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Review article

The use of intelligent database systems in acute pancreatitis – A systematic review

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ABSTRACT

Introduction: Acute pancreatitis (AP) is a complex disease with multiple aetiological factors, wide ranging severity, and multiple challenges to effective triage and management. Databases, data mining and machine learning algorithms (MLAs), including artificial neural networks (ANNs), may assist by storing and interpreting data from multiple sources, potentially improving clinical decision-making.
Aims: 1) Identify database technologies used to store AP data, 2) collate and categorise variables stored in AP databases, 3) identify the MLA technologies, including ANNs, used to analyse AP data, and 4) identify clinical and non-clinical benefits and obstacles in establishing a national or international AP database.
Methods: Comprehensive systematic search of online reference databases. The predetermined inclusion criteria were all papers discussing 1) databases, 2) data mining or 3) MLAs, pertaining to AP, independently assessed by two reviewers with conflicts resolved by a third author.
Results: Forty-three papers were included. Three data mining technologies and five ANN methodologies were reported in the literature. There were 187 collected variables identified. ANNs increase accuracy of severity prediction, one study showed ANNs had a sensitivity of 0.89 and specificity of 0.96 six hours after admission – compare APACHE II (cutoff score $\geq$8) with 0.80 and 0.85 respectively. Problems with databases were incomplete data, lack of clinical data, diagnostic reliability and missing clinical data.
Conclusion: This is the first systematic review examining the use of databases, MLAs and ANNs in the management of AP. The clinical benefits these technologies have over current systems and other advantages to adopting them are identified.

1. Introduction

Severe acute pancreatitis (AP) is a common disease that carries with it significant morbidity and mortality [1–3]. Research and clinical decision-making in patients with AP are hampered by a variety of factors including the wide range of aetiological factors [4], difficulties in severity prediction with complex and labour intensive scoring systems [5], multiple treatment guidelines of variable quality [6], and, as examples, a relative lack of high quality evidence relating to fluid therapy [7] and nutritional support [5].

Electronic databases are now commonly encountered tools across many industries, including healthcare. The power to rapidly extract, assimilate, analyse and convey information derived from data stored within these systems has wide application across the health sector. Intelligent electronic databases with real-time analysis of data can be particularly useful in complex diseases processes, such as AP, for clinical management, research and administration. Clinical management and decision making in AP would be enhanced by efficient assimilation and real-time analysis of a multiple clinical and laboratory findings, as well as a growing number of molecular and genetic markers, by artificial neural networks (ANNs) [8]. Merging information into national or international databases would allow clinicians and researchers to work together more effectively and aid in producing high quality clinical guidelines and collaborative research.

The aim of this paper is to conduct a systematic review of the literature pertaining to AP databases and data analysis systems in order to 1) identify database technologies that have been used to store data in AP, 2) collate and categorise the range of variables that have been stored in AP databases, 3) identify the specific machine learning algorithms (MLAs), including ANN technologies, that have

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been used for analysing data in AP, and 4) identify the non-clinical benefits and obstacles involved in establishing a national or international database for AP.

2. Methods

2.1. Literature search

A comprehensive and systematic search was performed of the online databases Medline, PubMed, EMBASE, and The Cochrane Library using the search string: ("Automatic Data Processing"[Mesh] OR "Software"[Mesh] OR "Computer Systems"[Mesh] OR "Artificial Intelligence"[Mesh] OR "Medical Informatics"[Mesh] OR "Computer Security"[Mesh] OR "Information Storage and Retrieval"[Mesh]) AND ("Pancreatitis"[Mesh]). Papers were then screened for relevance based on pre-defined inclusion and exclusion criteria.

2.2. Inclusion and exclusion criteria

Inclusion criteria were all papers published in human medical journals deal with the use of 1) databases, 2) data mining and or 3) machine learning algorithms (MLAs) – including artificial neural networks (ANN) in acute pancreatitis. Papers were excluded if they were published before 1990, were case reports, editorials or commentaries. There was no restriction on language.

2.3. Data extraction and analysis

Data were extracted on to a pre-defined pro-forma by two authors (MvdH and MH) and any conflicts resolved by a third author (AM). Papers were categorised into the three discrete sets: databases, data mining, and MLAs.

Papers that only deal with database systems were analysed for database technologies used and variables stored. Papers that deal with data mining were reviewed in order to identify the underlying database and the data mining algorithm used. Papers relating to MLAs were reviewed for the algorithm type and configuration, the inputs provided to the programs, and the traditional scoring systems against which their performance was benchmarked.

3. Key definitions

Data mining is the computational process of examining large databases with the aim of generating new or previously unknown information from the data [9]. For example, data mining applications may scan stored data, and attempt to identify trends and cohort characteristics in the data [10].

Machine learning algorithm (MLA) refers to a computational program belonging to a family of algorithms which use example data or past-experience to solve a defined problem [11]. Artificial neural networks (ANN) are a type of machine learning algorithm. An ANN is modelled on biological neural tissue [8,12,13]. It consists of a series of processing units known as 'neurones', each series of which are interconnected by links termed 'synapses'(Fig. 2). ANNs 'learn' the association between input variables (such as admission data for AP patients) and outcomes from training data. A 'back propagation' algorithm allows these systems to learn the patterns between inputs and outputs and adjust the weighting each synapse/connection in the sequence. The training is then verified by running another set of inputs (admission data) through the ANN and assessing the accuracy of the system's prediction against the known clinical course values.

4. Results

4.1. Search

Our initial search identified 590 papers, of which 43 met our inclusion criteria (Fig. 1). The characteristics of each included study are summarised in Supplementary Table 1. Thirteen papers discussed analysing clinical databases, 10 discussed research databases and 22 papers used administrative databases. One hundred and eighty-seven distinct database variables were collected in the 43 papers. These are listed in Supplementary Table 2. Table 2 categorises the variables and records the frequency with which they appear across the papers.

4.2. Clinical databases

Eleven papers discussed extracting data from clinical databases at single sites [14–24]. These were a mix of Electronic Health Record (EHR) systems and radiology information systems. Two papers discussed the extraction of data from EHR systems across multiple hospitals [25,26].

4.3. Research databases

Seven papers discussed the use of prospectively created research databases as the source of data used in their research [20,27–32]. Two papers discussed research databases containing data across multiple clinical research sites [33,34]. Both of the latter papers dealt with centres involved with the Dutch Pancreatitis Study Group which comprises 8 University medical centres and 16 large teaching hospitals in the Netherlands [35]. It has completed 3 multi-centre trials and the group is currently conducting a further 7.

4.4. Administrative databases

Of the 22 papers which utilised administrative databases, 2 discussed the use of administrative databases at a single site. Both made use of surgical audit databases at the respective hospitals [12,36]. Three papers extracted data from regional administrative databases [37–39]. One was an adverse drug reaction reporting database for regions in France [38], 1 was a regional branch of the Veteran's Administration Healthcare Network in the USA [39], and the other was the publicly available database of discharge data at the California Office of Statewide Health Planning and Development [37] (these were the only publicly accessible data across the papers reviewed). Sixteen papers utilised data from national administrative databases [1,2,40–52]. These were large government or institutional databases from the USA (10 papers) [1,40–43,45,46,48,50,53], Japan (2 papers) [47,49], England [52], Ireland [2], Denmark [44] and Sweden [51] (each mentioned in a single paper). One paper utilised an international administrative database, the World Health Organisation's database of adverse drug reactions [54].

Supplementary Table 3 outlines the characteristics of these large databases, and the researchers' evaluation of their utility. Of the papers which utilised regional or national databases, 9 discussed the large size of these databases as being a benefit [37,42–46,49,51,52]. Nine papers discussed the issue of incomplete data [1,2,38,40,44,45,47,51,53]. Three papers discussed a lack of access to clinical data [2,43,52]. One paper noted the shortcoming of being bound to the fields collected in the administrative database [45]. Three papers noted issues with reliability of diagnosis [42,44,46].

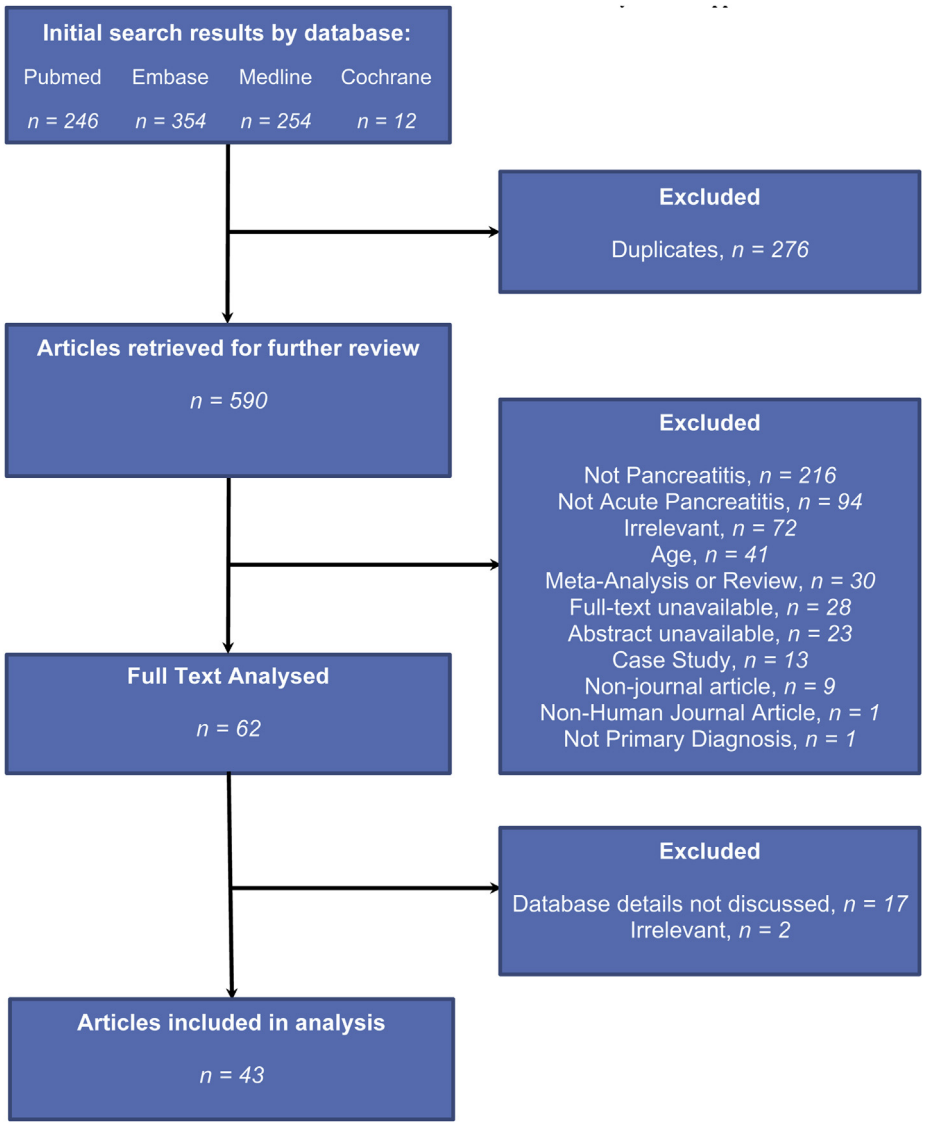

Fig. 1. Prospect diagram showing the flow of documents considered for systematic appraisal.

4.5. Data mining

Three papers discussed the use of data mining and employed various algorithms to perform disproportionality analysis of the data. All papers were attempting to discover statistically significant associations between drugs and AP to suggest an adverse drug reaction (ADR), i.e. drug induced AP. One paper utilised the Odds Ratio to generate signals of statistical associations between medications and AP across an EHR at a single site [14]. Another paper utilised a Bayesian confidence propagation neural network (BCPNN) [54]. BCNNs are a type of ANN, used to find strong relationships within the data being assessed using Bayesian statistical methods. The authors of this paper used the BCNN to find an association between selective serotonin re-uptake inhibitor treatment and pancreatitis in the World Health Organisation database on adverse drug reactions, the disproportionality being calculated using the information component (IC). The third paper used another Bayesian method known as the Multi-item Gamma Poisson Shrinker (MGPS) against the Adverse Event Reporting System database run by the United States Food and Drug Administration to assess the validity of the association found between pancreatitis and selected atypical antipsychotics by more traditional rule based methods of signal detection [41].

4.6. Artificial neural networks

Eight papers assessed the efficacy of ANNs against existing practice for diagnosis, severity prediction, and predicting length of stay (LOS) (Table 1).

4.7. Diagnosis

ANNs can accurately diagnose AP using clinical and radiological data [15,27]. Kazmierczak et al. found that when comparing the diagnostic accuracy of ANN models employing models utilising amylase, lipase or a combination that the use of lipase added greater diagnostic accuracy. Amylase alone had a diagnostic accuracy of 0.76 (95% CI: 0.71–0.81), lipase alone had 0.82 (95% CI: 77–87) [27]. Analysis of both amylase and lipase together did not significantly enhance the accuracy at 0.84 (95% CI: 0.79–0.89). Ikeda et al. used radiological findings extracted from a radiology image database to differentiate mass-forming pancreatitis from

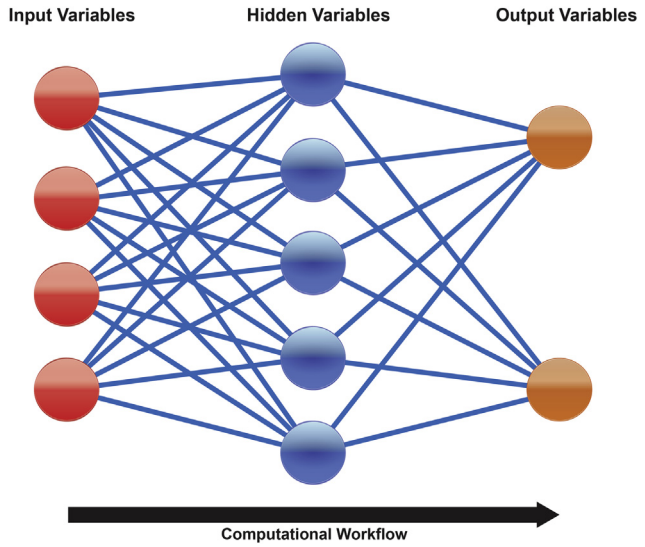

Fig. 2. ANN Multi-layer perceptron with back propagation. An ANN consists of a set of neurons (red circles) which store the value for a specific variable, a series of hidden neurons (blue circles) which can be configured by the ANN administrator and the output neurons (orange circles) which can contain either simple or complex data. The neurons in each layer are connected by synapses (blue lines). Initially, an ANN is an empty system and requires training data to allow it to learn the association between an existing set of patient data and outcomes. When the system modifies the weighting/significance of the synaptic connections between neurons and allows it to appropriately correlate a patient's admission data to observed outcomes in the training data – this is known as back propagation.

pancreatic ductal adenocarcinoma and found ANN to be comparable to experienced radiologists [15].

4.8. Severity prediction

Severity prediction was better with ANNs than APACHE II [12,19,32], modified Glasgow score (GS) [12,19] and Ranson's criteria [19]. ANNs can do so using fewer variables and within 6 h of the time of admission of the patient to the hospital compared with 48 h for clinical scoring systems [12]. Three papers used ANN in predicting the severity of disease on admission and found that ANN have better predictive ability [12,19,32]. Mofidi et al. compared an ANN model against the modified Glasgow (Imrie) score (GS) and APACHE II [12]. The study looked at severity of disease and found ANN to be superior with a sensitivity of 0.89 (95% CI: 0.83–0.93) and specificity of 0.96 (95% CI: 0.9–0.97). GS with a cut-off score of ≥3 had a sensitivity of 0.71 (95% CI: 0.62–0.79) and a specificity of 0.74 (0.67–0.81). APACHE II with a cut-off score of ≥8 had a sensitivity of 0.80 (95% CI: 0.72–0.86) and a specificity of 0.85 (95% CI: 0.77–0.90). It also compared the 3 scoring systems to predict persistent multi-organ dysfunction syndrome (MODS) within the first week of hospitalisation and to predict mortality during the index admission, and again found the ANN superior for both.

Halonen et al. developed an ANN model for severity prediction, with an area under the receiver operator characteristic (ROC) curve of 0.847 (95% CI: 0.741–0.953), substantially better than the Ranson scoring system, ROC = 0.6555 (95% CI: 0.503–0.808); the original GS, ROC = 0.536 (95% CI: 0.364–0.708); APACHE II, ROC = 0.817 (95% CI: 0.704–0.931); and the multi-organ dysfunction score (MODS), ROC = 0.781 (95% CI: 0.662–0.9) [19].

Andersson et al. created an ANN model to predict AP severity [32]. ROC curve analysis showed that the ANN model had a discriminatory power of 0.92 (95% CI: 0.85–0.99) which was significantly better than APACHE II with a discriminatory power of 0.63 (95% CI: 0.5–0.76) [32].

In addition to ANNs, other MLAs have also been used to accurately predict the severity of AP. For example, Pearce et al. used the Kernel Logistic Regression Model to predict the severity of AP, and it was found to be superior to APACHE II, when using the first clinical and laboratory findings at admission and with fewer inputs (only required eight) [21]. The MLA had a sensitivity of 0.71 and a specificity of 0.87 ($p < 0.33$ cut-off) compared to admission APACHE II (score ≥8) with 0.56 and 0.78 respectively for admission data [21].

4.9. Length of stay

ANNs are better than existing scoring systems at predicting length of hospital stay for AP patients. Keogan et al. used radiological and laboratory data, and their ANN was able to perform better than both the Balthazar and Ranson scoring systems [18]. The paper by Pofahl et al. found that their ANN model was able to predict whether a patient was going to have LOS longer than seven days using data available at admission instead of having to wait 48 h for the traditional severity scoring systems. ANNs had a sensitivity of 0.75 and specificity of 0.81 compared to the Ranson criteria with 0.63 and 0.94 respectively and admission APACHE II values of 0.63 and 0.84 respectively [16].

5. Discussion

This is the first systematic review to examine the role of databases, data mining and MLAs in AP in the published literature. It has demonstrated that AP researchers have relied on databases employed for predominantly administrative reasons, with only a small proportion of the literature pointing to the use of databases for clinical or research purpose. ANNs were shown to be more accurate in predicting severity using fewer variables and often providing this information at the time of patient admission, compared with current scoring systems that required collection of more variables and often necessitated a delay of 48 h before calculation.

5.1. Clinical benefits of using intelligent databases

Severity prediction in AP using traditional scoring systems falls short of what is required for the clinical management of acute pancreatitis, with an overall accuracy of 60–80% [55]. This is a significant barrier for both clinicians (unable to accurately predict patients who will develop severe AP) and also for researchers (unable to accurately classify patients for therapeutic studies) [55]. A significant application for ANN is the automatic optimised sequencing of prognostic scoring parameters in order to extract significantly better combined test outcomes from existing data [56]. The principle behind this approach is to improve the pre-test probability for each scoring system applied in sequence, thereby improving the post-test probability of the next applied scoring system [56]. The first scoring system in such a sequence would be one with a low false-negative rate to avoid excluding some patients with severe disease. For example, the Bedside index of severity in AP (BISAP) score might have such a role because of the high specificity (92%), which ensures that it is unlikely that those with severe disease will be excluded. The second scoring parameter, which might be more expensive or more difficult to perform, could then be applied to a smaller subset of patients, which with a high sensitivity could increase the accuracy of predicting severe disease. An intelligent database system would not only have automated collection of data, but with an integrated ANN to analyse the data to provide real-time support for clinician decision-making (Fig. 3) [32].

Another clinical benefit of intelligent database systems would be real-time access to current clinical guidelines and ANN

Table 1
Machine learning models assessed.[a]

Machine learning model	Reference	Year	Algorithm	Number of patients	Objective	Variables used for AP diagnosis or prognostication	Outcome
ANN	Kazmierczak et al. [27]	1993	3 layer, feed forward perceptron employed. 3 different models employed to deal with different permutations of inputs.	Training set: 254 Testing set: 254	Diagnosis of acute pancreatitis by serum activity of amylase and lipase	3 different models: 1. Lipase Only 2. Amylase only 3. Lipase and amylase in combination	ANN analysis of lipase activity provided the best diagnostic accuracy
ANN	Ikeda et al. [15]	1997	3 layer feed forward perceptron with back propagation algorithm employed. The most successful model was reported on with 15 inputs, 15 hidden nodes and a single output node.	32 with pancreatic inflammatory mass, 76 with pancreatic ductal adenocarcinoma	Differentiate pancreatic ductal adenocarcinoma from mass-forming pancreatitis using CT findings	15 input variables related to the characteristics of the pancreatic mass and parenchyma.	Neural network performed similarly to two other computerised classification systems and to radiologists
ANN	Pofahl et al. [16]	1998	3 layer, feed forward perceptron with a back propagation algorithm employed. A single model was used in the study with 71 input nodes, 71 hidden nodes and an output node for LOS >7.	Training set: 156 Testing set: 39	Predict LOS in acute pancreatitis	71 inputs from the time of admission	ANN model accurately predictedLOS >7 days with results similar to APACHE II and Ranson scoring system
ANN	Keogan et al. [18]	2002	3 layer, feed forward perceptron with back propagation employed. Model had 6 inputs, 2 hidden nodes and an output node for AP severity.	92 patients with acute pancreatitis	Predict LOS in acute pancreatitis using CT and laboratory data	6 input variables: fluid aspiration, extent of inflammation, serum creatinine level, presence of concurrent severe illness, blood pressure, and serum calcium level.	ANN model performed similarly to linear models
ANN	Halonen et al. [19]	2003	3 layer, feed forward perceptron with back propagation employed. 3 models used one with 4 inputs, one with 5inputs and another with 8 inputs.	Training set: 234 Testing set: 60	Predict fatal outcome of severe acute pancreatitis	Age, history of cardiovascular or anticoagulant medication, mechanical ventilation during the first 72 h, highest serum creatinine levels within 60–72 h of admission, whether transferred through to study hospital, requirement for pressor support during the first 72 h, gender and body mass index (BMI)	ANN model was significantly better than linear models (APACHE II, Ranson and GSS scoring systems)
ANN	Spigset et al. [54]	2003	Bayesian confidence propagation neural network (BCPNN), no further information on architecture available.		Investigate the association between SSRI treatment and pancreatitis	N/A	ANN analysis found no significant association between SSRI treatment and pancreatitis
ANN	Mofidi et al. [12]	2007	3 layer, feed forward perceptron with back propagation employed. Assessed models with $1 \leq N \leq 29$ clinical input variables. Sensitivity analysis found optimal model used a subset of 10 of these variables.	Training set: 498 Testing set: 166	Identify severe acute pancreatitis and predict fatal outcome	Inputs were patient age; initial admission values of arterial PO_2, LDH, serum glucose, serum urea, serum calcium, haematocrit, white blood cell concentration; along with assessments at 6 h after admission on hypotension refractory to fluid therapy and persistent systemic inflammatory response syndrome (SIRS).	ANN was more accurate than APACHE II and GSS at predicting severe course
ANN	Andersson et al. [32]	2011	~1.4million different Multi-layer perceptrons were assessed. The most successful model was the 3 layer perceptron using 6 of the 23 risk factors as inputs, 6 nodes in the hidden layer and a single output node for severity prediction.	200 patients with acute pancreatitis	Predict the severity of acute pancreatitis (AP).	6 admission variables – duration of pain (never utilised in a scoring algorithm before), serum creatinine, haemoglobin, serum alanine aminotransferase, heart rate and white blood cell count	ANN analysis was found to be superior to APACHE II
Kernel Logistic Regression Model	Pearce et al. [21]	2006	Kernel logistic regression (KLR) method was employed, models used both a number of commonly used kernels including linear and non-linear induced spaces. Final model was linear utilising 8 variables to predict severe attack.	265 patients	Predict severity of disease upon admission and include CRP as part of assessment.	8 Admission Variables: Age, CRP, respiratory rate, pO2 on air, arterial pH, serum creatinine, white cell count and Glasgow Coma Score	The machine learning model performed better than APACHE II at predicting severity of outcome from admission data. The model contained fewer inputs than the APACHE II and was easy to compute.

[a] Adapted from Bartosch-Härlid et al. [8].

Table 2
Type of variables across papers.

Category	Percentage
Demographics	13.2%
Administration/cost of care	1.2%
Severity of disease	7.8%
Patient history/co-morbidities	13.2%
Aetiology	10.1%
Genetic markers	0.7%
Clinical setting	5.6%
Admission and symptoms	8.5%
Interventions	10.2%
Diagnostic results	9%
Microbiology and infection	2.3%
Radiology	2.8%
Disease classification/coding	7.1%
Complications	1.2%
Clinical outcome/discharge	7.1%

recommendation for timely treatment and investigations based on individual patient data. There are multiple guidelines of varying quality for management of patients with AP [6]. However, compliance with these guidelines has previously been shown to be variable with poor compliance with recommendations regarding admission to intensive care units and various interventions. Application of an intelligent database system with an associated live ANN could allow for real-time recommendations being sent to the clinician based on guideline(s) chosen by the clinician's institution and individualised to each patient's data in an iterative manner.

5.2. Non-clinical benefits of using intelligent databases

Other potential benefits of utilising AP databases include reduction in entry errors of data, improved efficiency, easier conduct of multi-centre trials, enabling of concurrent laboratory and clinical research, and scalability.

Inaccurate data transcription are a common cause of data errors [57]. Use of multiple systems and information silos within hospitals force repeat entry by users (e.g. manual copy of clinical data into research databases). Modern database management platforms are able to minimise error through integration of administrative, clinical and research databases with automated extraction and upload of data, thus reducing duplication of effort and error rates. Modern database systems also enable complex data to be presented to administrators, clinicians and researchers efficiently, graphically and in an appropriate way for each group.

Collaboration across multiple sites can be facilitated through the use of a centralised online system, or a standardised model, deployed at each research site with centralised consolidation. The limitations of smaller database management system (DBMS) suites such as Microsoft® Access™ and FileMaker Pro™ include a restriction on the number of concurrent users, small size of the database, limited interface capability, poor security of data, and limited capability to backup data relative to enterprise level DBMS [58]. Modern enterprise level DBMS servers overcome these issues and allow for the expansion of the research database to be easily rolled out across multiple sites. Enterprise DBMS also allow for much higher throughput of data and are geared to cope with multiple concurrent datum updates and provide the ideal platform to build a bespoke AP database.

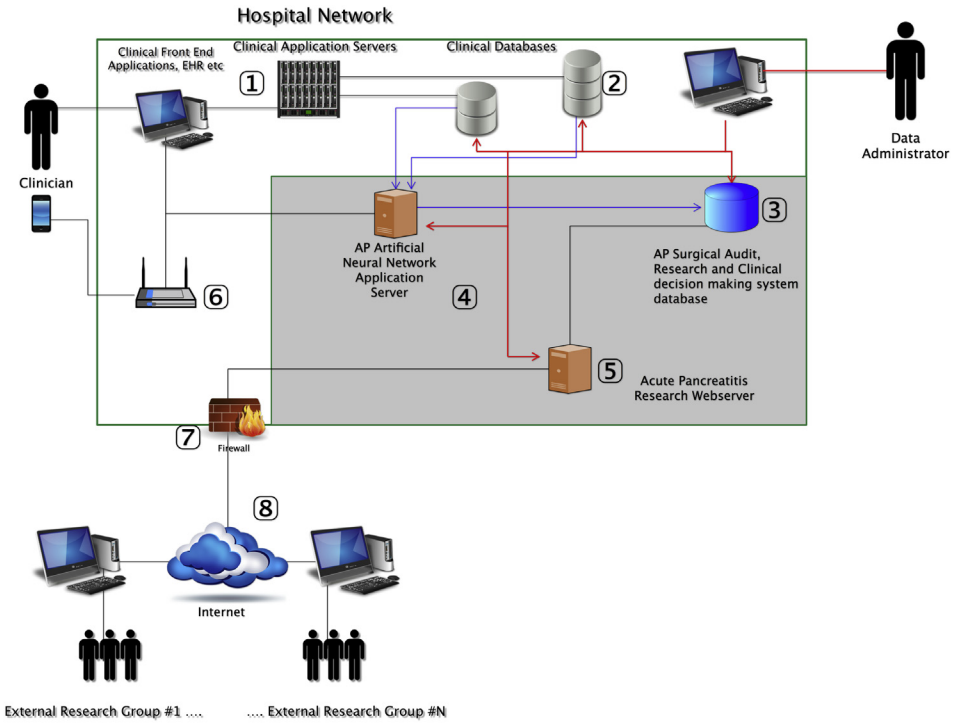

Fig. 3. Schema showing how an intelligent AP database could be used for both clinical and research purposes. The green rectangle represents the hospital's entire network. 1) represents the hospitals clinical systems which deliver the electronic health record and diagnostic applications. 2) Represents the hospital's clinical databases. The Grey shaded area represents that part of the network which houses the AP research systems – 3) the AP research database, 4) the neural network server and 5) the webserver which provides the online interface to the research database. The blue lines represent the unidirectional flow of data from the clinical source – the ANN system stores salient AP patient data into the research database for the purposes of both training the ANN and research purposes. The red lines show the points of auditing which the data administrator has to ensure appropriate access to data. 6) is a wireless router to allow clinicians to access the ANN on mobile devices at the bedside. 7) The firewall ensures that only appropriate traffic from affiliated research groups is allowed to gain access from the internet (8).

5.3. Obstacles to the widespread use of intelligent databases and potential solutions

Several obstacles exist to the widespread use of intelligent databases in the clinical management and research of patients with AP. These are a lack of clinical and research focused databases, lack of a common standard for transfer of data, security concerns and regulatory considerations. These obstacles and the potential solutions are summarised in Table 3.

Approximately half of the included papers reported on the use of administrative databases rather than repositories specifically engineered for clinical or research use. Researchers accessing large regional and national databases acknowledged that although they had the benefit of large patient numbers, there were definite drawbacks including incomplete clinical data and uncertainty around diagnoses where coding systems were used [1,2,28,38,40,42–47,49,51–54]. A potential solution to this problem is a combined database that would provide efficient and relevant collection of data, monetary savings and a secure repository of data that can be used by all. An independent party might be employed by all three groups and a governance structure established to ensure that the system meet the requirements of all parties.

A major obstacle to large centralised databases for AP is a lack of compatibility of data stored at various hospitals and the lack of a common standard for transferring data. This is compounded by the heterogeneous data collected and stored across individual institutions. While data might be stored at different centres in various custom made databases, there is a need for an agreed common format if the transfer of data are to be facilitated between all institutions. The standardisation of collecting data and the transfer processes across different sites requires a commitment to user training, and this is best to be centrally coordinated [57].

If patient information is stored within databases that sit outside a protected hospital intranet system it is possible that this information can be accessed by researchers not directly involved in patient care. It is imperative that the issue of patient privacy is made a priority in the design of database systems and that access to data is restricted to authorised individuals for an intended purpose [59]. This includes security at the network layer, with SSL/TLS (and wireless TLS for mobile devices) encrypting the data transmitted, not opening up the application to the internet itself but rather requiring virtual private network (VPN) access for remote users. Storage and encryption of data is another important security consideration. Furthermore databases need to be housed on a physically secure serve. The system should also have inbuilt logging of user activity to allow for retrospective auditing of the database usage.

There are commercial solutions to both transfer of data and security requirements. An example of this is the Health Level 7 (HL7) international organisation which develops and maintains communication protocols and standards for the healthcare sector across more than 55 countries (http://www.hl7.org).

It is important to be fully aware of and compliant with local regulatory requirements. In regards the conduct of clinical trials in the United States, compliance with FDA guidelines is a legal requirement (Supplementary Table 5). Lastly, patient consent is critical to collection of patient data in any database. Research has shown that patients are willing to participate in research with storage of their treatment data, but want to be consulted first on the use of information from their medical records [60]. The majority of patients were also concerned about secondary uses of their data, particularly for marketing and insurance purposes. Therefore it is important to gain the patient's consent prior to their data being stored in any database and limits set to the use of the data in accordance with the mandate of the consent.

Table 3
Problems and potential solutions.

Problem	Potential solutions
Transfer of data	Create/adopt a common open standard. Hl7 is a commercial common transfer protocol for data in health and could be adopted as the standard of data transfer. Creating a common open standard is an alternative, allowing users of the protocol to determine the message formats.
Security concerns	1) Utilise the appropriate industry level of encryption for transfer and storage of sensitive data. 2) Ensure that the network security prevents internal exploitation. 3) Ensure that the physical storage of the sensitive data are adequately protected. 4) Ensure that use of the system is able to be audited and tracing is available for information accessed.
Regulatory considerations	FDA (USA) as well as local institutional ethics boards for research [61].
Financial barriers	Reduce costs when possible by use of open source software Pooling resources into developing a common standard amongst datum sharing partners, common physical storage units etc. can spread costs as well.

5.4. Conclusion

In conclusion, this systematic review of the published literature relating to the use of databases in the clinical management and research relating to AP, has found a disparate and somewhat haphazard approach. These databases were mostly designed for administrative purposes, and had very limited value to the clinician or researcher. This review should promote wider discussion, collaboration and research towards the adoption of intelligent database systems in AP that will automate collection of data, facilitate multi-centre data collection and with integrated ANNs allow automated analysis of data to support clinical decision-making in real-time.

Conflicts of interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.pan.2013.11.010.

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