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Respiratory decision support systems

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Introduction

Respiratory diseases are considered, in general, as complex conditions, as their initiation and progression are multifactorial and driven by the interaction between genetic factors, comorbidities, environmental exposures, treatments, etc.

Various respiratory conditions, such as asthma, COPD, cystic fibrosis (CF), sleep apnea, or malignant conditions like lung cancer and respiratory infections (influenza or COVID-19) affect many individuals in all age groups. In addition to acute respiratory care, these conditions pose a challenge for the health system resources, which requires careful and efficient management.

Decision-making, including diagnostic, treatment-related, and optimization of procedures and organization, is the core of clinical routine. The digital transformation in health promises to leverage decision-making.

As mentioned in Sutton et al. [68], “A computerized clinical decision support system (CDSS) is intended to improve healthcare delivery by enhancing medical decisions with targeted clinical knowledge, patient information, and other health information.”

Such a system may support clinicians, administrative staff, patients, caregivers, or other health-care providers involved in care, with individualized information specific for each patient and situation that requires a decision, thus helping to make more timely and accurate decisions and to avoid errors or adverse events.

As an example, expert systems (ESs) based on “IF...THEN” rules have been used to implement consistently evidence-based processes, including complex guidelines and protocols. Model-based decision support systems (DSSs) have been used in intensive care unit (ICU) for ventilation support.
Data-driven DSSs have been used when intensive data processing is required, for example, when the decision is heavily based on biosignals and bioimages.

Among the numerous examples, many success stories have been identified, as well as risks and pitfalls. Often criticism against a clinical DSS (CDSS) relates to “Alert fatigue” and clinical burnout [31], which happens when the CDSS overwhelms users with redundant or unimportant information, or unacceptable workflow freezes and burdens.

During the last years, the data-driven economy is being incrementally established, pushing for big data principles employment in digital economy applications in health. Several enabling technologies that play a role in this digital transformation can be identified, which play a role in the evolution of respiratory decision support systems (RDSSs).

Electronic medical records with advanced capabilities and computerized clinical workflows are increasingly adopted, thus increasing the volume of digital data to be considered for decision-making and facilitating the incorporation of CDSSs. These factors, together with the responsibility to deliver value-based care and the pressures for optimal resource use in more and more challenging conditions, make the CDSSs essential tools.

In parallel, connected health technologies (CHTs) can facilitate the patient—professional partnership in decision-making and offer opportunities for incorporating DSS in patient self-management [12]. In the previous years, CHT research was mainly focused on monitoring and measurement information, while the provision of feedback recommendation and prescriptive support in the context of CHT seem to be research priorities in the coming years [45].

The increased availability of health data enables the integrated data analysis (spanning from DNA to protein and metabolism, to physiology and external factors), which can address and lead to a better understanding of a range of phenomena, rather than a narrow symptom-based decision. This approach links to the systems medicine (SM) paradigm that considers the respiratory system as a complex system, and focuses on the interactions between the different components within it, functioning at different levels, and the interaction between organs or systems, e.g., between the cardiovascular and respiratory system in specific conditions [53]. SM and in silico modeling are fundamental pillars of information and knowledge for an RDSS.

Finally, AI’s role in a DSS in respiratory care cannot be overlooked. AI in medicine, both machine learning (ML) and deep learning, shows potential toward improving diagnosis, and support treatment decisions, provided that adequate quantities of data are available. In emergency situations, like the COVID-19 pandemic, AI-based prediction models and RDSS constitute promising solutions toward alleviating the asphyxiating pressure on health systems, provided that their reliability and trustworthiness can be ensured beyond preliminary results.

This chapter aims to provide an overview of the CDSS approaches and enabling technologies in respiratory care. This integrated view of the aspects...
that need to be considered when designing for RDSS includes (a) the continuum of decision between acute and chronic care, (b) the wealth and added value of biomedical data to be employed, and (c) the complementarity of methods to be pipelined or aggregated.

A variety of methodological aspects are discussed, along with RDSS cases in chronic and acute care. Challenges in the maturation of RDSS are identified along with future research directions of interest.

**Overview of the RDSS domain**

A wide range of diseases and conditions implicate the respiratory system and require decision support, spanning in the whole range between acute and chronic care or even transition care.

**Emergency and intensive care**

The emergency COVID-19 pandemic has put pressure on health systems and led to the fast implementation of prediction models, for diagnosing COVID-19 in patients with suspected infection, for predicting hospital admission, for prognosis of diagnosed patients, and for detecting people at risk of becoming infected. As discussed in a recent review [77], preliminary prediction models may prove unreliable, and future high-quality model development and validation are needed, taking into account quality of reporting, risk of bias, and extended performance evaluation.

Currently, the vast majority of widely applied decision support approaches in ICU are limited to basic alarms, which are both unreliable, considering the false alarms, and insufficient. A characteristic effort to improve arrhythmia alerts in ICU was the CINC challenge 2015 [15].

The gap in the efficiency of critical care DSS is highlighted by the alarm fatigue problem [76], raised by a high number of clinical alarms to which the clinical staff is continuously exposed, and thus desensitized. Although this phenomenon is widely observed, it is not accurately measured with direct metrics. In order to reach a higher accuracy and meet the emerging needs, research is turning to more sophisticated methods, including (a) integration of data, (b) complicated calculations, and (c) continuous analysis of waveforms, rather than sparse data.

Some major issues in a respiratory ICU are described below to better sketch the RDSS needs and challenges.

**ARDS diagnosis**

Acute respiratory distress syndrome (ARDS) is a critical condition, with substantial mortality. It is a characteristic case of in-hospital patient deterioration. However, its routine diagnosis remains a challenge, due to the variety of risk factors and etiologies, including the lack of diagnosis support tools and
the gaps in CT image radiomics. It is considered an underdiagnosed condition in ICU [21], which has negative consequences in treatment decisions. Recently, a number of ARDS diagnostic models were proposed, using, for example, routinely collected clinical variables and information from radiology reports [40] for early prediction, or “sniffer” systems that automatically analyze electronic medical record data recognize ARDS in clinical practice [75].

**Mechanical ventilation optimization**

Conflicting clinical goals and competing risks that change dynamically for each ICU patient under mechanical ventilation make its management a complicated task. Overall, the aim is to offer adequate ventilation without creating damage. DSSs may help clinicians find the correct balance when complex decisions need to be made.

Important insights on mechanical ventilation CDSS have been previously discussed [34], using a particular example (Real-time Effort Driven ventilator management [REDvent]) to illustrate the concepts. Overall, the main points highlighted are the need to provide simple and explicit instructions, a transparent knowledge base, to understand the decline of recommendations, and provide a reevaluation and adjustment mechanism.

Pediatric ventilation is a particular case. In an older work [69], the CDSS tools for mechanical ventilation in children are distinguished into two categories. The first category refers to commercial CDSS built into specific ventilators, as proprietary fixed rule systems, lacking mechanisms to modify or adapt the rules or report reasons for disagreement with recommendations. Such systems are likely to gradually show decreased acceptability and efficiency. The second one is about ventilator agnostic tools, focusing on a particular ventilation phase (e.g., initiation or weaning) or ventilation mode (e.g., pressure support). The latter can be closed-loop systems. The effectiveness of pediatric RDSS has been variable with no apparent benefits, and, as also suggested in Hartman’s DSS evaluation of DSS for weaning mechanical ventilation in children, acceptability is low, and recommendations are not often followed [24]. These facts suggest the need for more maturation steps for improvement and broader adoption.

**ARDS treatment**

DSS has been considered among the strategies to improve a protective ARDS treatment, i.e., low tidal volume (LTV) mechanical ventilation [66]. The DSS mainly focuses on customizing electronic health records to provide LTV ventilation reminders or alerts at convenient times (i.e., when the respiratory data page is viewed on patients receiving mechanical ventilation, at the time of initiation or change of a ventilator order) or alerts if ARDS patients received injurious tidal volumes for more than 1 hour. Such approaches tend to be
useful, although still with variable results and low acceptability. Supporting better ARDS recognition can be combined with the support of more advanced ARDS therapies.

**ICU-telemedicine**

In recent years, telemedicine ICU programs have been deployed [11], mainly linking a highly expert (potentially academic) ICU to smaller nonacademic ICUs, for patient monitoring, recognition of complex conditions (e.g., ARDS), and staff education purposes. Such systems were considered promising, but many open issues were pinpointed regarding their cost-effectiveness and the broad deployment applicability.

Such issues can potentially be alleviated based on data analysis and decision support tools. Based on data collection from such networks [18], including a significant number of ICU stays, research is conducted to develop and test new predictive and prescriptive analytical solutions and DSSs, that will help to better coordinate care for critically ill patients, and optimize resources and processes of the critical care telemedicine network. Leveraging telemedicine intensive care units (tele-ICUs) may prove particularly useful in the future, in extreme health conditions, like the COVID-19 pandemic.

**Chronic care**

In chronic care, future digital health systems aim to support predictive, preventive, personalized, and participatory medicine (“P4-medicine”). Decision-making challenges pertain to clinicians, nurses, patients, and caregivers, especially in integrated care settings, including telehealth solutions.

**Lung cancer diagnosis and management**

Lung cancer is among the most common cancers among men and women in the world, as well as a major cause of death. Early-stage detection can improve survival probability, but it is heavily dependent on quantitative assessment of lung nodules by radiologists, which is time-consuming if manually performed. Therefore, trustful automated detection of lung lesions is a need, and a number of studies have focused on solving this problem, mainly in CT imaging modality [47]. The combination of multiple modalities, including ET/CT and pathology images, has recently gained attention [70] for accurate diagnosis and treatment support.

Considering treatment support, different RDSSs have been proposed, specific to cancer types. The review by Ref. [61] studies RDSS for treatment of metastatic non—small cell lung cancer (NSCLC), which predicts overall survival and/or progression-free survival, for the whole group or subgroups. Gaps are identified regarding performance, coverage of the entire treatment spectrum, incorporation of genetic and biological markers, and evidence on toxicity and cost-effectiveness.
COPD and asthma diagnosis and management

Chronic obstructive pulmonary disease (COPD) is a widespread respiratory disease in the aged population, causing chronic airflow limitations, often interlinked with other chronic conditions. Personalized medicine in COPD has been focused in dealing with heterogeneity of disease trajectories, clinical presentation, and response to existing therapies [19]. However, predicting and/or modifying the course of the disease (including exacerbations), and predicting response to specific interventions, are gaining attention [30] but are not yet resolved issues. These unmet needs may be answered via a SM approach, integrating data and phenomena at multiple scales in computational models. Such approaches can set the basis of new advanced RDSS for COPD.

Nurses often run patient management in COPD telemedicine programs, and an RDSS has a role in supporting clinical reasoning and avoiding nursing staff from being overwhelmed by the continuous patient monitoring data flow. In Ref. [2] the DSS was based on a combination of symptoms and measurements, and used a rule-based system to classify a patient as “stable patient” indicating change that need follow-up, and “unstable patient” indicating a severe change or a critical condition. This approach was evaluated in practice as useful for identifying health problems and prioritization. However, deeper clinical information regarding each patient’s health status is needed to fully promote the understanding of health changes and provide more certainty for a decision on actions.

In the case of asthma self-management, the myAirCoach system [35] has been presented. This is a promising system that monitors several physiological, behavioral, and environmental factors, which are further processed and aggregated to provide short-term prediction of asthma control level for daily and real-time personalized patient guidance, and long-term prediction of exacerbation risks, to support clinical decision-making and alert medical personnel [38]. While this monitoring and decision support approach was found to improve asthma control and quality of life, extended validation and evidence are missing.

Obstructive sleep apnea diagnosis and management

Obstructive sleep apnea (OSA) is a highly prevalent but underdiagnosed disease, with a complex pathophysiology. In order to provide a solution for underdiagnosis, a rule-based DSS based on straightforward questions for pediatric OSA detection in primary care is discussed in Ref. [29] as a feasible approach for automating OSA screening and detection.

In recent years, CHTs, including portable and wearable devices, from polygraphy to smartwatches, have been proposed for OSA diagnosis in the home environment, with various quality and accuracy, suggesting the need for an evaluation framework [54]. OSA continues to be investigated, regarding the various physiological traits, clinical presentations, and biomarkers, and research efforts bring more attention to the need for support of tailored and effective treatments [6].
Methods for respiratory DSS

Biomedical data for respiratory DSS

A variety of signal and sensor-based approaches have been developed and deployed in clinical environments and home monitoring schemes toward accessing information of value to an RDSS. These fall under different categories: estimation of breathing rate and content, lung function and structure, biological and clinical data, and intervention/treatment-related data, as well as data related to systems interaction.

Respiratory rhythm and content

Spirometry is a typical test that can assess lung function by measuring the volume of inhaled and exhaled air and exhalation speed, and its values are of diagnostic value according to medical guidelines (e.g., for asthma or COPD). It can be used in a clinical or ambulatory environment, as is nowadays feasible at homecare settings, although the unsupervised use may pose quality issues [14]. Pulmonary function is measured by spirometry via a challenging maximal breathing maneuver, which is not accurate or suitable for long-term unsupervised monitoring.

The respiratory signal can be used for the diagnosis of clinical state or assessment of treatment and recovery, both at clinical/intensive care and home setting. Continuous sensing by wearables strain sensors has been proposed. PPG-derived respiratory frequency is easily measured, but its accuracy depends on the measurement site and breathing pattern [25]. It is best measured at the forehead and finger, respectively, for normal and deep breathing patterns.

SpO2 signal can provide detailed information about blood oxygen level [71]. Hypoxia can be related to chronic lung conditions, including COPD and sleep apnea. A simple SpO2 drop has recently been proposed [58] to early detect COVID-19-related hypoxemia, before the manifestation of more severe symptoms such as shortness of breath. Statistical indices such as the oxygen desaturation index (ODI, number of desaturations per hour) are often used for apnea/hypopnea characterization. Other more sophisticated biosignal analysis methods have been proposed, based on detailed characteristics of desaturation events. Such analysis is vital for the accurate automated classification of OSA, the characterization of events severity, and relation with their clinical status, e.g., prediabetic insulin [55].

As for capnography, this semiperiodic waveform fluctuates between inspiration and expiration and measures how much CO2 a person is exhaling and is typically monitored in intensive care or homecare ventilation. In non-intubated patients, it can be used to assess the pulmonary vessels’ ventilation and perfusion, e.g., for asthma classification with ML and capnograph waveform features [65].
New sensors have been proposed as point-of-care diagnostics. In the review of Ref. [26], approaches are discussed to detect volatile organic compounds (VOCs) as biomarkers for respiratory diseases. Such approaches can identify the VOCs distinctive of several respiratory diseases, including COPD, asthma, lung cancer, pulmonary arterial hypertension (PAH), obstructive sleep apnea syndrome (OSAS), tuberculosis (TB), CF, and pneumoconiosis. The underlying sensing mechanisms involve several innovative techniques, including spectroscopy techniques, nanomaterials, chemiresistors, acoustic sensors, colorimetric sensors. On the other hand, electronic noses (e-noses) can distinguish VOCs based on pattern recognition or specific olfactory fingerprints, and human exhaled breath profiling by e-nose can support screening/diagnosis of respiratory diseases [17].

**Lung function and structure**

Lung sounds (auscultation) and cough have been considered as traditional means for diagnosis [62], as discussed in Chapter 5. Enabled by CHTs [12], the availability of digital lung sounds in broader monitoring conditions has enriched the knowledge and leveraged the use of digital auscultation. Automated lung sound detection is crucial for such analysis [57]. Adventitious sounds have been systematically studied during the last years concerning understanding of exacerbation and postexacerbation recovery, and monitoring of chronic conditions such as COPD across clinical and nonclinical settings. For example, in Ref. [52] it was found that inspiratory crackles seem to persist until 15 days postexacerbation.

In respiratory medicine, imaging is considered as the diagnostic cornerstone (see Chapter 6). A broad spectrum of imaging techniques is available. Chest imaging studies include X-rays, computed tomography (CT), magnetic resonance imaging (MRI), nuclear scanning, ultrasonography, and positron emission tomography (PET). The main modality is still CT, which allows fast and high-resolution assessment of the lung and surrounding structures, e.g., detection of lung nodules. Additionally, MRI and PET are gaining attention with regard to direct functional information, as elaborated in Ref. [41].

As discussed in Chapter 6, electrical impedance tomography (EIT) is a promising, noninvasive, and radiation-free technique with rich information content, applicable in a broad spectrum [20], in intensive and chronic care. EIT has been mostly studied in critical care, as a bedside functional imaging modality for continuous monitoring of lung ventilation and perfusion, mechanical ventilation, and detection of lung ventilation problems [72]. For example, EIT may improve (a) monitoring of lung function during ARDS, (b) assessment of patients’ responses to changes in ventilator settings and mode, and optimize mechanical ventilation settings, (c) detecting complications such as derecruitment and pneumothorax, and (d) providing estimates of perfusion distribution. While such studies have taken place, more extended
clinical validation studies are expected to explore the technology’s full potential and introduce EIT in practice. EIT shows potential in pulmonary function testing in patients with COPD, asthma, and CF in chronic care. Wearable solutions aim to bring chest EIT to home monitoring [13].

**Biological and clinical data**

The EHR is a useful tool to enable the rapid deployment of standardized processes. Beyond usual care, it has also proven an essential tool in extreme cases, as in supporting the clinical needs of a health-care system managing the COVID-19 pandemic.

In Ref. [60] the design and implementation of EHR-based rapid screening processes, laboratory testing, clinical decision support, reporting tools, and patient-facing technology related to COVID-19 outbreak management are discussed. Multiple COVID-19-specific tools were proposed to support outbreak management, including scripted triaging, electronic check-in, standard ordering and documentation, secure messaging, real-time data analytics, and telemedicine capabilities.

Ref. [75] examines six automated ARDS “sniffer” systems and tools that can automatically analyze electronic medical record data to detect ARDS and discusses their role in improving recognition of ARDS in clinical practice. The reported sensitivity for ARDS detection spans a wide range (43%–98%), and so does the positive predictive value (26%–90%), while a potentially high risk of bias was estimated. The need for robust evaluation of ARDS sniffer systems and their impact on clinical practice remains ongoing.

Another work [48] proposes an integrated point-of-care COVID-19 Severity Score. Using clinical data, biomarker measurements of C-reactive protein (CRP), N-terminus pro B type natriuretic peptide (NT-proBNP), myoglobin (MYO), D-dimer, procalcitonin (PCT), creatine kinase-myocardial band (CK-MB), and cardiac troponin I (cTnI) combined in a statistical learning algorithm to predict mortality. Based on this, clinical decision support tools for COVID-19 can prioritize critical care in patients at high risk for adverse outcomes.

**Intervention and treatment related data and interaction with other organs/signals**

In critical care, ventilator data can be of use for smart decisions. In Ref. [39], the continuous ventilation data are used through using ML for the generation of smart alarms, that predict in the short term (next 5 min) the presence of high/low driving pressure of mechanically ventilated patients, therefore suggesting the need for increased/decreased attention and adaptation of ventilation parameters.
Ventilation data together with physiological respiratory parameters can be utilized for tools that support optimizing ventilation, including weaning decisions [53], or minimization of asynchronies [67].

In Ref. [16], rapid learning (Rle) concepts were discussed toward improving treatment decisions. Rle involves reusing clinical routine data to develop models that can predict treatment outcomes, and then clinically applying and evaluating these models via DSSs. The Rle approach in focus deploys a previously developed DSS in a typical clinic for NSCLC patients, and it uses routine care data to validate the system. The prognostic groups are identified based on patient and tumor features, and for each group therapy can be individualized based on the model predictions.

**RDSS enabling technologies**

*Databases and knowledge bases*

A number of respiratory sounds databases have been generated and made available for the training of digital lung auscultation diagnostic support [62]. Lung medical imaging collections can be found at the Cancer Imaging Archive,¹ including data, mainly CT, at different time-points the care pathway, diagnosis, pre/during/posttreatment.

In Ref. [56] a freely available ICU database is described. Although not specific to respiratory care, it can help in new knowledge discovery on the dynamics and system interplay. However, it is not easy to find multiparametric data, temporal data, especially data recorded in home environments. An overview of relevant datasets is available in Table 10.1.

When it comes to knowledge bases, several works are dedicated to generating disease ontologies, mainly of diagnostic value. Ryerson et al. [63] proposes a standardized ontological framework for fibrotic interstitial lung disease, aiming to homogenize the diagnostic classification of patients.

This is also important in domains of emerging knowledge, like COVID-19 [27]. The Coronavirus Infectious Disease Ontology (CIDO) is a community-based ontology that supports coronavirus disease knowledge and data standardization, integration, sharing, and analysis.

The COPD Ontology is a biomedical ontology used to model concepts associated with COPD in routine clinical databases.²

The approach followed by Ref. [36] provides a representation of semantically enriched EHR data for COPD and comorbidities, based on an OWL ontology built upon HL7 FHIR resources, that can also support SPIN rules and constraints.

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¹ [https://www.cancerimagingarchive.net/](https://www.cancerimagingarchive.net/).
² [https://bioportal.bioontology.org/ontologies/COPDO/?p=summary].
A deeper understanding of the respiratory phenomena can be of use in a more personalized RDSS approach. Systems biology or SM is an approach complementary to the classic reductionist approach followed in medicine that focuses on the interactions between the different components within one organizational level (genome, transcriptome, proteome) and among levels. SM [9] contributes to the interpretation and understanding of the pathogenesis and pathophysiology, biomarker discovery, and design of innovative therapeutic targets. This is very relevant in the case of respiratory diseases, as they are generally related to the interaction of multiple factors at different levels. Such opportunities for the adoption of SM approaches in COPD management, focusing on proteomics and metabolomics, are proposed in Ref. [44]. As suggested, SM approaches can be incorporated in an RDSS, and support the identification of disease subclusters, as well as the selection of effective therapies.

TABLE 10.1 Example datasets for AI model training for RDSS.

| Data                        | Description                                                                 | References                                                                 |
|-----------------------------|-----------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Respiratory sounds          | COPD, pneumonia, Bronchiectasis, Bronchiolitis, Upper/Lower respiratory Tract infection, healthy | https://bhichallenge.med.auth.gr/                                           |
| Chest imaging               | Cancer Pneumonia COVID-19                                                   | https://luna16.grand-challenge.org/                                         |
|                             |                                                                             | https://www.cancerimagingarchive.net/                                      |
|                             |                                                                             | https://www.kaggle.com/paultimothymooney/chest-xray-pneumonia              |
|                             |                                                                             | https://bimcv.cipf.es/bimcv-projects/bimcv-covid19/                         |
|                             |                                                                             | https://github.com/ieee8023/covid-chestxray-dataset                         |
| ICU/ventilation             | ICU patients including vital signs, ventilation data, and other treatments and events | https://eicu-crd.mit.edu/                                                   |
|                             |                                                                             | https://github.com/AmsterdamUMC/AmsterdamUMCdb                            |
| Biosignals                  | OSA                                                                         | https://physionet.org/content/ucddb/                                       |
|                             |                                                                             | https://physionet.org/content/apnea-ecg/                                   |
|                             |                                                                             | https://physionet.org/content/mimic3wdb-matched/1.0/                       |
| Biological (-omics)         | Cancer Chronic                                                              | https://www.cbioportal.org/                                                |
|                             |                                                                             | http://pulmondb.liigh.unam.mx/                                             |
In a recent work [74], a comprehensive COVID-19 network (CovMul-Net19) is proposed. It contains all available known interactions involving SARS-CoV-2 proteins, the related diseases and symptoms, and compounds that can potentially target them. While not a DSS, it can be considered a knowledge tool that can support educated treatment decisions, especially in view of a precision medicine approach.

A precision medicine approach requires systems-level understanding, integrating phenomena at multiple scales, ensuring diagnosis and treatment support in an individualized manner. In silico modeling enables the generation of mechanistic hypotheses using patient-specific computational models that incorporate a unique patient’s profile (omics, physiological, and anatomical), and can study treatment strategies. In Ref. [33], following this paradigm, an agent-based, asthmatic virtual patient is described that predicted the impact of multiple drug pharmacodynamics at the patient level, paving the way for personalized RDSS.

**Connected health technologies in RDSS**

The evolution of CHT, including sensors, mobile systems, and cloud computing, has allowed the extension of services and decision-making in the whole continuum between daily life at home, clinical setting, and acute care.

In Ref. [37], the application of CDSSs in a tele-ICU is considered. The use of multiple data streams and cloud computing would be basic components of a tele-ICU, toward supporting the analysis, management, and decision support of multiple remote units. ML algorithms are expected to have an important role as an integral part of tele-ICU CDSS. Such systems are expected to capitalize and grow upon the big volumes of data generated and made available by tele-ICU systems. When policies for sharing data are in place, the higher data availability can be exploited for better learning in ML/AI-based solutions.

With respect to telehealth and self-management of chronic respiratory conditions, RDSS can offer automated treatment advice to the chronic patient without a health-care professional’s interference. This approach is presented in Ref. [5], concerning COPD self-management of symptom worsening and exacerbation, based on 12 symptom-related yes/no questions and the measurement of SpO₂, forced expiratory volume in one second (FEV₁), and body temperature. The automated treatment advice is based on expert knowledge and Bayesian network modeling. The system was validated and showed high sensitivity and negative predictive value, and in many cases provided patients with useful advice for day-to-day symptom management.

**DSS technology**

DSSs can follow a rule-based approach, a model-based approach to optimize a specific treatment, or a data-driven approach.
Model-based DSS

Mechanistic models, including compartmental models, can simulate at physiological organ level, the lung function, the respiratory function, or some aspect of it. Model parameters can be fine-tuned to the individual patient, by fitting the models to real measurements and thus estimating optimal model parameters. The ’what-if’ scenarios can be explored via simulation, to support decisions. Both open-loop and closed-loop approaches can be supported.

In Ref. [32], a characteristic computerized model-based DSS is presented and evaluated. It offers advice on inspired oxygen fraction, tidal volume, and respiratory frequency, with personalized parameters. It can automatically provide advice about the ventilation strategy with minimal risks. It is based on physiological models simulating the effect of ventilation strategies and penalty scores to increasing the risk for various adverse effects, e.g., hypoxemia, or acidosis/alkalosis. While such approaches can be valuable, providing accurate and robust advice, it is always important to recognize the model assumptions and limitations, for example, patient parameters in transitional status.

Computerized guidelines and rule-based/expert systems as RDSS

The main advantage of this category of approaches is the incorporation of existing knowledge, interpretability of decisions, and potential applicability in low computational resource settings, for example, in primary care or mobile health settings.

Several technical approaches are applicable. Drools3 is a Business Rules Management System (BRMS) solution. The semantic knowledge bases can make use of Semantic Web Rule Language (SWRL), or Owl reasoners Jena4, Hermit,5 RDfox.6 Several open-source python-based projects can also be of interest, as lightweight options: like experta7, or durable_rules8.

ESs have been considered for chronic diseases screening. In Ref. [7] the different pulmonary diseases that include persistent obstruction of lower airways are considered, under the umbrella term chronic obstructive lung disease (COLD), like chronic bronchitis and emphysema, and specific asthma patterns, all of them often underdiagnosed, especially in primary care. An ES was proposed and validated, aiming at COLD diagnosis support, based on symptoms and standard measurements, and was found as a safe and robust supporting tool for COLD diagnosis in primary care settings.

3. https://www.drools.org/.
4. https://jena.apache.org/.
5. http://www.hermite-reasoner.com/.
6. https://www.oxfordsemantic.tech/.
7. https://github.com/nilp0inter/experta.
8. https://github.com/jruizgit/rules.
In Ref. [1], asthma and COPD are considered as major chronic diseases, excessively underdiagnosed. An expert diagnostic system was proposed that can differentiate among patients with asthma, COPD, or a normal lung function based on measurements of lung function and information regarding patient’s symptoms. Data from 3657 patients were used to build the system and then independently verified using data from 1650 patients. The system shows a high accuracy for all three classes, which contributed to a 49.23% decrease in demand for conducting additional tests, therefore decreasing financial cost.

Concerning computerized clinical guidelines, a characteristic example is the hybrid system Lung Cancer Assistant that includes guideline rule—based recommendations (implemented with the LUCADA lung cancer ontology) and a probabilistic DSS based on a Bayesian network trained on the English Lung Cancer Audit Database, to aid clinicians achieve more informed treatment selection decisions [64].

As already stated by Luger and Stubblefield [46], typical ESs present some core “deficiencies” They do not include necessarily in-depth knowledge of the domain, in the sense that they cannot explain the underlying mechanisms. They cannot learn from experience to continue evolving. They are rigid, in the sense that they function only in problems contained in their knowledge bases.

**ML/AI and data-driven RDSS**

AI, and ML as part of it, follows the data-driven research paradigm that capitalizes on the availability of large nonhumanly processable datasets, to generate models of diagnostic or predictive value, to support health-care professionals in making clinical decisions [49]. In an RDSS, these ideas may apply, for example, to chronic conditions with regard to diagnosis, staging, exacerbations, and survival. Such models are particularly useful in cases of gray zones, or cases where current knowledge and evidence do not support thoroughly decision-making, allowing for ML approaches to improve clinical decisions and even minimize patient risk. A data-driven RDSS can involve one or more of the following technologies:

**A.** Classic approaches, which involve: (i) analysis of respiratory data [50], e.g., wavelet analysis for respiratory sound analysis, (ii) selection of the most informative features, (iii) employment of features in ML-based models (e.g., random forest or support vector machine classifiers), and potentially rule-based systems that employ as high-level concepts the diagnostic outcomes of ML models.

**B.** Deep learning, with a variety of neural network architectures (with CNNs and LSTMs among the most typical ones) and applications in images, biosignals, text recognition, generation of synthetic data [22,23].

**C.** Transfer learning, which literally means that experience gained from one domain can be transferred to other domains, and fine-tune part of the
model for the specific problem. This is typically used for the detection of structures in imaging, e.g., lymph nodes [80] and for the classification of “objects,” and is usually based on previously known and successful architectures (e.g., VGG16) for which pretrained models are available for problem-specific fine-tuning.

**D.** Reinforcement learning (RL) is a goal-oriented learning method to solve complicated control problems. It uses a state at each time, an action to change the state, a transition probability, and a reward function per state-action. Based on that, it develops a policy, a set of rules for taking actions [43].

Some characteristic cases are discussed below.

**New approaches improving scoring and classification**

In Ref. [51], an ML method using a shallow neural network is proposed to accurately estimate apnea–hypopnea index (AHI) and ODI using only the continuous measurement of blood oxygen saturation signal (SpO$_2$). This improved estimation with affordable home-measured means can open the way for a more affordable screening of OSA and can help address underdiagnosis.

As clinical information systems may include errors, incorrect labels, missing values, ML systems evolve to cope with these issues. For example, in Ref. [59], an algorithm to detect ARDS is presented that accounts for the uncertainty of training labels existing in real life records.

**AI in pandemics and emergency**

AI methods have been proposed during the COVID-19 pandemic for identification of positive subjects, treatment, prognosis, and monitoring.

In Ref. [8], different CNN architectures of different depth are compared, as regards five chest related pathologies (the CheXpert dataset) and different types of pneumonia (toward distinguishing the COVID-19-related pneumonia). Interestingly, both shallow networks with a low need for resources and deeper and more complex ones can achieve excellent classification performances.

In Ref. [10] review, it is found that AI was applied to COVID-19 in four areas: diagnosis, public health, clinical decision-making, and therapeutics. However, several methodological and evaluation issues were identified in the proposed methods, including insufficient data for model creation and internal/external validation, as well as ethical, trustful, and efficient use.

**Treatment optimization and reinforcement learning**

In Ref. [43] survey on RL for clinical decision support in critical care, the RL-based decision support was applied to optimize the choice and dose of medications, the timing of interventions (e.g., ventilation), and for personalization
of laboratory values. Several challenges were identified, regarding RL system design (e.g., actions), realistic evaluation metrics (e.g., alternatives to mortality), model choice, and extent of realistic validation.

A characteristic deep reinforcement learning (DRL) pipeline for treatment-related RDSS is described in Ref. [73]. It aims for automated dose adaptation, and specifically automated radiation adaptation protocols for NSCLC patients, to maximize local tumor control at reduced rates of radiation pneumonitis. It includes three components: (a) a generative adversarial network (GAN) to create synthetic data for training from a relatively limited sample size, (b) a radiotherapy model RAE based on a deep neural network (DNN) to enable simulation of transition probabilities between its states when making decisions for adaptation of personalized radiotherapy treatment courses, and (c) a deep Q-network (DQN) for choosing the optimal dose. Careful validation of such systems is critical to their success and acceptance.

A detailed RDSS example

This section presents a generic RDSS framework applicable in Chronic Care that includes a galaxy of tools spanning between primary care, secondary care, and continuous monitoring. Table 10.2 summarizes this framework.

| Step                        | Need                                                                 | RDSS opportunities                                                                 |
|-----------------------------|----------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Primary care screening      | Early diagnosis, to address underdiagnosed cases, manageable and affordable resources | AI/ML model based on daily life data (signals and symptoms) and mobile technology—results to be shared with primary care doctor for shared decisions Tools for the primary care doctor to easily screen patients |
| Expert diagnosis and treatment | Precision diagnosis and personalized treatment, not contradicting but enhancing existing guidelines | ML to combine biological and physiological data, recognize disease subtype, and suggest tailored treatment DSS for respiratory and comorbidity treatment |
| Continuous monitoring       | Support patient in lifestyle changes and adherence and self-care support Manage transitions from/to secondary care Manage comorbidity | DSS using multiple sensors for daily lifestyle planning and adaptation DSS for symptom management—including guidelines Detect deterioration and guide patient—combine AI and knowledge systems AI/DSS for guiding patient in the transition from/to hospitalization |
An example is further elaborated with regard to OSA, inspired by the work of [6]. Primary care screening for OSA is essential, as it is a widely prevalent and highly underdiagnosed condition. Its early diagnosis can help in better management and will positively impact interrelated conditions, including obesity, cardiometabolic syndromes, as well as other respiratory conditions. The primary care RDSS can have two legs for diagnosis:

(a) Use electronic symptom-based screening tools, customized per age/gender, in the general population, administered via mobile health (mhealth) apps, and

(b) When opted-in, combine with affordable home-based sensors (e.g., wearable oximeter, activity, sound, heart rate) and ML to detect possible apnea.

Accurate diagnosis in secondary care can benefit from an RDSS that follows a personalized approach to OSA. This must consider the sparsity of sleep labs, and the difficulty of sleep lab exam. Thus, OSA diagnosis will need to employ, when acceptable, home-based recordings of the necessary sleep study type.

The diagnostic strategy can incorporate:

(a) An improved severity/stratification strategy, beyond AHI [6], based on day and night measurements and AI models,

(b) Determination of the OSA endotype, in terms of mechanisms underlying the condition (e.g., pharyngeal collapsibility, loop gain, arousal threshold) based on standard sleep measurements, wearable sensors, blood biomarkers, and AI methods [42], toward personalized medicine,

(c) Determination of OSA phenotypes or disease clusters [78] in terms of symptoms, comorbidities, lifestyle, and

(d) DSS to decide on treatment and secondary prevention based on “endophenotype,” as CPAP is not the treatment for all. Data-driven prediction of treatment adherence can be considered.

As OSA patients can benefit in the long term from lifestyle changes, a patient DSS to support and guide patients in achieving and maintaining healthy habits (sleep, activity), as well as adhere to treatment, is also part of the solution. The DSS will also detect deteriorations of OSA symptoms and physiology, together with other interrelated comorbid conditions like COPD, including causal information, and will guide patients accordingly for self-management or transition to other health-care services and treatments.

**Discussion: unmet needs and challenges for the future**

Much attention has been drawn both to the promises and perils of CDSSs during the past decades. Despite the attention of both technical researchers and clinical practitioners, the adoption of such systems has been sparse. Among
the main challenges identified in the CDSS in previous decades [3] was the technical complexity in accessing and integrating the data from diverse sources and in managing large datasets in a clinical context, the conceptual complexity and the wide range of problems to be dealt with (deterioration, optimization of intervention) in a real clinical environment, the lack of in-depth understanding of complex disease pathophysiology, which would enable building solid models, and the limitations related to regulatory issues [4].

Some of these challenges are present also in a respiratory DSS, due to: (a) the complex interaction of respiratory system with circulatory and other main systems, (b) the respiratory system decision-making spans in many directions and time scales, in acute and chronic care, and (c) a wealth of informative measurements and signals implicated.

In recent years, the concept of personalized medicine has gained popularity among respiratory clinicians, which implies an effort to address some of the fundamental challenges posed above, i.e., address the complexity and the multiscale nature of respiratory phenomena.

Emerging technologies in wearable sensors, -omics analysis, big data management, and computing, as well as AI methods, can leverage the RDSS research and development, but in acute and chronic care. In this direction, several issues must be considered:

**Challenges for AI in RDSS.** For AI methods to become trustworthy and adopted as part of routine RDSS, decision explainability, causability, and interpretability concepts must be incorporated [28].

**Level of personalization in decisions.** On the way to prediction medicine, the role of multiple sources of information in decision models must be recognized. This also has as a prerequisite the availability of rich and unbiased multiparametric data, which suggest the generation of integrated resources and data repositories as a necessary step. A synergetic use of clinical respiratory guidelines and AI, with the user in the loop, can be the basis for personalized decisions.

**RDSS for new organizational schemes and services.** RDSS ideas have been developing for critical care, or clinical setting. As models of care are being reorganized toward more efficient schemes, new RDSS tools need to be conceived developed, or integrated, to cover chronic care self-management services, tele-ICU, and transition care.

**RDSS as part of a learning health system.** The ability of an RDSS to learn from its mistakes [79] and improve its function, as well as improve its experience from ongoing use and data collection (i.e., via retraining), would be a valuable direction for development. This aspect can improve robust use in a real-life environment and can place an RDSS as a part of a learning health system, in which new knowledge gets embedded in daily practice and continuously improves systems and care.
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