COVID-19 and Oxygen: Selecting Supply Options in LMICs that Balance Immediate Needs with Long-Term Cost-Effectiveness

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Medical oxygen therapy is a core part of the treatment of patients with severe COVID-19. Particularly in low- and middle-income countries (LMICs), where supplies are likely to be inadequate in the face of the pandemic, boosting access to medical oxygen can save lives.

Much of the policy debate regarding COVID-19 medical equipment focuses on the question of which form of patient respiratory support is effective in low-resource settings. However, irrespective of the specific form of respiratory support used, the long-term and cost-effective functioning of all forms of oxygen therapy requires an appropriate system to supply oxygen to hospitals.

The sustainable and affordable supply of medical oxygen to hospitals has long been neglected in health services, especially in LMICs. With the increased attention to oxygen supply brought by COVID-19, there is an opportunity to build adequate infrastructure to deliver oxygen in a systematic manner.

AN OVERVIEW HOSPITAL OXYGEN SUPPLY SYSTEMS

Oxygen can be supplied to hospitals through a variety of methods, such as tanks of compressed liquid oxygen (LOX), compressed gas cylinders, on-site pressure swing adsorption (PSA) plants, and oxygen concentrators. Careful consideration of the context—including health system infrastructure, skilled health care work force, and available financing—should go into identifying the most appropriate option. Beyond the specific source of oxygen selected, some forms of oxygen supply also require particular products, such as flow splitters, flow meters, tubing, nasal prongs, and face masks. Further, oxygen therapy is used in coordination with pulse oximeters or patient monitors, resuscitators, suction devices, ventilators, and other tools essential for intubation. Oxygen delivery solutions vary in flow rates and pressure, and it is important to ensure compatibility among the various components of the respiratory care system.

OXYGEN SUPPLY IN HIGH-INCOME COUNTRIES

Many high-income countries such as Italy, France, Spain, and the United States have been hit hard by COVID-19. In considering how to boost access to medical oxygen in LMICs, it may be useful to start by...
looking at how high-income countries have coped with managing reliable oxygen supply, both during COVID and in normal times.

Large hospitals in the United States, the EU, China, and many middle-income countries have onsite liquid oxygen tanks that supply oxygen to the entire hospital. Most hospitals keep some compressed oxygen cylinders as backup in case the main tank stops working. Liquid oxygen to hospitals is provided by medical oxygen manufacturers such as Air Liquide, Linde Group (including Praxair), Nippon Gases.

At the peak of COVID-19 cases in China, local subsidiaries of liquid oxygen producers such as Air Liquide, Praxair, Linde, and other large industrial gas suppliers were central to ensuring reliable access to oxygen. As COVID-19 outbreaks spread globally, other countries struggled to ramp up production of bulk oxygen to meet patient needs. In parts of Italy, oxygen consumption tripled, forcing considerable increases in production and installation of bulk storage tanks onsite at designated COVID-19 treatment facilities. LOX suppliers have rapidly created new ways to ensure sufficient supplies of oxygen to existing and large makeshift hospitals in the EU, UK, and US.

While global production rates have so far met the unprecedented growth in demand (see Figure 1), utilization of oxygen at this rate places a strain on the supply system to ensure timely resupply.

**Figure 1. Increases in oxygen demand in the US and EU due to COVID-19**

![Image of Figure 1](source)

COVID-19 also accelerated the need for equipment maintenance and careful performance monitoring of system components, including oxygen conversion systems (e.g., ambient air vaporizer that converts liquid oxygen to gas oxygen) within health facilities that manage the flow of gas oxygen di-
rect to patients through bedside piping outlets. In two New York hospitals, the unusual consequence of peak liquid oxygen use led to frozen coils and the inability to manage the flow rate of this life sustaining commodity.

REGULATORY STANDARDS FOR OXYGEN AND OXYGEN EQUIPMENT

Patient safety and risk minimization are the top priorities in selecting appropriate medical equipment. Regulatory pathways for oxygen and related equipment vary considerably from one country to another.

In the United States, medical gases such as oxygen are regulated as finished pharmaceuticals by the FDA, requiring “current good manufacturing practices” that ensure drug safety, identity, strength, quality, and purity. Both air separation units (ASUs) that produce liquid oxygen in bulk quantities for medical and industrial gas applications and transfillers that take bulk oxygen (liquid or gas) and transfer it to a smaller container are regulated by the FDA. Oxygen concentrators, by contrast, are not considered to be medical gas manufacturing equipment and are instead regulated as a medical device under section 510(k) of the Federal Food, Drug, and Cosmetics Act, and is typically classified as a moderate risk (or class II) in the United States.

The regulatory infrastructure for medical devices in many low- and middle-income countries is still relatively nascent. In many countries, there is no designated regulatory authority to monitor medical devices. Often, the national drug authority or ministry of health will serve in this role. Some countries develop import/export requirements to ensure some degree of quality—often using reliance on or recognition of approval from a stringent regulatory authority, such as CE mark or a US 510(k) filing, as a proxy. In these cases, there is often no post-market surveillance.

CONSIDERATIONS IN SELECTING OXYGEN SUPPLY IN LMICS

To select an oxygen delivery solution that is most appropriate for a given country or specific hospitals in a country, it is important to understand the common challenges to reliable access.

Under normal circumstances, a mix of oxygen production and storage devices would be recommended to deliver oxygen to patients. The same is true for COVID-19 response planning. No single oxygen delivery solution will suffice for the range of treatment approaches required. For example, the commonly used 5 liter per minute (lpm) oxygen concentrator may be appropriate for treating some severe COVID-19 cases but would not be appropriate for many critically ill patients. Therefore, a nuanced approach to supply planning and procurement that accounts for the different oxygen flow rate requirements is recommended. Figure 2 (from WHO oxygen guide for COVID-19) provides an overview of the different oxygen sources and storage options.

Liquid oxygen tanks: Large hospitals can be equipped with bulk liquid oxygen tanks that are filled periodically with oxygen generated at a plant. This can be a cost-effective option if there are existing LOX plants in the area and delivery logistics can be managed by the LOX producer in a robust manner. LOX supply relies on uninterrupted transport from the plant to the hospital site and may not be feasible or cost-effective for health facilities located in regions with poor transport infrastructure. Liquid oxygen tanks also present the risk of flammability and explosion if adequate ventilation, well-maintained piping and auxiliary equipment, and trained professionals are not available.
PSA oxygen plant: At larger health facilities, an on-site pressure swing adsorption (PSA) oxygen plant can be installed. Such on-site PSA plants can also be combined with an oxygen compressor in order to fill oxygen cylinders for distribution within the same health facility and other smaller health facilities. An on-site PSA plant requires a higher capital investment and comes with considerable maintenance needs. While regular PSA plants require longer time to commission/install, many modular skid-mounted, PSA plants are now available that can be installed relatively quickly.

Oxygen cylinders: Compressed oxygen cylinders supplied periodically by an oxygen generation plant (ASU with conversion or PSA with oxygen compressor) are commonly viewed as a cost-effective oxygen source. However, cylinder rental fees and delivery costs add up substantially over time. Delivering oxygen via cylinders requires a pool of cylinders certified for medical oxygen service and complex logistics to transport cylinders and returning and reprocessing used cylinders. In times of emergency, such as the lockdowns now in place in many countries, oxygen cylinder delivery may face greater risks of disruption. Cylinders also require the government or private hospital to pay the suppliers on a routine basis, perhaps monthly or after each delivery invoice. Non-payment or tardy payments can lead suppliers to delay or stop deliveries. Because oxygen cylinders are frequently moved between production sites, storage depots, health facility stores, and eventually to a patient’s bedside, they create injury risks due to fall or rupture.

Oxygen concentrators: Because they are self-contained, quick to install, and once installed are not dependent on periodic resupply, oxygen concentrators have been the focus of a lot of attention during the COVID-19 pandemic. However, oxygen concentrators are not without their own flaws, and such a hasty focus on this delivery approach—without the systems to support their continued functionality (e.g., reliable power, training, maintenance)—may result in poor sustainability long-term. Patient safety requires an uninterrupted supply of oxygen. Hospitals in many LMICs have power cuts regularly. Concentrators generally do not have backup batteries. A power cut of any substantial duration will disrupt oxygen therapy and can be fatal for patients receiving oxygen via a concentrator. Therefore, concentrators should only be selected as the source of oxygen when they are accompanied by a reliable 24/7 power supply, whether a self-switching standby generator, a solar power inverter and battery, or a back-up battery.
<table>
<thead>
<tr>
<th>Description</th>
<th>Cylinders</th>
<th>Concentrators (PSA)</th>
<th>Oxygen plant (PSA)</th>
<th>Liquid Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>A refillable cylindrical storage vessel used to store and transport oxygen in compressed gas form. Cylinders are refilled at a gas generating plant and thus require transportation to and from the plant.</td>
<td>A self-contained, electrically powered medical device designed to concentrate oxygen from ambient air, using PSA technology.</td>
<td>An onsite oxygen generating system using PSA technology, which supplies high-pressure oxygen throughout a facility via a central pipeline system, or via cylinders refilled by the plant.</td>
<td>Bulk liquid oxygen generated offsite and stored in a large tank and supplied throughout a health facility pipeline system. Tank requires refilling by liquid oxygen supplier.</td>
</tr>
<tr>
<td><strong>Clinical application and/or use case</strong></td>
<td>Can be used for all oxygen needs, including high-pressure supply and in facilities where power supply is intermittent or unreliable. Also used for ambulatory service or patient transport. Used as a backup for other systems</td>
<td>Used to deliver oxygen at the bedside or within close proximity to patient areas. A single concentrator can service several beds with the use of a flowmeter stand to split output flow.</td>
<td>Can be used for all oxygen needs, including high-pressure supply</td>
<td>Can be used for all oxygen needs, including high-pressure supply and in facilities where power supply is intermittent or unreliable.</td>
</tr>
<tr>
<td><strong>Distribution mechanism</strong></td>
<td>Connected to manifold of central/sub-central pipeline distribution system, or directly connected to patient with flowmeter and tubing.</td>
<td>Direct to patient with tubing or through a flowmeter stand.</td>
<td>Central/sub-central pipeline distribution system, or can be used to refill cylinders that can be connected to manifold systems in the facility.</td>
<td>Central pipeline distribution system.</td>
</tr>
<tr>
<td><strong>Electricity requirement</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Maintenance requirement</strong></td>
<td>Limited maintenance required by trained technicians.</td>
<td>Moderate maintenance required by trained technicians, who could be in-house.</td>
<td>Significant maintenance of system and piping required by highly trained technicians and engineers, can be provided as part of contract.</td>
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</tr>
<tr>
<td><strong>User care</strong></td>
<td>Moderate: regular checks of fittings and connections, regular checks of oxygen levels, cleaning exterior.</td>
<td>Moderate: cleaning of filters and device exterior.</td>
<td>Minimal; at terminal unit only.</td>
<td>Minimal; at terminal unit only.</td>
</tr>
<tr>
<td><strong>Merits</strong></td>
<td>− No power source.</td>
<td>− Continuous oxygen supply (if power available) at low running cost.</td>
<td>− Can be cost-effective for large facilities.</td>
<td>− 99% oxygen obtained.</td>
</tr>
</tbody>
</table>

In addition to selecting the right mix of oxygen sources for a given context, it is also important to build redundancy and/or excess supply and backup sources in case of supply chain failure or device malfunction.

**PLANNING FOR OXYGEN SUPPLY FOR COVID-19 AND AFTER**

An effective response will include a combination of short-term, rapidly available supply sources where surge demand is anticipated and long-term infrastructure development such that oxygen supply is integrated throughout the health system.

**Immediate planning**

A significant number of ASUs and PSA plants are already installed throughout LMICs. Medical oxygen typically makes up a small portion of the total volume that can be produced at ASUs. Given that the process is the same to produce oxygen for industrial and for medical uses at an ASU, mapping available capacity and engaging with private firms to procure larger shares of the production capacity is perhaps the quickest opportunity for securing immediate medical oxygen supply. For PSA plants, transitioning capacity from industrial to medical oxygen production is more complex and would require further investments to purify the air for production given many industrial PSA plants are co-located at dusty mining facilities. For both, oxygen cylinders and/or tanks, a rapid increase in the number of cylinders together with reliable distribution and transport logistics may be required.

In addition to reallocation of existing large-scale oxygen production in-country or regionally, countries can explore immediate opportunities to bring non-functional oxygen concentrators back online through targeted maintenance and spare parts procurement.

Matching oxygen delivery sources to treatment use cases is an essential part of supply planning. Concentrators already deployed in most LMICs are likely to be 5 lpm models and so they may be allocated to COVID-19 cases that require routine oxygen therapy. Whereas compressed oxygen cylinders and/or tanks with direct piping may be regulated to support patient ventilation. When analyzing available oxygen capacity, it is crucial to take into account oxygen required for routine health services.

Once available supply is identified, countries will need to quantify shortfalls in access. Filling these gaps should consider equipment that requires minimal upfront installation and is familiar to staff to operate and/or training may be easily conducted for safe use. In most countries this will mean oxygen concentrators and additional oxygen cylinders.

**Intermediate planning**

Like concentrators, skid-mounted PSA plants are another turnkey solution that countries can employ to ramp up oxygen production. While the lead time is slightly longer than oxygen concentrators, it is far shorter than importing individual PSA plant parts and installing them from the ground up. These plants offer the advantages of larger volume production as well as the flexibility to reallocate that production post-COVID-19 demand surges. These plants can be connected to facilities with installed copper piping or utilized with flexible piping lines that can be connected and disconnected with the plant. They can also be paired with an oxygen compressor for cylinder filling capabilities which allow the flexibility to move cylinders within a large facility or distribute cylinders to neighboring health facilities. Effective technical staff for operation and maintenance, adequate spare parts supply,
an identified and pre-contracted repair and maintenance facility are important prerequisites for successful functioning of concentrators and PSA plants.

In addition to larger-scale production, large-scale storage solutions may also prove useful in the intermediate term. Liquid oxygen tanks, particularly in settings where oxygen demand is consistently high (as in referral facilities), are a cost-effective way to supply oxygen in bulk. Tanks are piped directly to facilities and routinely filled by suppliers according to terms laid out in service agreements. It is important to note that off-gassing can be considerable (3 percent per day) and so long-term storage at more remote facilities may not prove cost effective.

**Long-term planning**

Once the initial peak in COVID-19 cases subsides, it will be important for health systems to evaluate available supply again and consider more equitable redeployment of equipment across the country. Supply solutions should also be considered for any remaining gaps in access. Constraints in global manufacturing production are likely to have subsided and so product variants and feature options will increase. Time-intensive capacity investments including installation of larger scale PSA plants and/or regional ASUs may be deployed effectively during this timeframe. Regardless of the oxygen delivery source, all technologies will require maintenance and spare parts and consumable replenishment. Systems that enable efficient asset management and continued training for both biomedical engineers and health care staff will play an essential role in sustained access and utilization.

**COVID-19 AS A WAKE-UP CALL FOR OXYGEN SUPPLY**

Oxygen access has been a long-neglected element of health services, despite its essential role in the treatment of numerous conditions. COVID-19 has created an opportunity for substantial investment in this essential therapy. Robust responses will include a balance of both short- and long-term oxygen supply solutions. Planning, selection, and procurement of oxygen equipment requires experienced biomedical engineers and local clinical staff to combine knowledge of the local context, equipment ecosystem, and clinical guidelines to select the equipment that can best serve the needs for COVID-19 and build long-term oxygen supply capacity. Regardless of the oxygen delivery approach employed, systematic improvements to maintenance, supply chains for cylinder resupply, device spare parts, and associated accessories/consumables, and training for appropriate use, will remain essential.
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