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Machine Learning used in the field of Pharmacy

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ABSTRACT

The application of intelligence in technology is expanding to include machine-prevalent methods. It could reduce expenses and save time, all the while additionally enhancing our comprehension of how different formulations and process parameters interact. Artificial intelligence, which falls under the realm of computer science is concentrated on problem-solving through programming. It has evolved into a science of problem solving with applications in industries like technology, medicine and more. The research paper covers a range of topics such as discovering peptides from sources, managing and treating rare diseases ensuring proper drug adherence and dosage as well as discussing barriers, to implementing AI in the pharmaceutical industry. It also touches upon automated control procedures, manufacturing execution systems and using AI for treatment predictions.

Key words: Machine Learning, Pharmacy, Prediction, Artificial Intelligence, Drug, Robotics

1 .INTRODUCTION

A subfield of computer science, which is historical is artificial intelligence (AI)concentrates on utilizing programming, for problem solving. Over time It now functions as a problem-solving tool. discipline with applications in fields such, as business, medicine and engineering. The primary objective of AI is to identify and address real world challenges effectively[5].

The field of intelligence deals, with the challenges in processing information. Offers a conceptual approach to tackle them. There is a theorem that relates to such an explanation, known as a method. reference [4]. In the realm of studying intelligence algorithms are.Employed to analyze learn from and comprehend data. Artificial intelligence encompasses methods, machine intelligence methods, the identification of patterns, clustering and similarity based approaches. It's an expanding field of research, with applications.

2.HISTORY

The integration of intelligence, specifically artificial intelligence (AI), within the technological the environment has alteredstrikingly over theyears. Rooted in the realm of computer science, AI has surfaced as an effective instrument for problem-solving through programming. Its application spans varied industries, encompassing but not restricted to technology and medicine, where it holds thecapacity to streamline processes, save time and costs, and enhance our comprehension of complex interactions such as those between various formulas and procedures parameters.

The historical trajectory of AI in technology dates back to the mid-20th century. The term "artificial intelligence" was coined in 1955 by John McCarthy, an American computer scientist, during the Dartmouth Conference. Early developments in AI were marked by ambitious goals and expectations, envisioning devices that could imitate humans intelligence. However, progress during the initial decades was gradual due to limitations in computing power and the complexity of modeling human cognitive processes.

A significant breakthrough occurred in the 1980s with the advent of expert systems, AI programs designed to emulate the decision-making abilities of a human expert in a specific domain. This era witnessed increased interest and investment in AI technologies, paving the way for applications in various industries.

The 21st century has witnessed a resurgence of interest in AI, driven by advancements in machine learning and neural networks. Big data, coupled with more powerful computing capabilities, has enabled AI algorithms to examine extensive quantities of information and derive meaningful insights. This comeback has been especially pronounced in fields such as medicine, where artificial intelligence is utilized to examine medical data, assist in diagnostics, and even predict treatment outcomes.

Applied to the pharmaceutical industry, artificial intelligence has become a focal point of research and development. The utilization of AI in discovering peptides from diverse sources, managing and treating rare diseases, ensuring accurate drug adherence and dosage, and overcoming barriers to implementation within the pharmaceutical sector is a testament to the expanding scope of AI.

Research papers within this domain delve into automated control procedures, manufacturing execution systems, and the use of AI for treatment predictions. These topics reflect the multifaceted applications of AI in optimizing pharmaceutical processes, from drug discovery to manufacturing and treatment protocols. As AI's incorporation into the pharmaceutical sector continues to advance, it holds the promise of revolutionizing how we approach healthcare, providing more efficient solutions to complex challenges and improving patient outcomes.

3. ARTIFICIAL INTELLIGENCE DRUG DISCOVERY

During the drug discovery procedure, assessment of chemicals substances against specimens of ill cells traditionally entails a time-intensive endeavor. The identification of physiologically active compounds worthy of subsequent investigation requires meticulous scrutiny. To expedite this process, research teams at utilize machine learning techniques that that analyze images, providing predictive perceptions of the possibilities of untested chemicals for further exploration[5].

The utilization of machine learning in this context proves advantageous, as computational systems can discern patterns and gather important information from the data sets at a pace far exceeding traditional human analysis and laboratory experimentation. The expeditious discovery of new data sets allows for the rapid identification of novel and efficacious medications. This strategy not only quickens the availability of promising pharmaceutical candidates but also contributes to a reduction in operational expenses, as compared to the manual examination of each substance. The integration of machine learning algorithms in drug discovery exemplifies a paradigm shift, leveraging computational efficiency to enhance the efficiency and cost-efficacy of the medication investigation and creation process. Figure 1 below shows the drug discovery cycle.

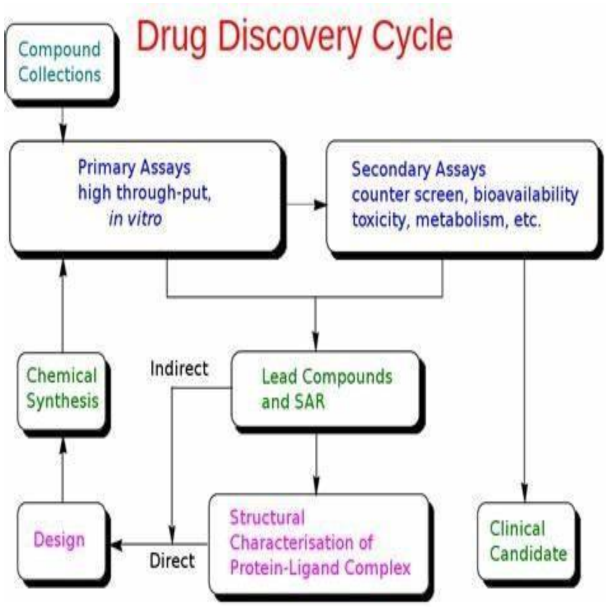

Figure1: Drug discovery cycle

4. COMPONENTS OF AI

4.1 Robotics Pharmacy

The Medical Center at UCSF has implemented robotic technology in the pharmaceutical manufacturing and monitoring processes, demonstrating a commitment to advancing patient safety. These technologies' application has led to the accurate preparation of an impressive 350,000 dosesof medication[3]. Notably, the robotic system exhibits superiority over human counterparts in both scale and precision in drug administration.

The robotic technology employed by UCSF excels particularly in the manufacture of pharmaceuticals, including hazardous chemotherapy drugs for both oral and injectable use. This capability not only enhances the efficiency of drug production but additionally reduces the dangers connected to the management of potentially harmful substances[4].

A distinctive benfits of this robotic approach is its liberating effect on the professional roles of UCSF's chemists and nurses. By automating certain aspectsof pharmaceutical manufacturing and monitoring, these skilled professionals can redirect their focus towards direct patient care and collaboration with medical practitioners. This shift allows for a more nuanced application of their expertise in patient- oriented tasks, ultimately contributing to an elevated standard of healthcare delivery.

In essence, the integration of robotic technology at UCSF exemplifies a strategic alignment oftechnological innovation with the imperative of patient safety. By leveraging automation for pharmaceutical processes, the medical center not only achieves operational efficiency but also empowers its healthcare professionals to dedicate their expertise to the direct benefit of patients.

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Figure.2: Robot Pharmacy

4.2 MEDI Robot

By integrating elements of AI-like interaction, MEDi seeks to enhance the overall experience for pediatric patients undergoing medical procedures. The robot's ability to engage with children in a relatable and comforting manner serves as a testament to the potential of merging medicine and engineering to address not only the physical aspects of healthcare but also the psychological and emotional well-being of patients, particularly in the context of pediatric care. Consequently, the robot for pain management represents a noteworthy intersection of medical and technological innovation, offering a promising approach to improving the overall quality of healthcare experiences for young patients[5]. Figure 2 above shows the Robot Pharmacy.

4.3 ERICA Robot

A researcher at Osaka University named Hiroshi Ishiguro created the new care robot Erica in Japan. Beyond its technical capabilities, Erica exhibits peculiar human-like desires and preferences, such as an affinity for watching cartoon films, expressing a wish to travel to Southeast Asia, and harboring a desire for a life partner with whom it can engage in conversation. This nuanced integration of human-like traits adds a layer of relatability to Erica, aligning with the broader goal of creating robots that can operate with ease incorporate into human social contexts.

In essence, the creation of Erica underscores the interdisciplinary collaboration between academia and technology institutions to push the boundaries of humanoid robotics.

4.4 TUG Robots

The TUG robots are made to autonomously move throughout the hospital delivering meals, medications, specimens, supplies, and heavy loads like trash and linen. Renowned researcher Hiroshi Ishiguro at Osaka University spearheaded the development of Erica, a cutting-edge care robot in Japan.[1] This collaborative effort involved key contributions from International Advanced Telecommunications Research Institute, the Japan Science and Technology Agency (ATR), and Osaka University itself. Erica represents a notable advancement in human-robot interaction, showcasing sophisticated capabilities in language processing and facialexpressions.

Designed with a linguistic proficiency in Japanese, Erica possesses a composite of facial features inspired by both European and Asian aesthetics. Despite being stationary and lacking autonomous mobility, Erica is endowed with a remarkable capacity to comprehend and respond to inquiries with facial expressions that mimic human emotions, fostering a more natural and relatable interaction.

4.5 BERG

Berg, a company located in Boston is, at the forefront of incorporating AI into its operations. They have developed a drug discovery platform that leverages AI technology and utilizes a patient database. This platform aids in identifying and validating biomarkers responsible for causing diseases allowing them to make treatment choices based on the gathered information.. The ultimate goal of Berg is to harness the power of intelligence (AI) to expedite the drug discovery process while minimizing costs by eliminating the guesswork inherent, in drug development methods.

5. MANUFACTURING EXECUTION SYSTEM (MES)

Utilizing MES offers benefits such, as production cycles improved resource use, managed and observed production stages, and optimized batch release. Additionally it ensures compliance with laws[2]. Manufacturing executing systems in shown in figure 3 and various rare diseases are shown in figure 4.

5.1 AI to Forecase new Treatments

Verge is addressing the complexities in the realm of drug discovery through the integration of automated techniques for the collection and analysis of data. Essentially, they are adopting a strategy to chart numerous genes pivotal in brain-related disorders

Figure. 3: Manufacturing execution systems

such as Alzheimer's, Parkinson's, and ALS. Verge posits that by amassing and scrutinizing gene data, they can significantly improve the experimental phase of drug research. Their overarching goal is to harness AI technology for closely monitoring the side-effects of medication treatments on the brain, commencing from the phase. This approach enables pharmaceutical companies to swiftly glean insights into the impact of drugs on cells. Verge is steadfastly focused on employing intelligence to meticulously track and assess diverse treatment outcomes on the brain during the preclinical stage.

5.2 New PEPTIDES generated from Natural Food

Irish startup Nerites pioneers the incorporation of AI and state-of-the-art technology to expedite the quest for innovative, highly resilient foods and nutritious elements. Through this partnership, The goal of BASF (Baden Aniline and Soda Factory) is to create completely unique functional peptides using ingredients found in organic food. In order to forecast, examine, and validate peptides with natural origins, BASF makes extensive use of Nuritas' AI and DNA analysis capabilities. The main focus of BASF is the investigation and launch of peptide- based medicines intended to help treat diseases like diabetes.

5.3 Care and Management of very rare Illnesses

Advancements in AI and the increasing focus on addressing rare diseases are currently at the forefront. Presently, over 350 million individuals globally grapple with more than 7,000 uncommon diseases. In spite of these difficulties, there are positive developments on the horizon. Heal, a biotech a UK-based business has obtained $10 million in Series A funding to implement AI in the quest for innovative treatments for rare disorders. Meanwhile, there's positive updates for those suffering from uncommon diseases as Swiss biotech startup Thera Chon has attracted $60 million in investment to leverage AI in the development of medicines targeted at treating rare genetic illnesses[4].

Figure 4: Rare diseases

6. DRUG ADHERENCE AND DOSAGE

In a strategic collaboration aimed at enhancing treatment adherence and bolstering vigilance in drug trials, AbbVie has partnered with New York-based Acura. In this alliance, AbbVie has implemented the AiCure mobile Software as a Service (SaaS) platform, utilizing facial and image recognition algorithms to monitor adherence. To elaborate, the AI-powered platform ensures that the correct individual has indeed ingested the appropriate medication, confirmed through smartphone- recorded videos of patients taking their pills. The outcomes have been astounding, with adherence rates soaring by up to 90% as reference [6].

Similarly, numerous clinical trials have adjusted dosages for specific individuals to optimize outcomes by leveraging Genpact's AI solution. In a collaborative effort, Bayer is employing Genpact's Pharmacovigilance Artificial Intelligence (PVAI) to not only track medication compliance but also to detect potential adverse effects much earlier in the process.

7. APPLYING AI TO CLEAN UP CLINICAL DATA AND GENERATE IMPROVABLE ANALYTICS

Apple's ResearchKit offers a convenient avenue for individuals to participate in clinical trials and studies without the need for traditional, in-person enrollment processes. This ecosystem for clinical research is centered around Apple's key devices, namely the iPhone and the Apple Watch. A notable example is Duke University, which utilizes an AI- driven facial recognition algorithm and patient data collected from Apple devices to identify autistic youngsters. The ResearchKit simplifies the interpretation of gathered health data, streamlining the process of making sense of valuable information for research purposes. Figure 5 below shows Challenges to the use of AI in Pharma.

7.1 Finding more reliable patients faster for Clinical trials

Despite the abundance of available patient data, The pharmaceutical sector must deal with major obstacles identifying suitable candidates for clinical trials. The process of finding and recruiting suitable individuals can prolong the typical length of time for clinical trials to 7.5 years and escalate the cost per medicine to a range between $161 million and $2 billion. Regrettably, clinical trials often experience an 80% rate of missing deadlines. The clinical trial sector, valued at $65 billion, is in need of a substantial overhaul, especially with over 18,000 ongoing clinical studies recruiting participants in theUS.

8. CHALLENGES TO THE ADOPTION OF AIINPHARMA

Although AI has significant potential to help reshape the pharmaceutical sector, adoption is not a simple process.

Obstacles pharmaceutical companiesen counter when attempting to use AI**:**

- The technology's unfamiliarity — due to itsyouth and esoteric nature, AI still appears to be a "black box" for many pharmaceutical companies.
- The absence of appropriate IT infrastructure is a result of the fact that the majority of IT systems now in use were not created or designed with artificial intelligence in mind. Even worse, pharmaceutical companies must invest a lot of money to improve their IT infrastructure. The use of AI in in the pharmaceutical sector, while promising, is not without its challenges. These are a few of the hurdles that pharmaceutical companies face in integrating AI into their processes:

1. Unfamiliarity with the Technology: AI, being relatively young and complex, can often be perceived as a "black box" by many pharmaceutical companies. Understanding and trust in the technology may be lacking due to its esoteric nature.

2. Lack of Appropriate IT Infrastructure: The current IT systems in use were not initially designed with AI in mind. Upgrading the existing infrastructure to accommodate AI capabilities needs a substantial expenditure of resources, both in terms of money and time.

3. Data Format Challenges: A substantial amount of data in the pharmaceutical industry exists in free text format, making it challenging to compile and convert this data into a format suitable for AI analysis. This steps can be resource-intensive.

Despite these challenges, there is a consensus that AI is already making transformative changes in the biotech and pharmaceutical industries. Over the next decade, it is anticipated that AI will becomea standard and commonplace technology inthe pharmaceutical sector as companies overcome these initial obstacles and recognize the capacity benefits of AIintegration.

Figure. 5: Challenges to the use of AI in Pharma

9. PHARMA SHOULD CONSIDER IMPLEMENTING ARTIFICIAL INTELLIGENCE

The pharmaceutical sector has the potential to spur innovation through the utilization of novel technologies, such as artificial intelligence. emerging as a key player. AI involves the development of computer systems able to carry out tasks that usually call for human intelligence, such as visual perception, speech recognition, decision- making, and language translation. As of 2011, the healthcare industry already possessed a staggering 161 billion GB of data, according to estimates by IBM.

The abundance of data in the healthcare sector provides a ripe opportunity for AI to play a crucial part role in data analysis and result presentation. This, in turn, facilitates informed decision-making, leading to significant savings in time, money, and human effort, ultimately contributing to saving lives.

One notable artificial intelligence in healthcare is inthe forecasting of the onset of epidemics.. With the use of AI and machine learning, researchers can examine past outbreaks, study social media activity, and accurately forecast the occurrence, location, and timing of potential outbreaks. This Capability has enormous potential for proactive and effective publichealth measures.

Certainly, treatment customization is a significant area where artificial intelligence (AI) can contribute to the development of new tools for various stakeholders, including patients and doctors. Here are some key aspects:
1. Personalized Medicine AI is capable of analyzing enormous volumes of patient data, including Personalized treatment plans, lifestyle factors, and genetic information.. This enables healthcare professionals to tailor interventions to individual patients, potentially improving efficacy and minimizing side effects.

2. Drug Development and Discovery: Artificial Intelligence is essential to accelerating the process of discovery. Artificial intelligence algorithms can find

promising drug candidates by evaluating intricate biological data. more efficiently, leading to the development of targeted and effective treatments.

3. Treatment Monitoring: AI-powered tools can continuously monitor patients during treatment, providing real-time feedback to healthcare providers. This can help in adjusting treatment plans promptly based on the patient's response and minimizing adverse effects.

4. Predictive Analytics: AI can predict disease progression and identify high-risk patients, allowing for proactive and preventive measures. This is particularly valuable in chronic conditions where early intervention can significantly impact outcomes.

5. Virtual Health Assistants: AI-driven Virtual assistants are able to offer customized health advice, reminders for medication, and guidance on lifestyle choices. This enhances patient engagement and adherence to treatment plans.

6. Clinical Decision Support: AI systems can help medical professionals make well-informed decisions by examining treatment guidelines, medical literature, and patient data. This may result in more precise diagnosis and optimized treatment strategies.

10.THE APPLICATION OF AI TO HEALTHCARE

Personalization has enormous potential for Increasing patient outcomes and the effectiveness of healthcare delivery, and advancing medical research and innovation. Utilizing predictive analytics to identify possible clinical trial subjects found via social media and physician visits is an innovative approach reference [5] that leverages data-driven insights for more effective participant recruitment. Here's how this process might work:

1. Social Media Analysis:

- Targeted Recruitment: Predictive analytics can use social media data analysis to find people who fit particular requirements for clinical trials. This could include demographic information, health indicators, or lifestyle factors relevant to the study.

- Sentiment Analysis: By assessing social media posts, sentiment analysis can be employed to gauge individuals' attitudes towards healthcare, clinical trials, or specific medical conditions. This information can help tailor recruitment strategies.

2. Electronic Health Records (EHR) Integration:

- Patient Eligibility Assessment: Predictive analytics can be applied to electronic health recordsto assess patients' eligibility for clinical trials based on medical history, conditions, and other relevant factors.
- Identification of Potential Participants: Algorithms can identify patients who may be suitable for a particular trial, streamlining the recruitment process by proactively reaching out to eligible individuals.

3. Doctor Visits and Electronic Medical Records (EMR):

- Physician Engagement: Predictive analytics can help in identifying potential trial participants during routine doctor visits. Physicians can be alerted to ongoing clinical trials relevant to their patients, facilitating discussions about potential participation.

4. Integration with EMR Systems:

- Electronic medical records can be integrated with predictive analytics tools to assess patient profiles and identify those who align with the criteria for specific trials.

5. Patient Outreach and Engagement:

- Personalized Communication: Predictive analytics can guide the development of personalized communication strategies for patient outreach. Tailored messages can be delivered through various channels, enhancing the likelihood of participantengagement.

6.Feedback Loops:

-Continuous analysis of engagement data allows for refining outreach strategies over time, ensuring a more effective and efficient recruitment process.

7. Privacy and Ethical Considerations:

- Data Security: Given The delicate aspect of health data, a robust data security framework must be in place to protect individuals' privacy and comply with regulations such as HIPAA.

8. Informed Consent:

Transparency in communication and obtaining informed consent remain crucial ethical considerations, ensuring that potential participants fully understand the implications and voluntarilychoose to participate.

By combining predictive analytics with social media insights and healthcare data, researchers can enhance participant recruitment strategies, potentially increasing the efficiency and success of clinical trials. However, it's crucial to navigate ethical considerations and privacy concerns to ensure the responsible use of personal health information.

10.1 Limitations

Organizing electronic records for efficient streamlining necessitates an initial cleanup process due to their current disorganized state and dispersion across multiple databases.

Clarity: In light of the intricacies involved in artificial intelligence-driven procedures, healthcare recipients demand transparency in the healthcare services they receive.

The confidentiality and legal accessibility of medical data fall under the purview of data governance. Securing public approval is imperative.

10.2 Benefits and Issues

• Mastery of incomplete datasets, swift data analysis, adaptability to preferences and constraints, and the ability to generate coherent rules.

• Economical enhancements to product performance and quality.

• Accelerated time-to-market, innovation in product creation, heightened client feedback, and augmented confidence.

• When meticulously coded, AI boasts a lower error rate compared to humans. It exhibits remarkable speed, accuracy, and precision.

• Immune to adverse conditions, AI can undertake hazardous tasks, explore uncharted realms, and confront challenges that pose threats to human safety.

• Involves navigating through materials perilous to humans.

• Substituting humans with machines in arduous and monotonous tasks..

• AI application in numerous video games serves asa tangible example.

• Robotic animals with the capability to communicate with humans can combat sedentary behavior and alleviate feelings of sadness.

• Offers avenues for sexual satisfaction.

• Possesses the capacity for sound decision-making with minimal or no errors, as it operates with clarityand devoid of emotion.

10.3 Applications

(1) In Formulation Controlled-Release Tablets

With reference [6] in the realm of formulation, the University of Cincinnati's Hussain and team in Ohio, USA, spearheaded the utilization of undetectable AI in the development of controlled-release tablets. Their groundbreaking work harnessed neural networks to model the in vitro release properties of various medications incorporated into matrices constructed from diverse hydrophilic polymers. Across multiple studies[1], it was consistently observed that undetectable AI, characterized by a singular hidden layer, demonstrated commendable efficacy in accurately predicting drug release outcomes.

Immediate-Release Tablets

Around three years ago, the inaugural endeavors in the field were initiated through two studies. One study, led by Turkoglu and collaborators from the University of Marmara in Turkey and the University of Cincinnati, employed undetectable AI alongside statistical methods to predict various compositions of hydrochlorothiazide tablets.

In the pursuit of optimizing tablet strength or selecting the most suitable lubricant, the created undetectable AI networks were instrumental in constructing three-dimensional plots. These plots encompassed massing time, compression pressure, crushing strength, drug release, and more. Despite discernible patterns, no ideal formulations were explicitly provided, mirroring outcomes produced by traditional statistical approaches.

(2) In Production Development

A prime example of an undetectable AI challenge in the realm of multivariate optimization is the advancement of medicinal products. This involves navigating various variables in formulation and process optimization. Undetectable artificial neural networks (ANNs) exhibit a commendable trait in their ability to generalize, making them particularly well-suited for addressing challenges in formulation optimization within the pharmaceutical production domain[1].

In investigations assessing the impact of diverse elements, such as formulation and compression parameters, on tablet qualities like dissolution, undetectable AI models, specifically ANNs, showcased superior fitting and predictive capabilities in the development of solid dosage forms.[2] Leveraging undetectable AI, particularly ANNs, proved to be a valuable tool in efficiently constructing micro-emulsion-based drug delivery systems, minimizing the need for extensive experimental work.

11. CONCLUSION

The human body stands as the pinnacle of intricate machinery ever fashioned. The human brain tirelessly strives to create entities surpassing human efficiency in any designated task, achieving noteworthy success to a certain extent. The landscape has undergone substantial evolution through the integration of undetectable AI tools like the robotic pharmacy, pull robot, and Watson for cancer. As the healthcare domain expands, the requisite infrastructure will demand heightened sophistication and technological advancement. The creation and use of algorithms for data analysis, learning, and interpretation constitute artificialintelligence.

REFERENCES

[1] Smith AB. Applications of artificial intelligence in pharmacy and medicine. 1992;27:312-5, 319-22 Hospital.

[2] Johnson X., Krishnan S., Palmer J., Artificial Intelligence Strategies for Rational Drug Design and Discovery. Current Pharmaceutical Design, 2007;13:00.

[3] Garcia France The Pharmaceutical Journal December 2007.

[4] Nowakowski P. An Introduction to Machine Learning 1st ed. Switzerland: Springer International Publishing; 2016.

[5] DataWorld. Machine Learning and Its Applications. Available from: https://www.dataworld.com/machine-learning-and-its-applications-study-report/. [Last accessed on 2017 Jun 24].

[6] Thompson M. (2017) Evaluating the Impact of Watson's Victory on 'Jeopardy'. The Times of NewYork.