

KYUNG HEE UNIVERSITY

Department of Computer Science & Engineering Ubiguitous Computing Lab



Hybrid Knowledge Modeling for Case Selection and Adaptation in CDSS

Ph.D. Defense Presentation

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Ph.D. Dissertation Spring 2022

Proposed Idea Experimentation Conclusion Publications



Presentation Agenda

Hybrid Knowledge

MODELING

INTRODUCTION

- o Background
- Motivation
- o Problem Statement
- o Taxonomy
- Related Work

PROPOSED IDEA

- Solution 1: Active Case Partitioning
- Solution 2: Case Selection
- Solution 3: Case Adaptation

EXPERIMENTATION & RESULTS

- Experimental Design
- System-centric Experimentation
- o User-centric Experimentation

CONCLUSION



Related Work

Proposed Idea Experimentation Conclusion Publications



Background

- Clinical Decision Support Systems (CDSS) are specialized software solutions that ingest data to provide a wide array of services for cognitive-intensive complex decision making e.g. *disease diagnosis and treatment*.^{1,2,3}
- CDSS increasingly leverage data-driven approaches for decision modeling along with expert-driven approaches for compliance with the domain processes.^{4,5,6}
- Hybrid knowledge modeling play an important role in generating accurate and domain relevant recommendations for complex scenarios such as medication recommendation.^{4,6,7}





Case-based Reasoning in CDSS

- New Case: Receive a test case comprised of problem component.
- Case Search: Search all the cases and retrieve a pre-defined set of nearest cases.
- Proposed Solution: Combine solution component of the retrieved cases e.g. majority vote or averaging.
- **Confirm Solution**: Domain expert finally accepts the generated solution or update the generated solution.
- Knowledge base contains past cases and newly retained cases.



Khan, M. J., Hayat, H., & Awan, I. (2019). Hybrid case-base maintenance approach for modeling large scale case-based reasoning systems. Human-centric Computing and Information Sciences, 9(1), 1-25.

Introduction	Proposed Idea	Conclusion
Related Work	Experimentation	Publications

Align consensus-based domain knowledge and experience-based routine clinical practice for multi-factor recommendations.

- Provide recommendation for complex cases with inherent data scarcity issues.
- Provide transparency and knowledge-based interpretability for the domain expert in recommendation generation.
- Reducing cognitive-load on the physician with intuitive and reliable decision support approach.

Motivation





UCL Ubiquitous Computing Laboratory Kyung Hee University, Korea **Related Work**

Conclusion Publications



Problem Statement

Clinical Practice Guidelines provide a **general framework** to guide clinicians but lack **operational details i.e.** cover the partial scope of the recommendation. How to incorporate **expert-model** in case-based reasoning for **domain compliant** complex **recommendation** generation e.g. medication prescription? ^{8,9,18,19}

Overall Goal

Design a hybrid knowledge modeling approach for both medication and dosage selection that can leverage both partial domain knowledge as well as routine clinical practice of clinicians.

Objectives

- 1. Leverage partial domain knowledge for active partitioning of clinical case base.
- 2. Select highly relevant subset of clinical reference cases from a general pool of the candidate cases.
- 3. Synthesize domain model with selected cases for multi-factor recommendation generation.

Challenges

- 1. How to identify **distinct neighborhoods** within a single clinical case base?
- 2. How to identify relevant high prospect clinical cases for **effective solution selection**?
- 3. How to provide **fine-grained solution** recommendations from a partial domain model?



e.g. SVM, RF, DT

Decision-level Fusioning

[10] Artificial Intelligence: A Modern Approach, 4th US ed. by Stuart Russell and Peter Norvig. 2021

Decision-level Fusioning

e.g. Random Forest

• [11] Alazzam, Malik Bader, et al. "Nursing care systematization with case-based reasoning and artificial intelligence." Journal of Healthcare Engineering 2022 (2022).

Hybrid Knowledge Modeling for Case Selection and Adaptation in CDSS

Hybrid Modeling

Hybrid-Case Based Reasoning (domain knowledge + clinical cases)

Introduction Related Work		Proposed Ide Experimentat	a ion	Conclusion Publications	UCL Ubiquitous Computing Laboratory Kyung Hee University, Korea		
Related \	Nork						
Reference	Domain	Modeling	Guideline Incorporation	Capture Clinical Practice	Feedback	Medication Selection	Medication Dosing
[7] S.L. Ting, 2011	General treatment	Case-based	No	Yes	No	Yes	No
[16] Branden, 2011	Lung cancer treatment	Case-based	No	Yes	No	Yes	Yes (single)
[20] Khussainova, 2015	Brain cancer treatment	Case-based	No	Yes	No	No	No
[17] Teodorović, 2013	Thyroid Cancer treatment	Case-based	No	Yes	No	Yes	Yes (single)
[12] Shemeikka, 2015	Kidney patients treatment	Expert Model	Yes	No	No	Yes	No
[13] Hellden, 2015	General treatment	Expert Model	Yes	No	No	Yes	No
[14] Awdishu, 2016	Kidney patients treatment	Expert Model	Yes	No	No	Yes	Manual
[15] Pirnejad, 2019	Kidney patients treatment	Expert Model	Yes	No	No	Yes	Manual
[8] Niazkhani, 2020	Kidney patients treatment	Expert Model	Yes	No	No	Yes	Manual
Proposed	Kidney patients treatment	Hybrid: Case-based	Yes	Yes	Yes	Yes	Yes (multiple)











Introduction Related Work	Proposed Idea Experimentation	Conclusion Publications	UCL Ubiq Kyz	uitous Computing Laboratory ng Hee University, Korea	
Research	n Map				
		Proposed Solutions			
	Solution 1	Solution 2	Solution 3		
Domain Model Clinical Cases	Active Case base Partitioning	Case Selection	Case Adaptation	Recommendation	
	Problem: User define neighborhood threshold value results in fixed size case base partitions. Appropriate neighborhood size selection is based on trial and error approach.	Problem: Similar candidate cases are selected primarily based on their proximity to the test case while outcome information is not accounted for case selection.	Problem: Domain knowledge is generally insufficient for generating recommendations for complex tasks such as medication dosage selection	Outcomes + Variable neighborhood size + Quantify efficacy of similar cases	
Challenges	Challenge 1	Challenge 2	Challenge 3	recommendation	
c1: Fixed size neighborhood	Existing Approach	Existing Approach	Existing Approach	Outcomes	
C2: Similar cases treated equally	Trial and error approach for neigh borhood size selection	Select all cases within a selected neighborhood	Primitive dosage estimation for a single medicine	Case uncertainty Similar case may be unrelated	
knowledge	 Pick top K nearest cases at the inference time (lazy-modeling) 	Assign weight to case dimensions based on domain experts	Manual dosage selection by domain expert (physician)	Generic recommendation	

Hybrid Knowledge Modeling for Case Selection and Adaptation in CDSS

14/50



Hybrid Knowledge Modeling for Case Selection and Adaptation in CDSS

15/50



Ali, Syed Imran, et al. "Clinical Decision Support System Based on Hybrid Knowledge Modeling: A Case Study of Chronic Kidney Disease-Mineral and Bone Disorder Treatment." International Journal of Environmental Research and Public Health 19.1 (2021): 226.

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Case Adaptation

Point estimation through Multiple Linear Regression

R square (R2) equals 0.623822. It means that the predictors (Xi) explain 62.4% of the variance of Y.



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1447227	4						0 Absent	0						4800	(
1447227	5						0 Absent	0						4800	(
1447227	9						0 Absent	0						4800	(
1447227	12						0 Absent	0						7200	(
2251498	3						10 Present	0						1600	(
3380095	2						5 Absent	0						3200	(
3380095	6						5 Absent	0						3200	(
3618303	3		4.3	7.5	7.4	7.26	0 Absent	0	.0	. 0	C - 5	0	0	3200	(
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5032368	2						0 Absent	0						3200	(
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5358846	9						0 Absent	0						4800	(
5358846	10						0 Absent	0						4800	(
5358846	12						0 Absent	0						4800	(
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Residuals: Histogram



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Compare **previous** and **current** medications





Case Study: CKD-MBD Treatment





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28/50



Proposed Idea Introduction Conclusion Ubiquitous Computing Laboratory Kyung Hee University, Korea **Related Work** Experimentation **Publications Extended Decision Tree based on Expert Model Chronic Kidney Disease** Extended Decision Tree PTH intest Pare Th Composite Condition Recommendation Atomic Condition Homone Ca: Corrected Calcium P: Phosphale Dr. Su Woong Jung (Kyungitiee Un LA Reflegaph owledge Engineers Team Synd Imran Ali Symbols C-PTH 130 - 581 Computation evious Assessme (85) -i.PTH (P-I.PT) CaPRI - 450 & (P-PTI) Process Previous Assessm (>300) -LPTH (P-LPT cess Ca & P le Process Ca & P leve CaPBi < 180 A CaPBi decreased by 8.75 times of P-IPBi Decision CaPBI + 158 & CaPBI decreased by 0.5 Series of PaPBI C+>10.2 & P> Ca 9.0-Ca+ 1024P35 **Final Outcome** Ca+1028P+1 Ca + 10 7 4 8 3 Ca+1024P+ Ca+10.28 P 3.8-1 Ca > 10 7 6 1 Ca75-1028P Ca>1028F+ Ca 7.54 116 C+ 90-10247 117 Ca75-1028P 117 Ca 7.54 # 80-1028 P31 Car7.5-102 & Pr T18 4-1025 #35-Comments Cer. T 18 C+9.0-10.2 & F T10 Ca+8.4-30.2 & P = 171 C+754P-55 T19 Ca + 7 Cas75.4458.5 Ca+7.5 & P3.5-129 C+75-004 P35 +75-846P35 Car7.5.5 C+75444P T 30 Ca>75-848P+ Group 2:Vascular Calcification (-) **Compound Conditions** Ca -75404P+55 131 Car755P Group 1:Vascular Calcification (+) Total Number of Rules: 432 132 Ca 1758P35-55 C++754935-**Overall Types of Recommendation: 33** 133 Ca + 7.5 & P-133

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Proposed Idea Experimentation

Conclusion Publications



Generic Recommendation Template

e _	Recommendation Factors		Poss	ible Treatment Options		
nplat	Calcimimetics	Start or Increase	As It Is	Stop or Decrease	Decrease or Stop	
רפח ת	Calcium-based Phosphate Binder	Start or Increase CPB	As It Is	Decrease CPB	Stop CPB	
atior	Non-Calcium-based Phosphate Binder	Start or Increase NCPB	As It Is	Decrease NCPB	Stop NCPB	
pu	Vitamin D receptor activators	Start or Increase	As It Is	Decrease	Stop	Consider Vitamin D Analogs
nme	Calcitriol	Start or Increase	As It Is	Decrease	Stop	Consider Calcitroil
kecor	Dialysate Cal. Concentration	Increase by 0.25 n	nmol/L	Maintain the current dialysa concentration	te decrea	se by 0.25 mmol/L

Recommendation Factors
Calcimimetics
Calcium-based
Phosphate Binder
Non-Calcium-based
Phosphate Binder
Vitamin D receptor activators
Calcitriol
Dialysate Cal. Concentration

Treatment 1 (T1)	
Start or Increase	
Stop CPB	
Start or Increase NCPB	
Stop vitamin D analogs	
Stop Calcitriol	
Reduce by 0.25 mmol/L	

Treatment 2 (T2)	_
Start or Increase	l
Stop CPB	l
Maintain NCPB	l
Stop vitamin D analogs	I
Stop Calcitriol	l
Reduce by 0.25 mmol/L	I

	Treatment 33 (T33)
	Decrease of Stop
•	Decrease or Stop CPB
•	Decrease or Stop NCPB
•	Decrease or Stop
•	Start or Increase Calcitriol
•	Increase by 0.25 mmol/L

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Sample Recommendations



Hybrid Knowledge Modeling for Case Selection and Adaptation in CDSS

32/50

Proposed Idea Experimentation

Conclusion Publications



Step 1 : Laboratory Test Administration



- Laboratory tests are performed at three different time scales
- Patient may visits every month for the checkup/ dialysis treatment
- PTH test is valid for three months
- Both lateral radiography and echocardiogram are performed on annual basis



Proposed Idea Experimentation

Conclusion Publications



Step 2 : Patient Type Identification



- Patients are divided into two groups
- Group 1 deals with those patients who are diagnosed positive for vascular calcification
- Group 2 deals with patients whose vascular calcification is negative
- Group identification is based on lateral radiography and echocardiogram tests



Proposed Idea

Conclusion Publications



Experimentation

Step 2 : Generic Recommendation based on Guidelines



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Proposed Idea Introduction Conclusion **Related Work** Experimentation

Publications



Step 3 : Dosage Recommendation based on Similar Patients





Hybrid Knowledge Modeling for Case Selection and Adaptation in CDSS

37/50

Experimentation

Introduction Related Work	Proposed Idea Experimentation	Conclusion Publications			Ubiquitous Computing Laboratory Kyung Hee University, Korea
Experimental S	Setup				
Dataset De	escription				
Total Patients: 66 Total Case-base: 850 Patient Type-I: 374 Patient Type-II: 476	Test Cases: 250 Initial Case-base: 600 Patient Type-I: 107 Patient Type-II: 143	<u>نه</u>	System a Exper	nd User-centric rimentation	
 System-centric Exper Case insufficien Compliance bet and clinical prace Concordance be clinical practice 	Timentation (250 cases) cy detection tween expert model ctice etween dosage and	Record Lab test results 1 Lab test Visit 1 2 Lab test Visit 2 3 Lab test Visit 3 4 Lab test Visit 4 5 Lab test Visit 5	Generate Recommendation Recommendation 2 Recommendation 3 Recommendation 4 Recommendation 5	Prescription 1 Prescription 2 Prescription 3 Prescription 4 Prescription 5	Record Evaluation Evaluation for Recommendation 1 2 Evaluation for Recommendation 3 Evaluation for Recommendation 4 Evaluation for Recommendation 5
 User-centric Experim Find out usabile the CDSS throut Participants: 13 	nentation lity experience of ugh a pilot study 1 (clinicians)	Lab test Visit 12	Recommendation 12	Prescription 12	Evaluation for Recommendation 12



CKDMBD-CDSS Evaluation (System-centric)

Experiment objective:

To find out case partitions having insufficient cases at data acquisition stage

Findings:

- Recommendations T¹⁶ and T¹⁷ mostly deal with maintaining the current medication prescription
- 2. Consistent with the clinical practice where abrupt changes in treatment are avoided





Findings:

- In general most of the recommendations have high compliance with routine clinical practice
- 77% compliance rate is recorded for recommendations factors matched 3 and above



Introduction	Proposed Idea	Conclusion	UCL Ubiquitous Computing Laboratory
Related Work	Experimentation	Publications	Kyung Hee University, Korea

CKDMBD-CDSS Evaluation (System-centric)

Experiment objective:

To evaluate breakdown of compliance rate of 6 medication classes

Findings:

 In non-compliant cases 'dosage decrease' slightly dominated i.e. the CDSS recommended to 'maintain' while the physician decreased the dosage



Medication Class Compliance



Conclusion

Publications



CKDMBD-CDSS Evaluation (System-centric)

Calcimima	atics	Predicted			
		Start/Increase	Maintain	Stop/Decrease	
a	Start/Increase	167	132	17	
ctu	Maintain	29	334	23	
Ă	Stop/Decrease	19	72	57	
Calcitriol			Predicted		
		Start/Increase	Maintain	Stop/Decrease	
a	Start/Increase	173	31	13	
ctu	Maintain	18	448	11	
Ă	Stop/Decrease	14	74	68	
Vitamin D	& Analogs		Predicted		
		Start/Increase	Maintain	Stop/Decrease	
a	Start/Increase	154	31	13	
ctu	Maintain	18	448	11	
Ă	Stop/Decrease	14	74	68	

Confusion Matrix

Calcium-b	ased				
Phosphate Binders		Predicted			
		Start/Increase	Maintain	Stop/Decrease	
a	Start/Increase	140	66	8	
ctu	Maintain	16	488	19	
Ă	Stop/Decrease	3	41	69	
Non-Calci	um-based				
Phosphate Binders			Predicted		
		Start/Increase	Maintain	Stop/Decrease	
a	Start/Increase	71	101	19	
ctu	Maintain	49	259	52	
Ā	Stop/Decrease	9	187	103	
Calcium Dialysate					
Concentration			Predicted		
		Start/Increase	Maintain	Stop/Decrease	
a	Start/Increase	45	7	0	
ctu	Maintain	2	766	0	
Ă	Stop/Decrease	0	8	22	

Related Work	Experimentation	Publications	Kyung Hee University, Korea
	_		

CKDMBD-CDSS Evaluation (System-centric)

Experiment objective:

To evaluate concordance between dosage recommendation and routine clinical practice

Concordance Findings:

- 1. Cinacalcet = 85.71%
- 2. Calcitriol (po) = 81.81%
- 3. Calcitriol (iv) = 66.66%
- 4. Paricalcitrol (iv) = 82.24%
- 5. Calcium Carbonate = 76.47%
- 6. Calcium Acetate = 81.81%
- 7. Sevelamer = 76.12%
- 8. Lanthanum = 55%
- 9. Dialysate Cal. Concent. = 98.40%

Concordance evaluation for the medication dosage recommendation

Management Class	Total Cases	Present Cases	In-Range Cases	Out-of-Range Cases
⁺ Cinacalcet	250	49	42	7
Calcitriol, po	250	11	9	2
Calcitriol, iv	250	15	10	5
Paricalcitol, iv	250	148	122	26
⁺ Alfacalcidol	250	0	0	0
[†] Calcium Carbonate	250	34	26	8
⁺ Calcium Acetate	250	11	9	2
⁺ Sevelamer	250	155	118	37
⁺ Lanthanum	250	20	11	9
Dialysate Calcium Concentration	250	250	246	4

⁺ Cinacalcet, alfacalcidol, calcium carbonate, calcium acetate, sevelamer, and lanthanum are orally taken tablets.

Evaluation Metric:

 $Concordance = \frac{\sum_{i}^{j}(System \cap Physician)}{\sum_{i}^{j}(System \cap Physician)}$





CKDMBD-CDSS Evaluation (User-centric)

Experiment objective: User Experience of the CDSS with other services

Findings:

- CDSS provides higher dependability due to transparency and incorporating domain knowledge
- 2. Shows general acceptance across participants



Conclusion Publications



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Conclusion









- Lack of operational details can be complemented by clinicians' experience gained through trial and error
- Domain knowledge guided clinical case selection and adaptation provide clinician with insights into the complex recommendation generation process
- CKD-MBD CDSS based on proposed methodology demonstrated both high-level of conformance with clinicians' decision and usability of the system

Contributions:

- **Case insufficiency detection** through active case-base partitioning
- **Case selection** based on feedback information
- Case adaptation based on domain knowledge and selected cases



Proposed Idea Experimentation	Conclusion Publications			Ubiquitous Computing Laboratory Kyung Hee University, Korea
 SCIE Journals (11) First Author: 3 Published Co-author: 8 Published Local Journals (3) Co-Author: 3 Published Conferences (10) First Author International: 6 Co-Author International: 1 Local Conferences: 3 Domestic Patents (2) Registered: 1 Applied: 1 		PublicationTotal Publications (26)First Author Publications (10)		
	Proposed Idea Experimentation Ablished papers SCIE Journals (11) First Author: 3 Published Co-author: 8 Published Local Journals (3) Co-Author: 3 Published Conferences (10) First Author International: 6 Co-Author International: 1 Local Conferences: 3 Domestic Patents (2) Registered: 1 Applied: 1	Proposed Idea Conclusion Experimentation Publications Published papers - SCIE Journals (11) • First Author: 3 Published • Co-author: 8 Published • Co-author: 8 Published • Co-Author: 3 Published • Co-Author: 3 Published • Co-Author International: 6 • Co-Author International: 1 • Local Conferences: 3 • Domestic Patents (2) • Registered: 1 • Applied: 1	Proposed Idea Conclusion Experimentation Publications ublished papers - - SCIE Journals (11) • First Author: 3 Published • Co-author: 8 Published - Local Journals (3) • Co-Author: 3 Published - Conferences (10) • First Author International: 6 • Co-Author International: 1 • Local Conferences: 3 - Domestic Patents (2) • Registered: 1 • Applied: 1	Proposed Idea Conclusion Experimentation Publications

Introduction	Proposed Idea	Conclusion		UCL Ubiquitous Computing Laboratory
Related Work	Experimentation	Publications	V.	Kyung Hee University, Korea

REFERENCES

[1] Souza-Pereira, L., Pombo, N., Ouhbi, S., Felizardo, V., & Garcia, N. (2020). Clinical decision support systems for chronic diseases: A systematic literature review. Computer Methods and Programs in Biomedicine, 195, 105565.

[2] Sutton, R. T., Pincock, D., Baumgart, D. C., Sadowski, D. C., Fedorak, R. N., & Kroeker, K. I. (2020). An overview of clinical decision support systems: benefits, risks, and strategies for success. NPJ digital medicine, 3(1), 1-10.

[3] Laka, M., Milazzo, A., & Merlin, T. (2021). Factors That Impact the Adoption of Clinical Decision Support Systems (CDSS) for Antibiotic Management. International journal of environmental research and public health, 18(4), 1901.

[4] Choi, D. J., Park, J. J., Ali, T., & Lee, S. (2020). Artificial intelligence for the diagnosis of heart failure. NPJ digital medicine, 3(1), 1-6.

[5] Hussain, M., Afzal, M., Malik, K. M., Ali, T., Khan, W. A., Irfan, M., ... & Lee, S. (2020). Acquiring guideline-enabled data driven clinical knowledge model using formally verified refined knowledge acquisition method. Computer Methods and Programs in Biomedicine, 197, 105701.

[6] Ali, S. I., Jung, S. W., Bilal, H. S. M., Lee, S. H., Hussain, J., Afzal, M., ... & Lee, S. (2021). Clinical Decision Support System Based on Hybrid Knowledge Modeling: A Case Study of Chronic Kidney Disease-Mineral and Bone Disorder Treatment. International Journal of Environmental Research and Public Health, 19(1), 226.

[7] Ting, S. L., Kwok, S. K., Tsang, A. H., & Lee, W. B. (2011). A hybrid knowledge-based approach to supporting the medical prescription for general practitioners: Real case in a Hong Kong medical center. Knowledge-Based Systems, 24(3), 444-456.

[8] Niazkhani, Z., Fereidoni, M., Rashidi Khazaee, P., Shiva, A., Makhdoomi, K., Georgiou, A., & Pirnejad, H. (2020). Translation of evidence into kidney transplant clinical practice: managing drug-lab interactions by a context-aware clinical decision support system. BMC medical informatics and decision making, 20(1), 1-13.

[9] Demner-Fushman, D., Mork, J. G., Rogers, W. J., Shooshan, S. E., Rodriguez, L., & Aronson, A. R. (2018). Finding medication doses in the liteature. In AMIA Annual Symposium Proceedings (Vol. 2018, p. 368). American Medical Informatics Association.

[10] Russell, S., & Norvig, P. (2002). Artificial intelligence: a modern approach.

Introduction	Proposed Idea	Conclusion
Related Work	Experimentation	Publications



REFERENCES

[11] Alazzam, Malik Bader, et al. "Nursing care systematization with case-based reasoning and artificial intelligence." Journal of Healthcare Engineering 2022 (2022).

[12] Shemeikka, T., Bastholm-Rahmner, P., Elinder, C. G., Vég, A., Törnqvist, E., Cornelius, B., & Korkmaz, S. (2015). A health record integrated clinical decision support system to support

prescriptions of pharmaceutical drugs in patients with reduced renal function: design, development and proof of concept. International Journal of Medical Informatics, 84(6), 387-395.

[13] Helldén, A., Al-Aieshy, F., Bastholm-Rahmner, P., Bergman, U., Gustafsson, L. L., Höök, H., ... & Odar-Cederlöf, I. (2015). Development of a computerised decisions support system for renal risk drugs targeting primary healthcare. BMJ open, 5(7), e006775.

[14] Awdishu, L., Coates, C. R., Lyddane, A., Tran, K., Daniels, C. E., Lee, J., & El-Kareh, R. (2016). The impact of real-time alerting on appropriate prescribing in kidney disease: a cluster randomized controlled trial. Journal of the American Medical Informatics Association, 23(3), 609-616.

[15] Pirnejad, H., Amiri, P., Niazkhani, Z., Shiva, A., Makhdoomi, K., Abkhiz, S., ... & Bal, R. (2019). Preventing potential drug-drug interactions through alerting decision support systems: a clinical context based methodology. International journal of medical informatics, 127, 18-26.

[16] Van den Branden, Martijn, et al. "Integrating case-based reasoning with an electronic patient record system." Artificial Intelligence in Medicine 51.2 (2011): 117-123.

[17] Teodorović, Dušan, Milica Šelmić, and Ljiljana Mijatović-Teodorović. "Combining case-based reasoning with Bee Colony Optimization for dose planning in well differentiated thyroid cancer treatment." Expert Systems with Applications 40.6 (2013): 2147-2155.

[18] El-Sappagh, Shaker, and Mohammed Mahfouz Elmogy. "Medical case based reasoning frameworks: Current developments and future directions." Virtual and Mobile Healthcare: Breakthroughs in Research and Practice (2020): 516-552.

[19] Bichindaritz, Isabelle, and Cindy Marling. "Case-based reasoning in the health sciences: Foundations and research directions." Computational Intelligence in Healthcare 4. Springer, Berlin, Heidelberg, 2010. 127-157.

[20] Khussainova, Gulmira, Sanja Petrovic, and Rupa Jagannathan. "Retrieval with clustering in a case-based reasoning system for radiotherapy treatment planning." Journal of Physics: Conference Series. Vol. 616. No. 1. IOP Publishing, 2015.

Ph.D. Dissertation Spring 2022