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Application of intelligent agents in health-care: review

Sajid Iqbal[1,4] · Wasif Altaf[2] · Muhammad Aslam[1] · Waqar Mahmood[3] · Muhammad Usman Ghani Khan[1]

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Abstract The successful use of intelligent agents in healthcare has attracted researchers to apply this emerging software engineering paradigm in more advanced and complex applications. Main success factor is the natural mapping of real world medical problems into cyber world. Multi-agent architecture can easily model the heterogeneous, distributed and autonomous health care systems. The multi agent systems have been applied from single healthcare activity like knowledge based medical system to complex, multi-component based systems like complete healthcare unit. The use of multi agent systems in health care domain has also opened the ways to find out new applications like personalized and socialized health care systems. This versatile use of multi agent systems has also posed new problems for researchers like; security, communication, and different social issues. This work reviews recent years' research and applications of multi agent systems in healthcare published in different research journals, international conferences, and implemented practically. We reviewed

✉ Sajid Iqbal
sajidiqbal.pk@gmail.com; sajid.iqbal@bzu.edu.pk

Wasif Altaf
malikalamgirian@gmail.com

Muhammad Aslam
maslam@uet.edu.pk

Waqar Mahmood
director@kics.edu.pk

Muhammad Usman Ghani Khan
usman.ghani@kics.edu.pk

1 Department of Computer Science and Engineering, University of Engineering and Technology, Lahore, Pakistan

2 Department of Computer Science, University of Gujrat, Gujrat, Pakistan

3 Al-Khwarizmi Institute of Computer Science, University of Engineering and Technology, Lahore, Pakistan

4 Department of Computer Science, Bahauddin Zakariya University (Sahiwal Sub-Campus), Multan, Pakistan

five subdomains and three systems in each subdomain. A set of common parameters of these systems has been extracted and compared to analyze systems' merits and deficiencies. Based on our analysis, we have provided recommendations for multi agent systems applied in healthcare domain. Future research directions for interested researchers and practitioners are also discussed. As our own future research work, we intend to study healthcare and multi agent systems in e-commerce.

Keywords Software agents · Multi agent systems · Health informatics · Patient monitoring

1 Introduction

Human health being human capital is of primary concern and central point of focus for all human efforts (Gardner and Gardner 2012; Becker 2007). Therefore, most of the human attention and efforts are directed towards healthcare and social wellbeing. Computation or computerization is one of the technologies which has proved its impact on human life by providing assistive, collaborative, and automated healthcare systems (Isern et al. 2010). The development of healthcare systems is one of the challenging (Johnston et al. 2001) as well as controversial task considering the patient data privacy, cultural, legal, and technical issues (Datta et al. 2010). A technical deficiency in quality of service (of healthcare systems) results in negative economic effect (Lee et al. 2006). Conventional health care systems built on traditional computing paradigms fall short when they try to model the complex and distributed nature of health care systems (Gupta and Pujari 2009). This is due to inherent problems with healthcare systems that mainly include: presence of physically distributed knowledge, asynchronous communication among distributed system components, absence of natural modeling, scalability, collaboration issues and absence of artificial intelligence (AI) techniques (Moreno 2006).

Agent based systems are one of the new analysis, design, development, and deployment paradigm for complex and distributed systems. In this paradigm, software components are not tightly coupled with one another and can work in an autonomous way, even in unpredictable environments. The multi agent systems (MAS) are the natural choice for dynamic and open environments that are characterized with heterogeneous systems and their interactions, enterprise wide span, effectively operating in dynamically changing environments, rapidly growing data quantity, different data representation forms, ambient intelligence and self-service (Luck et al. 2005). Agent technologies provide the right architecture for two major computing domains: artificial intelligence (AI) and pervasive (seamless) computing (Hagalisletto and Steinar 2010). Despite the attractive benefits, agent based systems do exist with dark sides that warns the technology users to design agent based system in very careful way (Zambonelli and Luck 2004).

The use of intelligent agents in health related systems has provided the value addition to their primary functionality. In literature, the use of intelligent software agents has been proposed to deal with a variety of medical and health related problems i.e. patient scheduling, organ and tissue transplant management, community care, patient and treatment information access, decision support systems (DSS), training, hospital management, senior citizen care, self-care and automatic health monitoring (Nealon and Moreno 2003). Moreover, use of autonomous software components in medicine systems has become one of the hot research areas (Isern et al. 2010).

This study presents the adaptation of intelligent agents in health care systems, their merits, limitations, associated issues, and future research directions. Rest of the paper is organized as follows: in Sect. 2, application and mapping of MAS to healthcare is discussed along with classification of reviewed MAS systems, Sect. 3 presents the study methodology and parameters used for comparison, Sect. 4 categorizes and compares the systems based on these parameters, Sect. 5 enlists the limitations and issues of MAS in healthcare domain, and finally the Sect. 6 provides the conclusion with future research directions.

2 Agent technology and applications in healthcare domain

A piece of software that works autonomously in given environment, gets perception from environment, translates it into representable form based on its knowledge base and performs actions to achieve its design goals is known as software agent (Nwana 1996). In a multi-agent system, given task is divided into sub-tasks that are further assigned to different agents based on coordination mechanism (Bourne et al. 2000) (i.e. partial global planning) supported by communication and negotiation protocols (Chopra et al. 2013). Each agent produces output based on allocated task which is combined with output of other agents to make the result output of larger task (Vlassis 2007). In a multi-agent system, every agent could be designed differently. This heterogeneity, among agent designs, creates flexibility in the system to operate in heterogeneous environment using distributed cooperative methods of coordination.

Stakeholders and components of a healthcare system could be considered as agents. This provides a natural mapping in manual healthcare system and multi-agent systems (Ivanović and Budimac 2012) by modeling real life system agents as software agents and if AI component is included, it will also be able to take rational decisions. Software agents have to face some additional technical issues that are key performance parameters for a typical health care system. These include security, reliability, confidentiality, scalability and efficiency. Among these data security, privacy, and confidentiality are major concerns because the practitioners are reluctant to share patient medical data (Johnston et al. 2001).

There is no single well defined taxonomy of multi-agent systems. They may be classified into as many classes as the number of features required. Considering various features and aspects, researchers have classified MAS into different groups. The grouping criteria may include style of resource sharing, functional description, structural description, behavioral description and coordination mechanism. Moreover, there is a variety of granularity of classifying features used in MAS categorization. Fulbright and Stephens (1994), have defined eight classes of MAS based on resource sharing criteria. The list includes Type1: Autonomous Agents, Type 2: Perceptually Coupled, Type 3: Inferentially Coupled, Type 4: Distributed Cognition, Type 5: Cognitively Coupled, Type 6: Distributed Inference, Type 7: Distributed Perception and Type 8: Single Agent. Andreadis et al. (2014), have also worked on MAS taxonomy by classifying them into Centralized and Decentralized classes where Decentralized class is similar to Type 1 class of Fulbright et al. Carabelea et al. (2003), has also defined sub-classes of autonomous agents. Stone and Veloso (2000), have described four classes of MAS based on their communication and structural/functional description that are (1) Homogeneous Communicating, (2) Homogeneous Non-communicating, (3) Heterogeneous Communicating, and (4) Heterogeneous Non-communicating. Examples of more fine grained classifications are Cabri et al. (2011) and Byrski et al. (2015).

The work reviewed is categorized into five groups based on functional characteristics. Different sub-domains studied include medical data management, data pre-processing, data collection, data communication and security, ambient medical intelligence, knowledgebase and decision support systems, operational systems for health care, health care resource planning and management. Multiple sub-domains which are very close to one another have been aggregated under a single category. Multifunction healthcare systems are considered as separate category that involves more than one subdomains to form single integrated system. Given below, is the list of these aggregated sub-domains with brief description:

1. *Planning and resource management* These systems focus on planning medical processes, monitoring of staff and performance measurement, patient health monitoring, hospital and clinical resources management.
2. *Decision support systems/knowledge base systems* This category includes such systems which utilize knowledgebase (KB) and apply some type of data analysis techniques (using AI or machine learning), pattern recognition algorithms, and also might often use knowledge inference techniques.
3. *Data management systems* These systems focus mainly on health data extraction, representation, organization, storage, retrieval, and presentation.
4. *Remote care/self care systems* This area includes systems designed for automated patient monitoring remotely, and patient self-care.
5. *Multifunction systems* Literature review identified that various systems perform multiple tasks related to a complete healthcare solution. And these systems may be composed of two or more sub-domains given above; hence they have been categorized under this title.

3 Study methodology and MAS evaluation parameters

As a first step of review, we identified different sources of relevant scientific publications and domain specific resource providers. The list of these publishers include ACM transactions, IEEE Xplore, Citeseer, PubMed, SpringerLink and ScienceDirect. Google scholar search engine provides a platform to search scholarly articles from various research publishers, research journals, websites, universities, and research groups (https://scholar.google.com/intl/en/scholar/about.html) (Falagas et al. 2008) and therefore is used as main search platform. In addition, proceedings of relevant conferences like International Conference on Machine Learning and Cybernetics (ICMLC), IEEE International Conference on Information Theory and Information Security (ICITIS), International joint conference on Ambient Intelligence (AmI'10) are also examined. Websites and published work of different societies and research groups, resource providers like Artificial Intelligence and Medicine Society (AIME), IEEE working group, Foundation for Intelligent Physical Agents (FIPA), IEEE Power and Engineering Society (PES), Java Development Framework (JADE), and Agent Oriented Unified Modeling Language (AUML) are studied. Related articles published between 2010 and 2014 and references therein are considered. The search in databases is made with keywords: "agent healthcare", "multi-agent healthcare", "intelligent agents in healthcare", "multi-agent systems", "distributed healthcare", "intelligent agents in medical", "medical expert systems" and "medical and multi-agent systems". The inclusion of conferences focused on industrial and relevant areas of MAS applications helped to have a view from different perspective on use of multi-agent systems in healthcare. We collected 205 papers and among them 15+ core papers are selected for comparative study. The term "core paper" stands for the research paper that presents a system or component which could be listed among one of our defined categories and is selected for comparative analysis. Table 1 lists the different comparison parameters and their values.

The work studied is grouped under categories as described in Sect. 2. To analyze studied work and healthcare projects, a set of parameters is extracted. The reader may found missing values in comparison parameters. This deficiency is due to two basic problems (1) Most of

Table 1 Intelligent agent properties and parameters along-with possible values

Parameter	Possible values
Agent types by application domains	Distributed systems
	Personal software assistants
	Agents for workflow and business process management
	Agents for distributed sensing
	Agents for information retrieval and management
	Agents for ecommerce
	Agents for human computer interfaces
	Agents for virtual environments
	Agents for social simulation
	Personal information agents
	Web agents
Agent types by mobility	Static agents
	Mobile agents
Agent types based on reasoning	Symbolic agents
	Reactive agents
	Hybrid agents
Reasoning	Theoretical reasoning
	Deductive reasoning
	Practical reasoning
	Mean-ends reasoning
	Procedural reasoning
Multi agent interactions	
Agent dependence	Independence
	Unilateral
	Mutual
	Reciprocal dependence
Communication mechanism design	Guaranteed success
	Maximizing social welfare
	Pareto efficiency
	Individual rationality
	Stability
	Simplicity
	Distribution
Negotiation	One to one
	One to many
	Many to one
	Many to many
Negotiation domains	Task oriented domains
	Worth oriented domains

Table 1 continued

Parameter	Possible values
Dialogue types	Persuasion
	Negotiation
	Inquiry
	Deliberation
	Information seeking
	Eristic
	Mixed
Agent communication languages	KIF
	KQML
	FIPA
	XML
Agent programming languages	AGENT0
	PLACA
	AGENT-K
	META M
	April and mail
	Viva
	Go
	Agent speak
	Coo agent speak
	JASON
	AFAPL
	3APL
	2APL
	JACK
	JADEX
Agent platforms	ZEUS
	JADE
	AgenTool
	RETSINA
	JATLITE
	FIPA-OS
	MADKIT
	JAFMAS
	ABS
	OAA
	Cougaar
	AgentScape
	Cybele

Table 1 continued

Parameter	Possible values
Ontology definition	
Coordinated computing	Task division, sharing and result preparation mechanisms
	Contract nets: task is divided into sub tasks for SPECIFIC agents, distributed nature, every agent takes its task
	Auctions: centralized approach, more than one agents can do the same task, bid winner agents gets the task
Coordination mechanisms	Partial global planning
	Joint intensions
	Mutual modeling
	Norms and social laws
Handling inconsistency mechanism	
Multi agent planning	Centralized planning for distributed plans
	Distributed planning
	Distributed planning for distributed plans
Agent oriented analysis and design	
MAS frame works (listening)	
MAS standards and standardization bodies	

the systems published do not provide the internal materialization details of the MAS. (2) The area of Intelligent MAS is not standardized causing a large variation in characteristic parameters (Jorge 2011). The work in standardization direction is in progress like IEEE research group titled Foundation for Intelligent Physical Agents (FIPA), IEEE PES working group and OMG Agent Platform. Following is the list of characteristic parameters used for comparative analysis.

System architecture It is an abstract concept describing the components and their interconnections. The MAS agents base their operations on commitments, service level agreements and their data flow is modeled like conventional software systems (Chopra and Singh 2009). There are two types of system architectures (1) Open System Architecture (2) Closed System Architecture. The tools used in MAS development are also considered under this category.

Knowledge representation Multi-agent systems require a specific way of knowledge representation that is different from conventional systems. This is due to system required features like reasoning capabilities and distributed autonomous interactions, which not only covers the static data but dynamic information as well. Other considerations like minimum communication traffic generation, knowledge encryption and dynamically knowledge extraction from environment are also important aspects (Langevin 2010; Bench-Capon 2014).

Agent mobility In MAS, an agent may be static or mobile. A mobile agent possesses the three properties (1) Cloning: Ability to create an instance of itself (2) Instantiation: Ability to create an agent of other class and (3) Mobility: An ability of agent to move from machine to machine in network (Chopra and Singh 2009). A variety of agent migration protocols has been implemented by MAS implementers i.e. Simple Migration Protocol (SMP) by FIPA (Self and DeLoach 2003).

Intelligence mechanism There are different approaches that incorporate rational behavior and decision making. This parameter identifies the intelligence and learning mechanism used in the system under discussion (Zhong 2009).

Agent dependence (autonomy) Agent dependence is considered separate from agent independent actions or operations (Beavers and Hexmoor 2003). An autonomous agent possesses the motivations, the ability to create goals according to some changeable agenda (Luck and d'Inverno 1995) and is studied at different levels i.e. domain dependence, activity based dependence (Olfati-Saber et al. 2007), argumentation dependence (Witkowski and Stathis 2004), and relative versus absolute autonomy (Nowostawski and Purvis 2007). Witkowski and Stathis (2004) defines the concept of personality for agent considering its aspect of autonomy. Normally researchers assume complete autonomy in MAS. However, the systems built on agent frameworks may exhibit well defined but limited autonomy. Whereas, custom built systems are more prone to lack this feature (Beavers and Hexmoor 2003; Bonté et al. 2005; Nowostawski and Purvis 2007).

Agent interaction and communication model Communication among agents in a society must be rational (what, when, and with whom to communicate) (Gmytrasiewicz and Durfee 2001) and optimal (Xuan et al. 2001). The level and type of communication among agents depends on the nature of work i.e. tightly coupled task, team based task and long term tasks (Xu et al. 2006). Different agent communication protocols have been developed based on agent types (task type) that may include coordination (Ciancarini et al. 1999; Excelente-Toledo and Jennings 2004), cooperation (Ji et al. 2006), negotiation (Marzougui and Kamel 2013) and commitment based protocols (Kalia and Singh 2014). In negotiation, one of communication parties may decline to communicate completely or to some extent. No communicating party declines in guaranteed communication and finally in commitment based communication, at least underlying commitments will be fulfilled by the serving party (Berna-Koes et al. 2004).

System complexity and scalability System complexity consists of two sub-types: structural complexity and algorithmic complexity. First category refers to the number of agents, type of agents, static and dynamic relationships, and their interactions. Only structural complexity is considered in this study. Based on features defining the complexity, the system is categorized among simple, medium and high. The functional aspects like knowledge processing, sharing, coordination, task division and collaboration lie under second type of complexity (Far and Wanyama 2003; Sarkar and Debnath 2012). Maximum and minimum work load limits define the system scalability. Scalability is decomposed into three parts: Number of agents, amount of communication and amount of resource consumption that could be raised or lowered at run time (Deters 2001).

Security and privacy It is one of the major concern of healthcare systems. This characteristic analyzes the measures used to protect medical data in a MAS (Borselius 2002). Medical data privacy refers to keeping one's medical data confidential (Beutter et al. 2014).

4 Existing applications of intelligent agents in healthcare systems

This section provides comparative analysis of intelligent agent based systems proposed in literature, implemented practically in healthcare units or simulated. The comparison parameters outlined in Sect. 4 are extracted from the relevant literature.

4.1 Planning and resource management

Planning and resource management systems are mainly focused on patient monitoring and scheduling, planning medical processes, monitoring and management of healthcare staff, performance measurement, hospital and clinical resources management. This section reviews three MAS systems used for optimal resource scheduling based on patient conditions.

Agent based modelling and simulation of emergency department re-triage (AMSEDR) (Rahmat et al. 2013) is developed for the re-triage of patients who have come to hospital's emergency department and are queued for medical service provisioning. It is simulation based work using Common-pool Resources and Multi-agent System (CORMAS) (Page et al. 2000). The system proposes the runtime waiting queue evaluation to rearrange the queue based on patients' condition severity/deteriorating conditions to manage the resource (doctor or nurse) allocation optimally to the urgent job first (based on patient condition). The MAS system is based on nine agents. Patient simulator agent for data generation is based on the case study data presented by them. This data is provided to the patient agent that acts as real life patient. The data is forwarded to triage and re-triage queue manager agents. The triage queue manager agent prepares the queue of patients based on their deterioration conditions with the help of triage accessor that records the severity level of a patient based on the status of the agent's clinical condition. Re-triage queue manager agent manages the severity level of a patient dynamically, with the help of re-triage accessor, whose clinical condition has deteriorated while waiting to seek treatment or when the allocated waiting time has exceeded. The treatment queue manager agent manages the patient in the treatment queue. The treatment caller agent calls the next patient in the queue using the patient agent's ID provided by the treatment queue manager. Finally, the physician agent requests the treatment caller to call in a patient for treatment. The physician 'holds' the patient for specified time duration for the purpose of 'giving treatment'. Once completed, the physician signals the treatment caller for another patient.

Intelligent environment for monitoring Alzheimer patients, agent technology for health care (IEMAP) (Corchado et al. 2008). In this autonomous agent for monitoring ALZheimer patients (AGALZ) system, authors present another approach for scheduling of human resources (doctors, nurses, and attendants) in execution time and allocation to patients in outdoor departments of a hospital. Looking at the previous cases and current working conditions, the system is authorized to prepare new working schedule providing up to date optimal schedule. In AGALZ system, problem description and solutions are represented as believes that are stored in "Belief Base". The final states are represented as goals and stored in goal base. Plan base is repository of different types of action including retrieve algorithms, revise algorithms, intension plans, retain algorithms, and reuse algorithms. The case based planning (CBP) is implemented through goals and plans. When the MAS goal corresponds to one of the cases, an action or set of actions is triggered to achieve the goal. It is a cyclic process where each goal can produce a sub-goal that results in the execution of new plans/actions. AGALZ agents are provided with dynamic planning algorithms that plan considering the different factors like spatial location of patient to allocate nearest available resource. To identify the location of the patient, the system uses radio frequency identification (RFID) technology. The case based planning–belief, desire, intention (CBP–BDI) agent searches continually for the plan that can most easily be changed in the event of interruption. The system defines two models based on Gaia analysis (Wooldridge et al. 2000): role model and interaction model. The role model defines five agents called roles. patient role manages the patient's personal data and behavior, doctor role treats patients, nurse role schedules the nurse's working day by obtaining dynamic plans depending on the tasks needed for each assigned patient, security role controls the patients' location and manages locks and alarms and finally manager role manages the medical record database and the doctor–patient and nurse–patient assignments and schedules. Another agent known as AGALZ agent worked with mobile devices to schedule communication and patient record-keeping. Patient agents are considered to be most sensitive agents that save their data periodically, and if one fails, another is created from the backup information. The interaction model defines the agent dependence and their relations.

A dynamic patient scheduling at the emergency department in hospitals (DPSEDH) (Daknou et al. 2010): Daknou et al. in DPSEDH propose a multi-agent based system for better resource (doctors and nurses) allocation to the patients in an emergency department considering patient waiting time, cost reduction, and quality of service. The system consists of five types of intelligent agents. Home agent (HA) is related to the patient that ensures the patient's host and his medical record creation. Identifier problem agent (IdA) receives medical problem and identifies the skills needed for treatment. Scheduler agent (SA) makes the assignment of MSA agents to medical teams, monitor agent (MA) is in-charge of the patient's and the MSA agent, mobile staff agents (MSA) of medical team moves from team to team based on the need, provides the treatment and the follow-up of the patient. When a patient arrives, an agent society consisting of all five types of agents is created. If a HA remains inactive for a certain period of time, it is assumed that the patient has either been serviced or is absent so its relevant agent society is destroyed. In the first phase, the system prepares a priority based list of patients present in Emergency Department (ED). In second phase, on the arrival of new patient, its agent is created and the system reorders the priority service list. In the third phase, the system finds the most suitable and available staff (Doctor, Nurse) for job allocation by calculating their skills and assigns the job. The tasks executed by ED staff are divided into two categories: Direction Action tasks (these tasks require the medical actor to act directly on patient i.e. medication, tests) and Indirect Action tasks (no direction staff action is required i.e. reports, monitoring).

Discussion AMSEDR is simulation based work that re-triages the patients present in emergency service queue of an Emergency Department (ED). Although there is improvement in patient service waiting time, however it is not significant. The results obtained are based on simulation study that may further deteriorate when applied in real scenario. Secondly stable patients wait more in AMSEDR. The situation could be improved by dynamic resource allocation. In addition authors have also mentioned few system limitations like use of one time historical data and randomly generated patient deterioration rate. IEMAP case-study provides an agent based approach for outdoor patients that visit the hospital. This system incorporates more intelligence than AMSEDR and is technically more sophisticated, however industry standard tools are not used in its development. AMSEDR only iterates its schedule when new patient arrives whereas, schedule in IEMAP can change any time. The results are more complete and sound as the case study has been implemented and tested however, event driven scheduling could be improved using periodic scheduling along with patient driven scheme.

DPSEDH shows similar work, as that of AMSEDR, for ED patient scheduling. The strength of the work is that it is based on real implementation in health unit instead of simulation. Like AMSEDR, this work does not utilize specific learning mechanism (AI based decision making), whereas the DPSEDH is based on calculation strategy for best available resource allocation. DPSEDH uses industry standard JADE framework but its results are not significant. DPSEDH has considered different types of emergency departments. The system could be improved by providing customized solution for each department. If agent society remains inactive for some time, DPSEDH considers it as completion of current session jobs and shuts down the society. This process is compute intensive and assumes some society establishment time making initial system response time slow that is not suitable for emergency departments. AMSEDR is simple system with few static agents and no information is provided about security and privacy. IEMAP is structurally simple system but algorithmically more complex than AMSEDR. The system supports limited scalability with basic security measures like authentication. DPSEDH is structurally more complex than IEMAP but is simple with respect to algorithmic complexity.

All systems are homogeneous and with no heterogeneity support. All three, in scheduling phase, have not discussed the incorporation of more resources or variation in resources. In scheduling single priority queue is considered. There may be more than one priority queues in emergency department especially if there are multiple units available in ED. Resources could be categorized and category based resource allocation is not considered. Resource allocation may overlap i.e. a doctor has placed a patient on ventilator for some time and in meantime she can serve other patient. Basic scheduling algorithms are used using multi-agent approach. There is need to implement advanced scheduling schemes. Literature contains more advanced and sophisticated approaches like Wong et al. (2014), Azadeh et al. (2014), and Xiao et al. (2010). Table 2 presents the comparison of technical parameters of these three systems.

4.2 Decision support systems and knowledge based systems

Decision support systems are the computer systems based on knowledge about the domain for which they have been designed. By digging the data stored in data warehouse(s), these systems can find various patterns or trends by using data analysis techniques and produce information that maybe utilized by the executives and policy makers. So, these systems can be referred as decision making assistive tools. It is commercially viable and relatively large domain of application, where the size of system is large too. Various commercial software vendors have provided the solutions in this domain i.e. Siemens, IBM.

A high performance agent-based system for reporting suspected adverse drug reactions (AS-SADR) (Ji et al. 2012): AS-SADR is related to the study of adverse drug reactions (ADR), the system collects information from different users (doctors, specialists, pharmacists, etc.) and maintains a knowledge-base. This simple type of system is based on four types of intelligent agents. Assistant agent is associated with professionals. It uses Naranjo algorithm that can assess the degree of causal association between a drug and the potential ADR based on the retrieved patient data by contacting the data mining agent. It can feed the ADR report by auto filling the Naranjo Form in database on behalf of its user i.e. Doctor. Data mining agent is associated with manager who has knowledge of epidemiology or biostatistics and this agent collects statistical data through data collection and monitoring agents and calculates the value of an adopted interestingness measure for suspected drug ADR signal pairs. The agent stores and manages these data association pairs and makes these available to assistant agents. The management agent provides a central service for information sharing, service discovery and service publishing by other agents. While the data collection and monitoring agents serve as

Table 2 Comparison of planning and resource management MAS for healthcare based on evaluation parameters

Parameter	AMSEDR	IEMAP	DPSEDH
Design and development	AOSE and GAIA methodology used MAS simulation packages	Agent based UML (AUML), Gaia methodology, OOP custom developed system	JADE architecture simulation
Agent types	Reactive and proactive	Deliberative	Reactive
System architecture/ framework	CORMAS	Gaia based model	JADE
Knowledge representation	OO classes relational databases	OO classes	OO classes
Agent mobility	Static	Static	Static
Intelligence mechanism	Rule based no learning	Case-based reasoning, machine learning algorithms	Previous history based calculation. No Learning
Agent dependence	Semi dependent	Independence	Semi-dependence
Communication mechanism	Guaranteed	Independent request–response	Dependent
Complexity and scalability	Simple very limited	Simple limited	Medium intermediate
Privacy and security	–	Basic security	JADE default security settings

the bridge between database and other agents. It is responsible for English language query translation into database language and provision of retrieved data to other agents.

An agent-based knowledge discovery from databases applied in healthcare domain (AKDDH) Benomrane et al. (2013) presents an application of intelligent agents in knowledge discovery in databases (KDD). KDD process is divided into multiple sub processes and AKDDH deploys intelligent agents for each sub process. A typical KDD process includes the problem formulation phase to define the problem, data retrieval phase which is concerned connecting multiple databases and retrieving data into a central repository. The data selection phase selects the most relevant fields, data cleansing involves the removal of inconsistent data and filling the missing values of attributes; data transformation causes the transformation of data from heterogeneous representations to homogeneous representation. The data mining phase is heart of KDD process which searches out the patterns and finally the results evaluation and knowledge integration phase presents the results/patterns in human understandable format. For each of the KDD steps except the first two which are mostly done in manual way, an agent has been proposed with few additional agents as described in Table 3.

Implementing an integrative multi-agent clinical decision support system with open source software (IMACDS) (Shirabad et al. 2012). Clinical decision making is divided among data collection, diagnosis, evaluation and treatment planning. In IMACDS, authors present an integrative clinical decision support system (ICDSS) which provides decision support to span the whole decision making process. The authors have already presented two models titled methods of information in medicine-1 (MET1) and methods of information in medicine-2 (MET2). The work under discussion has been titled as methods of information in medicine

Table 3 Agent-based KDD MAS's agents along-with brief descriptions

KDD phase	Agent	Description
Data selection	Data preparation agent (DPA)	This agent prepares the data for use of data mining activity
Data cleaning		
Data transformation		
Data mining	Data mining agent	It performs the actual task of data mining by applying following data mining techniques: Case based reasoning, decision trees, Bayesian networks
Data evaluation	Data evaluation agent	It identifies the patterns of interest in the retrieved and mined data
Decision making	Decision maker agent	It uses the extracted knowledge to predict results and then use the prediction in real time to alter organizational behavior
	Coordinator agent	It is a broker that handles communication using the appropriate protocol of coordination between all the involved agents
	GUI agent	It assigns agents to data sources, and to allocate high level discovery goals and a way for user interaction

(MET3) incorporating the intelligent multi-agent technology resulting in new features in the system i.e. provision of integrated support for data collection, diagnosis formulation and treatment planning, platform interoperability and capability of interacting with hospital's existing information systems. The system consists of 8 types of agents. Access management agent (AMA) is access controller for the MET3 system. To handle requests from other agents and to respond them with models retrieved from MET3's knowledge base, model manager agent (MMA) is used. Data storage and retrieval of patient data is done by data management agent (DMA). HIS synchronizer agent is used to work as intermediary for maintaining synchronized data updates between external systems. The diagnosis suggester agent (DSA) suggests the agent diagnosis plan. Treatment suggester agent (TSA) suggests the treatment plans by using the treatment models created for specific health issues. Evidence provider agent (EPA) is aimed at providing clinical evidence related to a treatment plan for the specific patient. And the last agent, encounter assistant agent (EAA), allows the system users to access MET3's functionality by using graphical user interface.

ICDSS architecture, on high level, is as following. Access management agent controls the access to the system. Every user or agent can interact with the system after successful authorization. MET3 relies on a knowledge-base that is accessed through model manager agent. HIS synchronizer agent actively monitors information generated by HIS, and reacts accordingly by notifying other agents or external hospital systems. Data management agent uses this knowledge-base for maintaining patient data locally. Diagnosis suggester agent and treatment suggester agent use diagnosis and treatment models and associated solvers, these two agents delegate the logic of actual diagnosis to external programs created for each

Table 4 Comparison of decision support MAS/ knowledge-based MAS for healthcare based on evaluation parameters

Parameter	AS-SADR	AKDDH	IMACDS
Design and development technologies for MAS development	Model-view-controller (MVC) pattern, Java and JADE	JAVA/XML	O-MASE, AUML hibernate search
Agent types	Proactive and collaborative	Proactive	Reactive, proactive
System architecture/framework	JADE web based open system architecture	MADKit	JADE
Knowledge representation	Relational tables	Relational database	Ontology based data with underlying relational database
Agent mobility	Static	Static	Static
Intelligence mechanism	Case based and statistical decision support	Case based reasoning	Decision rules and decision trees
	Machine learning	Decision trees	
		Bayesian networks	
Agent dependence/autonomy	Dependent	independent	Limited (semi)
Communication mechanism	As specified by JADE	As specified by MadKit	As specified by JADE, HL7
Complexity and scalability	Simple good scalability for users	Simple very limited	Simple good scalability
Security and privacy	–	–	Basic security, no data privacy

decision model referred as solvers, while to provide clinical evidence, evidence provider agent relies on an evidence database. Authors have also provided a detailed view of MET3 design phase. Table 4 presents the comparison of technical parameters of these systems.

Discussion AS-SADR uses of better algorithm i.e. rule based and statistical, however its rule based approach is static. System performance can improve if dynamic learning based rule base is used. AS-SADR, however, is a prototype solution that does not reflect the actual operational results. Authors have discussed the usability of system but have not provided the details of efficiency measure in time and result domain. Work in AKDDH is strengthened by its real life implementation using systematic approach for data mining which is absent in AS-SADR. It is compute intensive due to KDD and statistical algorithms resulting in longer response time. The use of multiple decision making algorithms simultaneously seems over processing. The classification of results is better, however negative capacity of prediction is much higher. Moreover, authors have assumed structured data as input, whereas most of the medical data is present in unstructured form. Work in IMACDS shows the use of open source technology for cost effective MAS solution. Proposed system uses state of the art MAS technologies for system development. The system allows processing of multiple patients in parallel. This represents better scalability and has been tested in real environment.

For decision making, the system has used static models without any learning component. IMACDS is better work from technical perspective.

All three systems present different approaches for decision making. KDD with machine learning algorithms can perform better in case of large medical data (Domingos 2007). There is little information about security and privacy implemented in these systems.

4.3 Data management system

Simulation environment for the optimization of the data retrieval capabilities of an agent based system in a healthcare setting (SEODRH) Patriarca-Almeida et al. (2011) presents a simulation based study for optimization of MAS oriented data retrieval and integration system. The simulation environment aims at performance optimization of existing virtual electronic patient record (VEPR), which is based mainly on MAS for integration of data (MAID). Since, real-time data was not possible to be included in simulation environment, so anonymized archived data was used for system's tuning and analysis. Moreover, authors configured and executed simulated environment focusing mostly on scheduling algorithm based optimization, so that the system can perform efficiently in stress situations, e.g. when multiple departmental information systems (DIS) request and generate various reports concurrently. The results and performance evaluation of their simulation suggests that for effectiveness, more system optimization is required. As a continuance of this work, further optimized system has been presented in Patriarca-Almeida et al. (2012). Authors have provided very limited implementation details therefore evaluation parameters could not be fully extracted from their work for comparison with other systems. hence we extracted comparison parameters from their later work i.e. (Patriarca-Almeida et al. 2012).

Optimization of an agent based clinical data retrieval system (OACDRS) (Patriarca-Almeida et al. 2012) presents enhanced form of system simulated in Patriarca-Almeida et al. (2011) by proposing significant changes to MAID. Apart from behavioral changes in MAID, authors proposed and implemented a scheduling agent for optimization of production and retrieval of reports. Scheduling agent is aimed mainly at creation of weekly map of request list schedule of each hour of everyday. The simulated system was found to perform better in terms of report list requests, while the resource utilization improvement was not considerable. As the system was simulated only, so it still begs real-world deployment, testing, and performance analysis. Like SEODRH, not all evaluation parameters could be extracted for comparative analysis in OACDRS however, the work in OACDRS is more complete in simulation and analysis of performance, hence it is included in comparative study instead of SEODRH.

The study of secure agent-based scheme on health information systems (SASH) Chen et al. (2010) presents secure mobile agent based MAS for health information system. The work aims mainly at provision of secure, confidential, and efficient access to electronic health records (HER) in a distributed environment where patient health data is required to be shared among multiple healthcare units. Data communication and data security, in this situation, is basic requirement. Authors propose a key management scheme to provide security against various attacks such as security attacks, reversed attacks, cooperative attacks, and equation attacks. They analyze the proposed solution theoretically and conclude SASH usefulness against the aforementioned attacks. Since, the proposed solution is theoretical only, so performance analysis or comparative analysis based on evaluation parameters is not possible.

Research on integrating the healthcare enterprise based on multi-agent (HIIS-MA) (Zheng et al. 2010): HIIS-MA is a multi-agent system that is concerned with integration of EHR data to develop a healthcare enterprise. The problem statement is very interesting in terms that it has significant social implications, and if resolved, would revolutionize healthcare industry.

HIIS-MA is an abstract approach, provides abstract design and algorithmic description of MAS for integration of information. It leaves the complexities involved in integration of heterogeneous standard based systems as well as custom design based systems. The MAS proposed includes four agents namely user agent, management agent, integration agent and data agent, an XML wrapper, actor and interest store, and integration information store. User agent designs operational interface for user, handles complicated and flexible inputs and offers query results from integrated data. Management agent aims at management of all other agents and provides communication between all agents. Integration agent collects information from heterogeneous medical information databases and converts the information into unified XML format and stores into XML-based integration database. Data agent searches heterogeneous medical information databases and converts that data into XML which is then stored in XML-wrapper, as XML-wrapper has been designed to store XML-based medical information. The system is based on deliberative agents, and communication between agents is based on alliance mode. Since, the proposed MAS lacks implementation, so not all evaluation parameters for comparative analyses could be extracted.
The intelligent agents in the study of web-based medical information search system (IAW-MISS) Lin et al. (2012) present business intelligence (BI) using intelligent agents based medical information search system. They proposed a web-based system aimed at providing convenience to users' searching for proper medical-care centers specific to their health problems. As, not all medical centers excel in certain sort of treatments, so the system enables users to find health centers most relevant to their need based on symptoms and/or query. At abstract level, the proposed system consists mainly of intelligent agents, business intelligence components, data warehouse, OLAP server and web-based graphical user interface (GUI). IAW-MISS is important in terms that it intelligently processes the homogeneous data on web and provides filtered results to users. The system needs to be publically deployed so that its effectiveness and performance can be analyzed.

Discussion Different approaches for medical data management using MAS have been used in research and implementation. Important aspects of consideration for data management and integration include trust, security, anonymity and data encryption. SEODRH and OACDRS focus on the performance improvement of medical data management systems using MAS. These systems supports mobile agents and proposed infrastructure is scalable. The systems incorporate structural complexity because of mobile agents and scalability support. IAW-MISS is strong work as it uses heterogeneous data sources for data extraction and by using data warehousing techniques, converts the data into uniform format. All three systems have used plain text format for data storage and sharing. Medical data need proper security and trust treatment. None of the work is implemented in real environment. The comparative listening of parameters is given in Table 5.

Agents in MAS must possess *trust* on each other for their competence, reliability and originality of data. Medical data accuracy relies on verification of data source and origin. To ensure high level of trust, various trust relationship and reputation models for MAS have been proposed in literature. Pinyol and Sabater-Mir (2013) has studied the cognitive models for this task. Although cognitive models are more effective but these are complex therefore, mostly remain at descriptive level. Search for implementable cognitive models is an open area of work. Yu et al. (2013) have also presented a good work on the survey of multi-agent trust management systems and have formulated nine characteristics for good trust relationship model. Yu et al. (2013) has indicated integration of temporal aspect of agent reputation in future system designs. System security and data privacy insurance provision can be formidable and daunting, while being the very basic need of any MAS based healthcare

Table 5 Comparison of HIS data management MAS based on evaluation parameters

Parameter	OACDRS [44]	HIIS-MA [54]	IAW-MISS [55]
Design and development technologies for MAS development	Java, XML	XML	Custom development rapid prototyping model
Agent types	Reactive	Proactive	Reactive
System architecture/ Framework	JADE	–	Custom
Knowledge representation	Relational tables and XML	XML	Relational database
Agent mobility	Static	Static	Static
Intelligence mechanism	–	–	Rule based intelligence, knowledge based intelligence, learning approach to intelligence
Agent dependence/autonomy	Semi-autonomous	Semi-autonomous	Semi-autonomous
Communication mechanism	FIPA compliant messages	Collaborative	–
Complexity and scalability	Medium limited scalability	Medium limited scalability	Medium good scalability
Security and privacy	JADE default settings	–	–

systems. The security issues may arise due to agent architecture, communication mechanism (Jung et al. 2012), collaboration, and coordination methodologies (Bijani and Robertson 2014). Greenberg et al. (1998) has provided a detailed list of security issues in mobile agents. La et al. (2013), have also discussed security issues associated with mobile agents. Data and context privacy is major concern of patients and organizations managing patient history and related data. Huang et al. (2011) mentions two categories of privacy issues: content oriented privacy and contextual privacy. Content privacy refers to privacy of data whereas contextual privacy refers to relationships among various data items. If content is missing but the relationship information is available, content could be recreated. Kim (2014) has presented an enhanced version of (Huang et al. 2011) data and context privacy scheme. Jung et al. (2012) have presented a survey on MAS security issues. Researchers are putting efforts to find out better data model for agent based computing (Kim and Chung 2014).

4.4 Remote care/self-care systems

In *A small e-health care information system with agent technology (eHISAT)* (Subalakshmi et al. 2010) agent technology has been used to provide e-Health care services. The system creates connectivity on an anytime-anywhere-any-device-basis to meet patients' requirements by using various agents. The system consists mainly of patient agents (PA), doctor agents (DA), and controller agent (CA), and all the data transactions are provided by using these agents. The users use PA, to connect and communicate with networked controlling server(s) of the system. The CA is responsible for controlling the demand of patients, and also takes care of doctors' activity. When doctors want to check their patients, they connect with DA, and through DA doctors can prescribe medicines to patients, or can refer the patients to other doctors, if required. This system was aimed mainly at improving and enhancing healthcare system by provision of speedy and efficient response, as well as maximizing the system's availability. It was a very small system basically, simulated using JADE. It makes trivial use of MAS technology.

Intelligent agents in home healthcare (IAHH) Hudson and Cohen (2010) present usage viability and efficiency of intelligent agents in home healthcare systems. They provide theoretical architectures of IMAS for remote healthcare provision for patients with dementia, as well as for remote monitoring of cardiac conditions. Their system consists of three software agents namely reminder agent (RA), communication agent (CA), and surveillance agent (SA). As well, the system contains three human agents namely patient, caregiver, and medical professional. The system design also contains various devices which are required for data sensing, communication, storage, and output. As this work is of theoretical nature only, so no implementation details have been provided, although the authors held that the system architecture can be used in various other systems for provision of remote monitoring and healthcare. The actual and main contribution of this theoretical work is to present support and intervention for patients with dementia, and to provide automated remote analysis of cardiac data. This work lacks implementation, and hence is of very limited use for us to provide its comparative analysis based on evaluation parameters with other similar systems.

JADE implemented mobile multi-agent based, distributed information platform for pervasive healthcare monitoring (JMA-PHM) (Su and Wu 2011): JMA-PHM is, fairly large and comprehensive, aimed to meet openness and modularity requirements of MAS. To fulfil these requirements, the research work proposed and implemented a mobile multi-agent information platform (MADIP), which has been developed on top of JADE. MADIP allows agents to work in place of medical professionals, in such a way that distributed users' vital sign data can be collected and communicated to healthcare professionals in real-time if abnormal conditions are sensed. MADIP consists of six agents user agent (UA)—a stationary agent, which provides its users an intelligent gateway to the platform, resource agent (RA)—a stationary agent, which mediates access of resources between physician agent and host computers, physician agent (PA)—a mobile agent, used by medical staff to ubiquitously and virtually monitor the patients' conditions, diagnostic agent (DA)—a stationary agent, which is capable of analyzing patients' condition data and can predict or indicate sudden change of condition, as well it can communicate with external services agent to inform medical staff in real-time, knowledge-based data server (KBDS)—it contains of two main repositories namely, user profiles and user status, external services (ES)—contains hardware and software for the enablement of SMS, email, and call services. These services are requested by diagnostic agent, and are proposed to intimate physician agents in real-time. Researchers concluded that although the system's security was backed by JADE-S extension, there was still room for improvement in that dimension. And as the analysis of such systems' performance is a complex task and requires standard metrics, so they also analyzed the usability/readability of the system through questionnaires, and it was found that places for improvements exist in usability/readability enhancement too. Moreover, MADIP is a prototype system still to be deployed and tested in real world.

In *Software agent application to support the patient-at-home* (Lyell and Liu 2012) *(AAPAH)* authors have considered the needs of patients at homes (PAH). A PAH is a patient who needs fair amount of attention, such patients might have long lasting disease(s), might be elderly patients, or might be having trauma related injuries, etc. This research mainly uses agent oriented software engineering (AOSE) and Gaia methodology to propose a MAS namely patient-at-home supporting software agents (PAHSSA), in which PAH can be connected into healthcare support system. The use cases for PAHSSA have been developed by taking context of PAH into account, as well as the evolving standards. Moreover, system stakeholders and potential actors have been identified, usage scenarios have been created, functional requirements were analyzed and information flow was modeled as part of the design and modeling phase. Finally, the PAHSSA consists of 15 agents, which are, GUI agent (GA)—responsible for displaying information and allowing user actions, content module manager (CMM)—manages agents which provide information to PAH, expert subject module agent (ESMA)—wraps knowledge expertise, PAHSSA information help agent (PIHA)—replies to PAH queries, workflows support agent (WSA)—performs routing in cases of complex tasks, message agent (MA)—supports message extraction and enveloping, message content agent (MCA)—provides message content structure, message sending and receiving agent (MSRA)—manages messages exchange protocols, logging agent (LA)—logs system activities and communications, device manager agent (DMA)—supports communications with all medical device agents, device agent (DA)—provides transmission from a particular medical device, audit agent (AA)—manages audit reports, document manager and storage agent (DMSA)—manages documents storage and retrieval, PHR interaction agent (PIA) and information search agent (ISA). PIA and ISA agents enhance the basic functionalities of PAHSSA system provided by the rest of thirteen agents. Detailed responsibilities of all these agents may be seen in Table 1 of original work. The interaction mechanism among these agents has not been clearly described in PAHSSA, whereas the overall concept has been presented in an obscurely complex way. The provided solution is abstract in nature, so the usability/performance of the system cannot be analyzed until it has been practically implemented.

Discussion Since, usage of intelligent agent technology for remote healthcare is fairly complex and requires significant amount of effort, so proposing and implementation of such systems is a tedious and costly task. eHISAT doesn't fully utilize the benefits and characteristics of MAS technology, and is a system with rudimentary details; it lacks intelligence mechanism with shallow knowledge base and knowledge representation. It overlooks multiple essential requirements i.e. there is no scheduling plan for patient and doctor. Data security, encoding and encryption related information is missing and finally no communication protocol is mentioned however one can deduce that default functionality available in JADE is used. IAHH has presented theoretical architecture for intelligent multi agent system (IMAS) which is neither simulated nor implemented so that performance could be measured that makes its comparative analysis hard in context of this study. In contrast with eHISAT and IAHH, JMA-PHM presents a very detailed system for pervasive healthcare monitoring making significant use of MAS by providing implementation details. System presented in JMA-PHM differs from eHISAT and IAHH in development structure in a way that both eHISAT and JMA-PHM were developed using JADE, while IAHH was developed using AOSE approach. While eHISAT, JMA-PHM and AAPAH, all lack real-world deployment, which points out the fact that IA, MAS or IMAS based remote healthcare systems still require societal acceptance to get benefitted in daily life. From the systems studied, analyzed and compared in this section for remote healthcare domain, it is evident that performance evaluation of such systems is a very complex task, and the underlying complexity is because of variable evaluation criterion for each system or sub-system. It is also clear that, from system development point of view that IA, MAS and IMAS technology is fairly mature in this domain, but the systems developed require better implementations, so that they can be socially accepted. As, these systems have to exist in a wider health and medical care environment, so the standardization of interfaces is also required, only PAHSSA (Lyell and Liu 2012) took this issue into account

Table 6 Comparison of remote care/self-care MAS based on evaluation parameters

Parameter	eHISAT	JMA-PHM	AAPAH
Development	Mainly based on JADE remote monitoring agent (RMA)	Custom development on top of JADE	Custom development—AOSE, Gaia methodology
Agent types	Reactive	Proactive, reactive	Reactive
System architecture/framework	JADE	MADIP - extension of JADE	Custom
Knowledge representation	Shared file(s) Relational data	–	–
Agent mobility	Static	Static, mobile	Static
Intelligence mechanism	Non intelligent MAS	–	–
Agent dependence/autonomy	–	Independent/autonomous	–
Communication mechanism	As specified by JADE	Asynchronous communication channel (ACC)	Asynchronous interactions
Complexity and scalability	Medium good scalability	High good scalability	High good scalability
Security and privacy	JADE basic security, no data privacy	JADE enhanced security system	HL 7 V3 based data privacy

in detail while other systems have ignored it. Table 6 lists the parametric comparison of remote care/self-care MAS systems.

4.5 Multifunction MAS systems

Agent Hospital—health care applications of intelligent agents (Kirn et al. 2006) (AH) describes a high level introduction to numerous projects. Hospital logistics—an interest group founded under German Priority Research Program (GPRP) includes various projects and subprojects for the application of inter and intra-hospital information systems based on agent technology. Every project and its subprojects are focused to solve specific research problems of different hospitals. This group of projects resulted in creation of almost a complete virtual hospital model. This virtual hospital model along with MAS based sub-projects resulted in Agent_Hospital, the test-bed for agent technology in healthcare. Agent.Hospital consists of following projects. (1) Policy agents project that aims at automation of scheduling for operation theatres. Software agents negotiate autonomously in finding schedules, and try to reach efficient resource allocation. (2) Med Page project dealt with planning, coordination, and control of clinical procedures in all areas of a hospital. Software agents representing patients, negotiate autonomously with each other for limited hospital resources. Market mechanism was used as coordination mechanism. (3) The objective of EMIKA project is integration of emergency cases in radiology without disturbing the current schedule. The system comprised of autonomous agents communicating in decentralized environment. (4) ADAPT project provides solutions to clinical trial problems, using agent-based simulation system. The prototype system created supports medical professionals in scheduling, analysis and evaluation of clinical trials. (5) ASAinlog project utilizes multifunction software agents for provision of context-sensitive information to relevant personnel at the right time, and right place. Moreover, the project also supports processes for cooperation and coordination of information to enhance cooperation. (6) AGIL project modeled treatment processes using AGILShell (a Java based tool), and produced "agentified" process which improved the quality of software since agents carried out tasks which were previously done by humans. In addition to these projects, Agent.Hospital contained several infrastructural services, most of which are developed using JADE. To take full advantage of described individual projects, support and coordination is implemented using cooperation platform Real Agents. Agent.Hospital is a baseline for agent-based healthcare information systems. It is a complex group of highly useful projects, which begs deployment and details analysis in real world.

Isern et al. in *Agent-based execution of personalized home care treatments* (Isern et al. 2011) *(A.PHT)* present and discuss personalized homecare treatments and how they are created and executed through MAS in good detail. A.PHT is based on K4Care architecture, due to which it is complex from architecture point of view, but has significant practical implications and advantages. K4Care platform is based on layered architecture defining three layers known as knowledge layer (KL), data abstraction layer (DAL) and agent based layer (ABL). KL constitutes all the systems' data sources which include, an EHR in SQL format database and in XML-based database, ontologies which represent medical and organizational knowledge, repositories containing administrative services' procedures and formal intervention plans (FIP). DAL acts as an intermediary between knowledge layer and MAS, and provides MAS the data accessed from multiple data sources in formalized formats. Agent-based layer contains web-based application interface for users, while it uses servlets which call MAS based on JADE for execution of business logic in an autonomous fashion. The system developed uses SDA* formalism (a language developed as part of K4care project)(K4care.net) to represent administrative procedures and healthcare processes. As patients need customized treatments, so the system allows individual intervention plans (IIP) based on selection of specific procedures from formal intervention plans (FIP). Finally, the execution of IIP is done by various agents categorized under gateway agent (GA) and actor agent (AA). Another very important part of the work is the system's validation and performance evaluation. Through questionnaires filled by HC professionals, it is concluded that system outscored the set performance criterion. Also, through European Commission's evaluation and approval, the system is in deployment process after multiple revisions. The system would be tested in real-world (a community HC facility in Italy) initially.

Pegueroles et al. in *The TAMESIS project: enabling technologies for the health status monitoring and secure exchange of clinical records* (Pegueroles et al. 2013) *(TAMESIS)* has been proposed to improve some of the technologies which mainly required for state-of-the-art personal health systems (PHS). Authors present techniques for handling denial of service attacks, solving sensor node issues, and managing traffic injection. Moreover, they focused on how mobile agents can be used for efficient and secure exchange of medical documents between distributed databases in a networked environment. However, the nature of their work is theoretical only, and no implementation has been presented or carried out. Due to lack of implementation, the validation and evaluation of system design, architecture and performance are not possible. Also the extraction of evaluation parameters is not possible because the design and implementation details have not been provided. The system architecture basically consists of four modules namely personal monitoring system (PMS), data negotiation process (DNP), decision support system (DSS) and virtual agent (VA). PMS senses data from sensor node, processes the raw data into information, and communicates the data and information to other components while storing the data and information into data repository. DNP implements protocols aimed at finding ways in which multiple clinical databases can all exchange data for multilateral agreement, keeping in view patient's data privacy. DSS communicates with PMS and VA for enablement of treatment response for remote disease management. VA basically includes components for spoken interface with patients GUI based on user acceptance, and knowledge repository containing minimally DSS outputs, the clinical workflows and guidelines. The DSS is located at the health center, while PMS and VA are located at patient's home.

Kaluža et al. *An agent-based approach to care in independent living* (Kaluž et al. 2010) *(ACIL)* present a MAS aimed at provision of prolonged independent living of elderly people at home. The system is mainly based on seven groups of agents providing data on position and posture of the users and detecting and reacting to abnormal situations. It is aimed at detecting hazardous falls, as well as monitoring users' activities, so as to detect reduced movement. The agent groups contained in system are sensor agents (SA) that contain hardware to sense raw data through sensing agents and providing that to other processing agents. Refining agents - filter noise and correct coordination of body parts, then derive attributes which describe users' posture forming a basic uniform representation of all the data available about a user's body. Reconstruction Agents determine the posture and location of a person at a specific time by using machine learning agents and expert-knowledge agents. Interpretation Agents try to identify if the situation is dangerous for the user by using machine learning agents, expert-knowledge agents and integration agent. Prevention agents are meant for monitoring and analyzing user's movements and behavior so as to prevent them from developing any disabilities. Cognitive agents intend to construct the cognitive state of the integrated, although not implemented in the system currently. Communication agents perform user interaction activities, for example in case of critical situation; they automatically call relatives or professional help. These agents still have not been fully implemented and tested in the system. The system is tested for fall detection and disability detection; in first case system achieved good performance, while in second, it achieved accuracy of 100 percent. The authors expect that with the implementation, still to be completed, and performance to be tuned up, the accuracy of fall detection is likely to improve and upon completion and acceptance, the system shall be implemented in Europe, and elderly shall be able to benefit through it. Since, the authors presented high level design discussion, and not the specific implementation details, so we were not able to extract complete evaluation parameters required for comparison. The paper's contribution is very specific and significant, and it begs deployment.

Discussion Kirn et al. in Agent.Hospital study multiple projects resulting in virtual hospital, while Isern et al. A.PHT presents agents based personalized homecare treatments, both systems are very detailed and complex, as well as are similar with respect to various evaluation criterion as shown in Table 7. Uniform ontology based data representation provides communication and integration level scalability to the system. There is no discussion about data privacy and system security. In both systems, AH and A.PHT, JADE has been used as development framework, and the type of agents used in both systems are reactive static and mobile agents which act autonomously. Moreover, the knowledge representation in both systems is ontology based with task oriented MAS operational architecture. Framework proposed in A.PHT is secure, complex and highly scalable. Kaluža et al. ACIL is different from AH and A.PHT in various characteristics. ACIL uses semi-autonomous agents as opposed to fully autonomous agents used by AH and A.PHT. Another main difference between these systems is that of vertical abstraction usage by AH, which allows extension of system's functionally through agents that can be added to system later on. All three works are proposals with-

Table 7 Comparison of multifunction MAS for healthcare based on evaluation parameters

Parameter	AH	A.PHT	ACIL
Design and development technologies for MAS development	Custom development—JADE	Custom Development – JADE, AOSE, Gaia methodology, Java	–
Agent types	Reactive	Reactive	Reactive
System architecture/Framework	JADE	JADE	Custom
Knowledge representation	Ontology	Ontology	Ontology
Agent mobility	Static, Mobile	Static, Mobile	Static
Intelligence mechanism	–	–	–
Agent dependence/autonomy	Independent/autonomous	Independent/autonomous	Semi-autonomous
Communication mechanism	FIPA-Request, FIPAContractNet, JADE ontologies	FIPA-Request, FIPAContract-Net, JADE ontologies	Asynchronous messages
Complexity and scalability	High	High	High
	High	High	Medium
Security and privacy	Communication level security with no privacy measures	High level of data security with policy based data privacy	Basic security No data privacy

out solid implementation in production environment. This section review shows that idea of conventional healthcare has been revolutionized with the use of intelligent MAS. In next decade, we would be able to see systems such as AH, A.PHT and ACIL to be practically part of our society (healthcare industry) in developed nations at least, if not in developing or underdeveloped nations, as part of healthcare reforms (Table 7).

5 Limitations of MAS for healthcare domain and relevant recommendations

In this section, we discuss limitations, findings and recommendations in order of system sub-domains presented in Sect. 4.

First sub-domain discusses the planning and resource management. Our reviewed works have implemented basic algorithms. The focus or research is on modelling the system using multi-agent paradigm. Utilization of better planning and scheduling approaches have been overlooked. More sophisticated techniques may present their own merits and demerits in MAS.

Various approaches have been presented to incorporate intelligence in systems that may include rule based, case based and statistics based. We categorize these intelligence mechanisms into three groups: None, basic and advanced. In our reviewed work, few of the papers have not used any intelligence mechanism. Majority of papers use basic decision making techniques whereas few have used advanced (i.e. statistical) approaches.

Static rule based and case based approaches are popular. Very few of the systems have implemented statistical methods. Machine learning based approaches are promising and scalable. However, their use in MAS systems is not significant. Static rule based and case based systems can solve smaller problems but are insufficient for larger and complex problems. Dynamic and learning based algorithms may provide better results if implemented. New learning methods with continuous patient status need to be explored. MAS systems reviewed assume small amount of data transfer among stake holders however in real environment sound and image data is heavily transported that needs high end devices. Enough amount of drug related data is not available. Available data is present in unstructured form and needs lot of manual and computational work to bring it into structured form. It is big hurdle in the development of autonomous systems in medical domain. Moreover, there is lack of availability of data in required level of detail and accuracy. Usually decision support systems consume considerable amount of time to formulate the results, hence still not well suited to time constrained systems like patient scheduling and live diagnosis. Another technique for better decision making being considered recently is context awareness (Kaplan et al. 2012; Kim 2014; Manate et al. 2014).

Knowledge representation and remote health care are discussed in Sects. 4.3 and 4.4 respectively. A variety of data is dealt in healthcare information systems (HIS) like sensitive patient data, medical practitioner's data, as well as financial and management data. MAS for HIS are based mostly on distributed environments in which communication settings pose high trust, security, communication, collaboration, and coordination requirements when information is shared between different stakeholders.

Data and Information representation is not among the core issues of MAS however it becomes important when heterogeneous MAS need to communicate and share. Most of the systems discussed use either relational or XML based data representation or objects. Even few have used flat files. This heterogeneous data representation use more computation and need bridge software when communication among different systems is required. However, semantic data models are gaining more importance and as a result multi-agent system development platforms like JADE, MADKit and others are increasingly providing this support.

Trust is a cognitive concept in which one party keeps positive expectations regarding competence and favorable actions by other party. MAS design is based on human agents philosophy, hence HIS must be enriched with good level of trust relationship among stakeholders and system operators. We analyze this trust relationship at two levels: human-healthcare system and intelligent agent-agent trust. Patient health data is patients' personal privacy and they do not like it to be public or semi-public. It is highly required to keep patients' data safe while sharing. The granularity of data shared must be kept coarse or it must be anonymous in order to meet trust contact with patient (Chen et al. 2010). Better and effective methods for trust measurement are required to be conceived (Mohammed et al. 2014).

Various solutions to secure the MAS have been proposed and implemented. However, there are the areas like authorized collaboration, autonomous access control enforcement and data protection need more work. New security challenges also arise with invent of new technology (Jung et al. 2012). To summarize, all schemes focusing on privacy majorly present, authentication, encryption and encoding, context removal and data anonymity. Almost all systems in this study use basic security mechanism i.e. authentication. But, more security is required when an agent need to communicate out of society agent or remote agent. Another technique to manage the security or privacy issues is to setup and enforce privacy policies and limited usage policies based on specific system requirements. The granularity of data sharing must also be defined very carefully considering the medical ethics and patient concerns. The anonymity can be of great use while sharing patients' private health related data or information.

Most of the MAS based health care systems have implemented *static agents*. Static agents are normally applied for functional tasks in operating environment and provide faster response. Mobile agents are usually used for information collection and related purposes where real-time response is not expected. However, due to enhanced use of mobile devices, there is an increase in demand to use mobile agents. For example, a patient using its agent on laptop may need to move in open area where laptop usage is not possible, his agent need to be migrated on his mobile device. Similarly, in emergency department, most of doctors and nurses need to remain mobile. Agent development frameworks variably provide services or tools for security and privacy of MAS, for example JADE has an extension named JADE-S for provision of security features. While, through custom development, the level of security and privacy may be better controlled and specific to the context. Different vendors and researchers have developed frameworks for data privacy and sharing management. Miyagawa et al. (2014), Cristin et al. (2015), and Taweel et al. (2014) are few of the examples. It is to mention that among multiple agent development platforms, few consider the security and privacy. Among open issues in security and privacy domain are standardization of interoperability and openness, use of long life user/patient identity allocation, development of better disclosure decision making mechanisms, centralized information disclosure decision making and dynamic privacy learning (Such et al. 2014).

An architecture and organization of MAS depends upon the type and nature of underlying problem. That is why we see a variety in architectural implementations in our reviewed work i.e. JADE, CORMAS, GAIA based, MADKit, MADIP and Custom. This sometimes makes interaction and collaboration of agents belonging to one system with agents of another system difficult. MAS for healthcare define no strict or standardized architecture for healthcare communication. Most of the healthcare systems built using intelligent agent technology, use custom or underlying conventional network communication protocols. Agent platforms (APs) like FIPA, JADE and RESTINA, define communication protocols, however every platform works independently from other. Inter-enterprise integration requires specific communication protocols to be defined and standardized so that heterogeneous systems may be able to seamlessly communicate with each other. MAS have defined general purpose communication and coordination protocols where issues like information criticality, response severity, and reliable information delivery are not considered in healthcare context. Considering these and other secondary issues like enterprise wide context aware integration, agent guaranteed negotiation, conflict resolution and up to date information provisioning, it is required to design standardized protocols for HIS.

Since, MAS for medical care are fairly complex, so upgrading or maintenance is also cumbersome, tedious and hence costly (Patriarca-Almeida et al. 2011, 2012). The optimization of existing MAS for medical data management proved to be costly in terms of time, resources and effort requirements (Patriarca-Almeida et al. 2012). System maintenance can be costly, so as a golden rule—system architecture and design should be solid and comprehensive using MAS approach i.e. system development is maintainable and changes may be accommodated with no or little effect to the system architecture, while the costs remain economical.

MAS are not implemented at large in healthcare therefore we do not have any idea about its social acceptance. MAS performance benchmarks are not available that make performance measurement hard. Most of MAS are developed as a single homogeneous systems without considering its controversial side and very few MAS with complete heterogeneity have been developed for healthcare domain. As a result, we find it difficult to study a real effect of heterogeneous MAS systems. Multiple efforts to standardize MAS related issues are in progress however, there is no gold standard for implementation and realization of MAS. This deficiency opens the doors for research opportunity.

In following lines, we present recommendations for the application of MAS in healthcare:

- Tools and techniques specific for MAS development be used like AUML.
- Use more and specialized AI components i.e. machine learning algorithms, dynamic rule base algorithms.
- When presenting the work, technical details must be provided.
- Always consider the agent mobility
- Use popular MAS frameworks like JADE.
- Consider the openness and heterogeneity of the system.
- Consider the communication within and out of society.
- Trust, security, encryption and data sharing granularity must be properly defined.
- MAS are not implemented at large that raises question on its social acceptance. Consider this aspect when implementing MAS.
- Different medical services require different quality of service. Adoptable MAS communication protocols should be used.
- Semantic data models should be used for data representation.

6 Conclusion and future work

MAS in healthcare have wider practical applications which need to be realized globally. Nearly all healthcare domains can benefit from this MAS technology however implementation of MAS systems in healthcare is in infancy. Hybrid (software and hardware) agents are expected to become part of a standard HIS in few decades. It is hoped that, in next decade, MAS will become essential part of healthcare industry (Niazi and Hussain 2011). Moreover, emerging technologies such as wireless sensor networks, availability of high end mobile computing devices and internet of things also have potential practical implications in real-world healthcare systems. By delegation of human activities to MAS in healthcare industry, human resources required, would decrease, incorporating more accuracy and precision. Most of work included in this review is funded which shows the interest of public and private sector organizations.

On the other side, MAS in healthcare systems still need to be analyzed from human computer interaction (HCI) point of view so that usability of these systems can be ensured. No technology comes without dark side. Trust, security and information privacy are among major social and technical issues. Use of personal medical information without proper measures may raise many social, ethical, and legal issues for society (Sánchez-Garzón et al. AIME 2013).

As future work, we intend to analyze the local healthcare industry and application suitability of MAS systems to boost interaction among healthcare units and research centers.

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