20(4):390-6. https://doi.org/10.1038/gim.2017.122

69. Brown JS, Kahn M, Toh D. Data Quality Assessment for Comparative Effectiveness Research in Distributed Data Networks. Medical care. 2013;51(8 Suppl 3): S22-S9. https://doi.org/10.1097/MLR.0b013e31829b1e2c

70. Harris JG, Bingham CA, Morgan EM. Improving care delivery and outcomes in pediatric rheumatic diseases. Current opinion in rheumatology. 2016;28(2):110-6. https://doi.org/10.1097/BOR.0000000000000257

71. Wysham NG, Abernethy AP, Cox CE. Setting the vision: applied patient-reported outcomes and smart, connected digital healthcare systems to improve patient-centered outcomes prediction in critical illness. Current opinion in critical care. 2014;20(5):566-72. https://doi.org/10.1097/MCC.0000000000000139

72. Kaggal VC, Elayavilli RK, Mehrabi S, et al. Toward a Learning Health-care System - Knowledge Delivery at the Point of Care Empowered by Big Data and NLP. Biomedical informatics insights. 2016;2016(Suppl. 1):13-22. https://doi.org/10.4137/BII.S37977

73. Margolis PA, Peterson LE, Seid M. Collaborative Chronic Care Networks (C3Ns) to transform chronic illness care. Pediatrics (Evanston). 2013;131 Suppl 4(Supplement): S219-S23. https://doi.org/10.1542/peds.2012-3786J

74. Cumyn A, Barton A, Dault R, Cloutier AM, Jalbert R, Ethier JF. Informed consent within a learning health system: A scoping review. Learn Health Syst. 2020;4(2): e10206. https://doi.org/10.1002/lrh2.10206

75. Finlayson SG, Levy M, Reddy S, Rubin DL. Toward rapid learning in cancer treatment selection: An analytical engine for practice-based clinical data. J Biomed Inform. 2016; 60:104-13. https://doi.org/10.1016/j.jbi.2016.01.005

76. Seid M, Hartley DM, Dellal G, Myers S, Margolis PA. Organizing for collaboration: An actor-oriented architecture in ImproveCareNow. Learning Health Systems. 2020;4(1). https://doi.org/10.1002/lrh2.10205

77. Richesson RL, Horvath MM, Rusincovitch SA. Clinical Research Informatics and Electronic Health Record Data. Yearbook of medical informatics. 2014;23(1):215-23. https://doi.org/10.15265/IY-2014-0009

78. Richardson JE, Middleton B, Platt JE, Blumenfeld BH. Building and maintaining trust in clinical decision support: Recommendations from the Patient-Centered CDS Learning Network. Learn Health Syst. 2020;4(2): e10208. https://doi.org/10.1002/lrh2.10208

79. McLachlan S, Dube K, Kyrimi E, Fenton N. LAGOS: Learning health systems and how they can integrate with patient care. BMJ Health and Care Informatics. 2019;26(1). https://doi.org/10.1136/bmjhci-2019-100037

80. Rangachari P, Dellsperger KC, Karl Rethemeyer R. A qualitative study of interprofessional learning related to electronic health record (EHR) medication reconciliation within a social knowledge networking (SKN) system. Journal of Healthcare Leadership. 2019; 11:23-41. https://doi.org/10.2147/JHL.S198951

81. Borsky AE, Flores EJ, Berliner E, Chang C, Umscheid CA, Chang SM. Next steps in improving healthcare value: AHRQ evidence-based practice center program-applying the knowledge to practice to data cycle to strengthen the value of patient care. Journal of Hospital Medicine. 2019;14(5):311-4. https://doi.org/10.12788/jhm.3157

82. Greene SM, Reid RJ, Larson EB. Implementing the Learning Health System: From Concept to Action. Annals of internal medicine. 2012;157(3):207-10. https://doi.org/10.7326/0003-4819-157-3-201208070-00012

83. Solomon MZ, Gusmano MK, Maschke KJ. The Ethical Imperative and Moral Challenges of Engaging Patients and The Public with Evidence. Health affairs Web exclusive. 2016;35(4):583-9. https://doi.org/10.1377/hlthaff.2015.1392

84. Platt JE, Jacobson PD, Kardia SLR. Public Trust in Health Information Sharing: A Measure of System Trust. Health services research. 2018;53(2):824-45. https://doi.org/10.1111/1475-6773.12654

85. Gilmartin HM, Hess E, Mueller C, Plomondon ME, Waldo SW, Battaglia C. A pilot study to assess the learning environment and use of reliability enhancing work practices in VHA cardiac catheterization laboratories. Learning Health Systems. 2020. https://doi.org/10.1002/lrh2.10227

86. Kaushal R, Hripcsak G, Ascheim DD, et al. Changing the research landscape: the New York City Clinical Data Research Network. Journal of the American Medical Informatics Association: JAMIA. 2014;21(4):587-90. https://doi.org/10.1136/amiajnl-2014-002764

87. Ethier JF, Curcin V, Barton A, et al. Clinical data integration model. Core interoperability ontology for research using primary care data. *Methods of information in medicine*. 2015;54(1):16-23. doi:10.3414/ME13-02-0024

88. Friedman CP, Donaldson KM, Vantsevich AV. Educating medical students in the era of ubiquitous information. *Medical teacher*. 2016;38(5):504-509. doi:10.3109/0142159X.2016.1150990

89. Medicine I of, Care R on V and SDH, McGinnis JM, et al. Clinical Data as the Basic Staple of Health Learning: Creating and Protecting a Public Good: Workshop Summary. National Academies Press; 2011. doi:10.17226/12212