Limited options for low-global-warming-potential refrigerants

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Hydrofluorocarbons, currently used as refrigerants in air-conditioning systems, are potent greenhouse gases, and their contribution to climate change is projected to increase. Future use of the hydrofluorocarbons will be phased down and, thus replacement fluids must be found. Here we show that only a few pure fluids possess the combination of chemical, environmental, thermodynamic, and safety properties necessary for a refrigerant and that these fluids are at least slightly flammable. We search for replacements by applying screening criteria to a comprehensive chemical database. For the fluids passing the thermodynamic and environmental screens (critical temperature and global warming potential), we simulate performance in small air-conditioning systems, including optimization of the heat exchangers. We show that the efficiency-versus-capacity trade-off that exists in an ideal analysis disappears when a more realistic system is considered. The maximum efficiency occurs at a relatively high volumetric refrigeration capacity, but there are few fluids in this range.
Hydrofluorocarbons (HFCs), which are currently used as refrigerants in air-conditioning (AC) systems, are potent greenhouse gases, with high values of global warming potential (GWP). Although the present contribution of the HFCs to climate change is small, their contribution is projected to rapidly increase under various scenarios. A phase-down of HFCs is mandated in the European Union, and at an October 2016 meeting of the parties to Montreal Protocol, a global phase-down was negotiated. Thus replacement fluids must be found.

A refrigerant is the essential working fluid in a vapour-compression refrigeration cycle; it absorbs heat at a relatively low temperature in the evaporator (for example, the cooling coil in an air conditioner) and releases it at a higher temperature in the condenser (for example, the outside coil). HFC refrigerants were commercialized in the 1990s as replacements for the ozone-depleting chlorofluorocarbons and hydrochlorofluorocarbons. The HFCs are now the dominant refrigerants in new refrigeration, AC and heat-pump equipment. In particular, HFCs are used in small AC systems known as unitary systems: self-contained systems comprising a positive-displacement compressor, condenser, evaporator, and associated fans and controls. R-410A (a blend of HFCs) is currently the dominant refrigerant in such systems. R-22 (a hydrochlorofluorocarbon) was most commonly used prior to R-410A, and it is still commonly used in developing countries. (We use the shorthand nomenclature for these compounds specified in ANSI/ASHRAE Standard 34 (ref. 4); ISO Standard 817 (ref. 5) is substantially equivalent.)

A viable low-GWP candidate must possess a number of other attributes, including zero (or very low) ozone-depletion potential, chemical stability within the refrigeration system, thermodynamic properties matched to the refrigeration application, low toxicity and other practical considerations, such as compatibility with the materials of construction. Existing safety codes require nonflammable refrigerants for many applications, but that requirement is being reconsidered.

This work presents the results of a comprehensive search for the best single-component, low-GWP replacement fluids. We search for suitable replacement fluids by applying thermodynamic and environmental screening criteria to a comprehensive chemical database. The fluids passing these screens are then simulated in an AC system, with the calculated volumetric refrigeration capacity and energy efficiency serving as additional screens. We conclude that only a limited number of fluids possess the combination of chemical, environmental, thermodynamic and safety properties necessary for a refrigerant in small AC systems and that these fluids are at least slightly flammable. We argue that the presented list of refrigerants is essentially exhaustive. Our focus here is on single-component refrigerants (that is, pure fluids). Refrigerant blends are in common use and offer additional possibilities. We do not consider blends explicitly but, for the sake of completeness, do include several fluids that would not be suitable low-GWP fluids in their own right but that might be useful as a blend component. Our findings give certainty as to the options available to the AC industry in their transition away from high-GWP fluids. It is also important for policy makers to understand these limits and trade-offs as they consider phase-down schedules.

Results

The current work presents the results of a multi-year study to identify alternatives to the HFC refrigerants. We first briefly summarize interim results from our earlier work, as referenced in the following three subsections.

Optimal thermodynamic parameters. As a first step, we considered the optimal thermodynamic parameters for a refrigerant. By use of evolutionary algorithms, we examined the performance of hypothetical fluids in several idealized refrigeration cycles and applications. The performance metrics were coefficient of performance (COP, unitless), defined as refrigeration effect (that is, removed heat) divided by the work input to the compressor, and the volumetric capacity (Qvol with units of MJ·m⁻³), defined as the refrigeration effect per unit volume of refrigerant vapour entering the compressor. The COP determines the energy efficiency of an AC system, and Qvol has a large influence on the physical size of the equipment, with larger values of Qvol corresponding to more compact systems. We considered hypothetical fluids—as defined by the liquid–vapour critical temperature (Tcrit), critical pressure (p∗), heat capacity of the vapour on a molar basis (Cv) and other parameters—meaning that we were not limited to known fluids. The critical temperature was the most important parameter and revealed a trade-off between COP and capacity; a high value of Tcrit resulted in high COP but low Qvol and vice-versa. A high value of critical pressure resulted in both higher COP and Qvol. The optimum value of Cv was found with the refrigeration cycle; low values of Cv were optimal for the basic vapour-compression cycle, while higher values of Cv were optimal for more complex cycles. Low values of Cp are associated with simple molecules (for example, organic molecules with one or two carbons), and most current refrigeration and AC systems use the basic cycle.

Database screening. Our search relied on screening a comprehensive database of molecules by applying filters representing different refrigerant selection criteria. The search was carried out in the PubChem database—a listing with >60 million chemical structures. A first screening of this database is described by Kazakov et al.; we summarize here a second screening. All current refrigerants are small molecules, and McLinden provides a thermodynamic basis for this. Thus we limited our search to molecules with ≤18 atoms and comprising only the elements C, H, F, Cl, Br, O, N or S. The choice of elements follows the observation by Midgley that only a small portion of the periodic table would form compounds volatile enough to serve as refrigerants. Despite their ability to deplete stratospheric ozone, Cl and Br were included; a molecule which includes Cl or Br might have a negligible ozone-depletion potential and might be acceptable if it had a very short atmospheric lifetime. These restrictions resulted in 184,000 molecules to be considered further.

Further screens for 320 K < Tcrit < 420 K and GWP100 < 1,000 (GWP with a 100-year time horizon) yielded 138 fluids. The PubMed database does not provide these data for the vast majority of the compounds, so they were estimated using methods based solely on molecular structure; these estimations constituted a major effort of this project. The limits on critical temperature correspond to fluids usable in small AC systems, with an allowance for the uncertainty in the estimated values of Tcrit. Although refrigerants with values of GWP as low as possible are obviously desirable, fluids with GWP100 < 750 are, for example, permitted under EU regulations in AC systems with <3 kg of refrigerant. The full list of 138 fluids is given in Supplementary Table 1, which also lists the Tcrit and GWP100 for each fluid.

The next screens were for chemical stability and toxicity. Compounds with generally unstable functional groups were dropped from further consideration. For example, peroxides (compounds with the –O–O– group) are unstable. Ketenes (compounds with the –C=O group) are generally very reactive, and three such compounds were dropped. Allenes have the –C=C=– group and are characterized as ‘difficult to
prepare and very reactive. Compounds with a carbon-carbon triple bond are generally less stable than those with a double bond; for example, fluoroethyne (FC=CH) is described as treacherously explosive in the liquid state. There are exceptions, however, and trifluoropropyne was retained.

Attempts to automate the screening of toxicity were not successful. We tested the Toxicity Estimation Software Tool of the US EPA, but it estimated, for example, a higher lethal dose for perfluorobutene ((CF3)2C=CF2), an extremely toxic compound, than for R-134a (CF3CFH2), a molecule with very low toxicity. (Table 1 and Supplementary Table 1 provide the compounds of interest here. Fortunately, at this point, the number of compounds was sufficiently small to allow a manual examination of toxicity data. We considered published toxicity data, where available, making use of a variety of sources, including safety standards, compilations of toxic industrial chemicals, regulatory filings and safety data sheets of chemical manufacturers. We also dropped compounds with two specific groups. Molecules that included the ≡CF2 group were deemed ‘not viable candidates’ on the basis of Lindley and Noakes who discuss the ‘≡CF2 structural alert’ with regards to R-1225zc (CF2CH=CF2); this is the observation that the ≡CF2 group has a high reactivity which is often associated with toxic effects. The presence of a ≡CF2 group does not assure that a molecule is

Table 1 | COP and volumetric capacity of selected low-GWP fluids and current HFC and HCFC fluids in the basic, liquid-line/suction-line heat exchanger (LL/SL) and economizer (Econ.) cycles.

| IUPAC name | Structure | ASHRAE designation | GWP100 | COP/COPR-410A | Qvol/QvolR-410A |
|------------|-----------|---------------------|-------|--------------|----------------|
| Hydrocarbons and dimethylether | | | | | |
| Ethane | CH3=CH3 | R-170 | 6| | |
| Propene (propylene) | CH3=CH=CH3 | R-1270 | 2| 1.033 1.053 1.073 0.689 0.694 0.770 |
| Propane | CH3=CH2=CH3 | R-290 | 3| 1.014 1.042 1.058 0.571 0.579 0.640 |
| Methoxyethane (dimethylether) | CH3-O-CH3 | R-E170 | 1| 0.996 1.002 1.035 0.392 0.389 0.427 |
| Cyclopropane | -CH2=CH2-CH2- | R-C270 | 86| 1.018 1.021 1.045 0.472 0.467 0.510 |
| Fluorinated alkenes (HFCs) | | | | | |
| Fluoromethane | CH2F | R-41 | 116| 1| 1.038 1.026 1.070 1.084 1.057 1.191 |
| Difluoromethane | CH2F2 | R-32 | 677| 1| 1.026 1.031 1.062 0.601 0.594 0.658 |
| Fluoroethene | CHF-CF3 | R-161 | 42| 1.012 1.021 1.045 0.472 0.467 0.510 |
| 1,1-Difluoroethene | CHF2=CH3 | R-152a | 138| 1| 0.981 0.989 1.022 0.399 0.396 0.435 |
| 1,1,2,2-Tetrafluoroethene | CHF2-CF2 | R-134 | 1120| 1| 0.967 0.991 1.024 0.348 0.352 0.385 |
| Fluorinated alkenes (HFOs) and alkenes | | | | | |
| Fluoroethene | CHF=CH2 | R-1141 | <1| 1| 0.968 0.977 1.014 1.346 1.336 1.547 |
| 1,1,2-Trifluoroethene | CHF2=CH2 | R-1123 | 3| 0.956 0.988 1.014 1.054 1.074 1.230 |
| 3,3,3-Trifluoroprop-1-yn | CF2=CH-CF3 | R-1234| 1| 0.988 1.023 1.042 0.545 0.557 0.616 |
| 2,3,3,3-Tetrafluoroethene | CHF=CF=CF3 | R-1234| 1| 0.954 1.006 1.020 0.414 0.431 0.474 |
| (E)-1,2-Difluoroethene | CHF=CF=CF3 | R-1132(E) | 1| 1.016 1.019 1.051 0.591 0.585 0.646 |
| 3,3,3-Trifluoroprop-1-yn | CHF=CH=CF3 | R-1234| 1| 0.964 0.997 1.019 0.372 0.379 0.417 |
| 1,2-Difluoroethene | CHF2=CH2 | R-1252ye | 2| 0.973 0.996 1.021 0.355 0.358 0.392 |
| (E)-1,3,3,3-Tetrafluoroprop-1-yn | CHF=CF=CF3 | R-1234ee(E) | 1| 0.939 0.977 1.004 0.320 0.329 0.360 |
| 2,3,3,3-Pentafluoro-prop-1-yn | CHF=CF=CF3 | R-1225ye(Z) | 1| 0.922 0.972 0.986 0.273 0.285 0.310 |
| 1-Fluoropropane | CHF3=CF3 | R-12611e | 1| 0.975 0.983 1.018 0.353 0.351 0.385 |
| Fluorinated oxygenates | | | | | |
| Trifluoro(methyl)ethane | CF3-O-CH3 | R-E143a | 523| 1| 0.957 0.992 1.017 0.366 0.374 0.411 |
| 2,2,4,5-Tetrafluoro-1,3-dioxole | -O-CF2=O-CF=CF2 | NA | 1| 0.936 0.984 1.027 0.337 0.349 0.376 |
| Fluorinated nitrogen and sulfur compounds | | | | | |
| N,N,1,1-Tetrafluoromethaneamine | CHF2=NF2 | NA | 20| 0.965 1.007 1.027 0.807 0.831 0.937 |
| Difluoromethanethiol | CHF2=SH | NA | 1| 1.010 1.019 1.054 0.582 0.580 0.642 |
| Trifluoromethanethiol | CHF=SH | NA | 1| 0.977 0.997 1.026 0.418 0.421 0.464 |
| Inorganic compounds | | | | | |
| Carbon dioxide | CO2 | R-744 | 1.00| 1| 1.055 1.028 1.080 0.746 0.721 0.791 |
| Ammonia | NH3 | R-717 | <1| 1| 0.936 0.984 1.027 0.337 0.349 0.376 |
| Current HFCs and HCFCs | | | | | |
| Perfluorooctane | C2F5-CF2 | R-125 | 3170| 1| 0.913 0.979 0.995 0.746 0.784 0.889 |
| R-32/125 (50.0/50.0) Blend | C2F5-CF2 | R-410A | 1924| 1| 1.000 1.012 1.049 1.000 0.997 1.130 |
| Chlorodifluoromethane | CHF2=CF2 | R-22 | 1760| 1| 1.007 1.008 1.043 0.666 0.658 0.732 |
| 1,1,2,2-Tetrafluoroethane | CHF3=CF2 | R-134a | 1300| 1| 0.968 0.993 1.027 0.433 0.439 0.485 |

Values are for the ‘optimized’ cycle model and are relative to the performance of R-410A in the basic cycle. GWP100 are estimated by the method of Kazakov et al unless noted. The fluids are grouped by chemical class and, within classes, listed in the order of increasing critical temperature.

*Values are relative to those for R-410A in the basic cycle; COP R-410A = 5.35 and Qvol R-410A = 6.93 MJ m\(^{-3}\).

†Literature value from Myhre et al. or EU regulation.

‡ Fluid would be near-critical or supercritical in the condenser and was not simulated.

§ This fluid has cis (Z) and trans (E) isomers; the predicted values of both were the same.
toxic, but we are aware of only one possible counterexample of R-1123, which has an acute toxicity similar to that of the commercialized refrigerant R-1234ze(E). The chronic toxicity of R-1123 has not been reported in the public literature. The absence of a $\equiv$CF$_2$ group does not, however, imply that a molecule is of low toxicity. Fluids having the –OF group were also dropped. The –OF group is analogous to the –OH group that enhances the refrigerant heat transfer coefficient at an acceptable pressure drop, as described by Brown et al.

**Cycle simulations—ideal cycle.** The screening of the candidate molecules considered their simulated performance in equipment with operating conditions representative of AC systems, see Table 1. This list is a subset of the 138 candidates, with the deletion of those that have low $Q_{vol}$, low COP or are unstable or toxic. We also included in Table 1 four currently used refrigerants, as well as carbon dioxide, ethane, R-41 and R-1225ye(Z), as discussed in the Methods section. Refrigerant blends are currently in common use, and the fluids in Table 1 also constitute the components of future blends. The list includes a small number of novel molecules that have not been previously considered as refrigerants (at least publicly), but a majority of the fluids are well known, including ammonia (R-717) and propane (R-290), or are the focus of current research in the refrigeration industry, that is, the fluorinated alkenes (also known as hydrofluoroolefins or HFOs). The HFOs constitute the largest group in the list with nine fluids. The other fluids are halogenated alkanes, halogenated oxygenates, hydrocarbons, halogenated nitorgen and sulfur compounds and inorganic compounds.

The COP and $Q_{vol}$ of the candidate fluids, based on the optimized model, are presented in Table 1 and Fig. 3. The COP and $Q_{vol}$ analysis based only on thermodynamic properties is, however, more representative of a fluid’s performance in an AC system in commercial production, which would be optimized for the refrigerant being used.

This screening process yielded 27 low-GWP fluids we deem to be the best single-component low-GWP replacements for unitary AC systems, see Table 1. This list is a subset of the 138 candidates, with the deletion of those that have low $Q_{vol}$, low COP or are unstable or toxic. We also included in Table 1 four currently used refrigerants, as well as carbon dioxide, ethane, R-41 and R-1225ye(Z), as discussed in the Methods section. Refrigerant blends are currently in common use, and the fluids in Table 1 also constitute the components of future blends. The list includes a small number of novel molecules that have not been previously considered as refrigerants (at least publicly), but a majority of the fluids are well known, including ammonia (R-717) and propane (R-290), or are the focus of current research in the refrigeration industry, that is, the fluorinated alkenes (also known as hydrofluoroolefins or HFOs). The HFOs constitute the largest group in the list with nine fluids. The other fluids are halogenated alkanes, halogenated oxygenates, hydrocarbons, halogenated nitorgen and sulfur compounds and inorganic compounds.

**Cycle simulations—optimized cycle.** The second round of cycle simulations made use of the theoretical CYCLE_D model and provided a first estimate of volumetric capacity and COP. These simulations assumed an ideal cycle with 100% compressor efficiency and no pressure drops. To better elucidate general thermodynamic trends, these simulations were performed on the full list of 138 low-GWP candidates that includes those dropped as unstable or toxic as well as an additional 8 refrigerants in current use. These results are given in Fig. 2 and Supplementary Table 1. This figure clearly shows the COP (efficiency) versus capacity trade-off that results from an ideal analysis based only on thermodynamic properties. At this stage, we dropped fluids with a volumetric capacity less than one-third that of R-410A or a COP $< 0.5$. (For R-410A in the ideal cycle, $Q_{vol} = 6.62 \text{MJ} \cdot \text{m}^{-3}$ and COP $= 7.41$. The volumetric capacity of R-22 is 66% that of R-410A, so this would correspond to dropping fluids with a capacity less than one-half that of R-22.)

The stability, toxicity and performance screens yielded a set of 27 low-GWP fluids that were then simulated in greater detail.

These cycles are depicted in Fig. 1. For the representation of refrigerant properties, we used detailed equations of state (EOS) implemented in the NIST REFPROP database where available. However, for a majority of fluids we used the extended corresponding states (ECS) model, as discussed in the Methods section.

This screening proceeded in two rounds. The first round of cycle simulations made use of the theoretical CYCLE_D model and provided a first estimate of volumetric capacity and COP. These simulations assumed an ideal cycle with 100% compressor efficiency and no pressure drops. To better elucidate general thermodynamic trends, these simulations were performed on the full list of 138 low-GWP candidates (that includes those dropped as unstable or toxic) as well as an additional 8 refrigerants in current use. These results are given in Fig. 2 and Supplementary Table 1. This figure clearly shows the COP (efficiency) versus capacity trade-off that results from an ideal analysis based only on thermodynamic properties. At this stage, we dropped fluids with a volumetric capacity less than one-third that of R-410A or a COP $< 0.5$. (For R-410A in the ideal cycle, $Q_{vol} = 6.62 \text{MJ} \cdot \text{m}^{-3}$ and COP $= 7.41$. The volumetric capacity of R-22 is 66% that of R-410A, so this would correspond to dropping fluids with a capacity less than one-half that of R-22.)

The stability, toxicity and performance screens yielded a set of 27 low-GWP fluids that were then simulated in greater detail.

**Cycle simulations—optimized cycle.** The second round of cycle simulations made use of a more advanced ‘optimized’ cycle model that provided a more realistic representation of an air conditioner employing typical forced-convection, air-to-refrigerant heat exchangers, which were optimized for a particular refrigerant. In this type of heat exchanger, the refrigerant undergoes a phase change as it flows down the inside of a tube and exchanges heat with air on the outside of the tube. Specifically, the new model accounted for the effect of optimized refrigerant mass flux, which enhances the refrigerant heat transfer coefficient at an acceptable penalty of the pressure drop, as described by Brown et al.

The simulation model maintained the same heat flux in the evaporator through all simulations, which is a prerequisite for a fair rating of competing refrigerants. The isentropic efficiency of the compressor was a function of the refrigerant properties and averaged 70%. Here the relative ranking of fluids differs from a ranking based only on thermodynamic properties; it is, however, more representative of a fluid’s performance in an AC system in commercial production, which would be optimized for the refrigerant being used.

This screening process yielded 27 low-GWP fluids we deem to be the best single-component low-GWP replacements for unitary AC systems, see Table 1. This list is a subset of the 138 candidates, with the deletion of those that have low $Q_{vol}$, low COP or are unstable or toxic. We also included in Table 1 four currently used refrigerants, as well as carbon dioxide, ethane, R-41 and R-1225ye(Z), as discussed in the Methods section. Refrigerant blends are currently in common use, and the fluids in Table 1 also constitute the components of future blends. The list includes a small number of novel molecules that have not been previously considered as refrigerants (at least publicly), but a majority of the fluids are well known, including ammonia (R-717) and propane (R-290), or are the focus of current research in the refrigeration industry, that is, the fluorinated alkenes (also known as hydrofluoroolefins or HFOs). The HFOs constitute the largest group in the list with nine fluids. The other fluids are halogenated alkanes, halogenated oxygenates, hydrocarbons, halogenated nitrogen and sulfur compounds and inorganic compounds.

The COP and $Q_{vol}$ of the candidate fluids, based on the optimized model, are presented in Table 1 and Fig. 3. The COP
ranged from $-7.8\%$ to $+5.5\%$ relative to that of R-410A in the basic vapour compression cycle. Ammonia showed the highest COP, better than that for R-410A by 5.5%. Beyond ammonia, which is toxic, mildly flammable and presents materials compatibility issues, the COPs of R-32, propene (R-1270), R-161, R-1132(E), propane (R-290), cyclopropane (R-C270) and difluoromethanethiol are also above the R-410A baseline. The ‘Pareto front’ line shows the thermodynamic limit of performance for fluids in the ideal vapour compression cycle, as discussed by Domanski et al.\textsuperscript{9}.

The results for the LL/SL-HX and economizer cycles are qualitatively similar to the basic cycle and are listed in Table 1 and depicted in Fig. 4. Similar to the basic cycle (Fig. 3), the best COP values correspond to $Q_{\text{vol}}$ values that are at least 60% of that for R-410A; the upper range of optimal $Q_{\text{vol}}$ is somewhat extended above 110% for the economizer cycle because we normalized the data with R-410A values for the basic cycle. The LL/SL-HX cycle (Fig. 4a) provides a performance benefit to fluids with a high molar heat capacity and degrades the performance of fluids with a small molar heat capacity (which are best performers in the basic cycle). Consequently, the spread of COP values in Fig. 4a is smaller than that shown in Fig. 3. The economizer cycle (Fig. 4b) increases the COP for all refrigerants, although the increase is larger for the fluids having a high molar heat capacity.

**Discussions**

Unlike the COP versus $Q_{\text{vol}}$ trade-off observed for the ideal analysis (Fig. 2), the results of the optimized cycle simulations (Figs 3 and 4) show a maximum in COP corresponding to $Q_{\text{vol}}$ of approximately 60–110% that of R-410A. Relative to fluids with low values of $Q_{\text{vol}}$, the high-$Q_{\text{vol}}$ fluids have lower values of $T_{\text{crit}}$ and operate at higher pressures; the result is that the cycle operates near the critical point and suffers increased irreversibilities in the expansion process. This effect applies to both the ideal and more detailed analyses. However, the ideal analysis neglects the fact that the pressure drop in the heat exchangers (condenser and evaporator) extracts a smaller COP penalty on the high $Q_{\text{vol}}$ (that is, high pressure) fluids when the heat exchangers are optimized. (The benefit of this optimization will also be affected by the relative heat transfer resistance on the refrigerant side and air side of the heat exchangers, as discussed in the Methods section.) An additional effect is that the low-$Q_{\text{vol}}$ fluids tend to be more complex molecules (see Supplementary Table 1). For example, R-32 (one of the best fluids in Fig. 3) is based on a single carbon atom, and R-410A is a blend of the single-carbon R-32 and two-carbon R-125. In contrast most of the fluids with $Q_{\text{vol}} < 0.4 \cdot Q_{\text{vol,R-410A}}$ are three-carbon compounds; greater complexity is associated with higher values of viscosity, which would increase the pressure drop and lower the COP.

This preference for high-pressure fluids does not apply to all types of systems. For example, large central-plant chillers typically employ shell-and-tube heat exchangers that have very-low refrigerant-side pressure drops; they often employ low-pressure...
Carbon dioxide is also nonflammable (class 1), but exposures at the relatively low levels of 500 to 1,000 p.p.m. become large. Result in such a small compressor that mechanical losses would to-low-pressure refrigerants (for example, R-134a or isobutane) equipment is, however, impractical for small AC systems. Very refrigerants and achieve high COPs. The complexity of such equipment is, however, impractical for small AC systems. Very small systems, such as home refrigerators, typically use medium-to-low-pressure refrigerants (for example, R-134a or isobutane) because the use of a high-pressure fluid, such as R-410A, would result in such a small compressor that mechanical losses would become large.

Most of the candidate fluids identified are flammable or mildly flammable. The refrigerant classification standards assign a fluid to one of four flammability groups based on their lower flammability limit, heat of combustion and burning velocity. Ranging from nonflammable to most flammable, these are classes 1 (nonflammable) fluids, although the ‘mildly flammable’ class 2L fluids (for example, R-134a or isobutane) have low acute toxicity but it exhibited toxic effects upon longer heat of combustion and burning velocity.

Values plotted are relative to those for R-410A in the basic cycle (COP/R-410A = 0.85 and Qvol/R-410A = 6.93 MJ·m⁻³); (a) cycle with LL/SL-HX; (b) two-stage flash economizer cycle. We identified six novel molecules in the screening: tetrafluorodioxole, trifluoromethanethiol, trifluoropropyne, difluoromethanethiol, (E)-1,2-difluoroethene (R-1132(E)), and tetrafluoromethaneamine. Few data could be found on these fluids, and they present unknown risks. None of them are particularly compelling from a performance standpoint. Difluoromethanethiol and (E)-1,2-difluoroethene, for example, have predicted COPs slightly higher than R-410A but Qvol values that are about 40% lower than that of R-410A. They are flammable (in addition to possible other hazards), and their COP and Qvol are very similar to propane (R-290). This raises the question, why take on the unknown risks of these fluids when one could use the somewhat more flammable but well-known propane? R-134 has a relatively high GWP, of 1120. It was investigated in the 1990s but never used commercially; it may be of interest as a blend component.

Our major conclusion is that the viable candidates for single-component low-GWP alternatives for small AC systems are very limited, especially for refrigerants with volumetric capacities similar to R-410A. Fluids with good COP and low toxicity are available, but all are at least slightly flammable. Nonflammable candidates exist among the fluids with low volumetric capacity, but use of such fluids in small AC systems would require extensive redesign and may result in lower COP. Blends offer additional possibilities, and the refrigeration industry is actively investigating blends of HFCs and HFOs with the intent of reducing or eliminating flammability with the trade-off of increased GWP. Although our study focussed on unitary AC systems (that is, residential and small commercial single-package and split systems), the general conclusions would apply also to room AC units and to refrigeration and heat-pumping systems currently using R-410A or R-22. The list of suitable fluids for systems operating at high ambient conditions would be reduced (as presented in the Results section).

Accepting thermodynamic arguments that viable refrigerants are restricted to small molecules, there are a finite number of ways to combine the selected elements into stable molecules. It is our contention that the presented screening process has yielded a list (see Table 1) of the ‘best’ low-GWP fluids allowed by chemistry, that is, it is highly unlikely that any better-performing fluids will be found, and unknown risks associated with the lesser-known fluids may further reduce the list.

Refrigerant blends offer a compromise between flammability and GWP: for example, a low-GWP but flammable fluid blended with a nonflammable but high-GWP fluid could result in a nonflammable fluid with a moderate value of GWP (order of 500) or a slightly flammable refrigerant with a low GWP (order of 150). The list presented in Table 1 (with the addition of the ‘current’ HFCs listed) also encompasses the fluids that would serve as blend components. The refrigeration industry has been very actively developing such blends, and in parallel, significant work has been undertaken in support of refrigerant safety standards that could allow the safe use of flammable refrigerants in specific applications. The results of the present study have confirmed these courses of action.

Our findings give certainty as to the options available to the AC industry in their transition away from high-GWP fluids. It is also important for policy makers to understand these limits and trade-offs as they consider phase-down schedules.

**Methods**

**Database screening.** The PubChem database is a listing of 157 million chemical substances and 60 million unique chemical structures, and we considered it as exhaustive for the small molecules that would be viable as refrigerants. The entries in PubChem are provided by a wide variety of contributors, including chemical vendors, university laboratories and government agencies, including the US President's Committee on Cancer.
Environmental Protection Agency. More than 16 million chemical structures were obtained from six million US, European and World Intellectual Property Organisation patent databases. In addition to the chemicals, it includes compounds that have been synthesized only on a laboratory scale and also entirely hypothetical molecules.

We carried out two screenings of this database. The first screening is described by Kazakov et al.14, who generated a subset of 95,203 molecules of ≤15 atoms and comprising only the elements C, H, F, Cl, Br, O, N or S. Also excluded at this stage were ions, radicals and molecules enriched in specific atomic isotopes. Kazakov et al.15 developed a method for predicting the GWP100 of compounds based only on their molecular structure; the method combined estimates of the radiative efficiency and atmospheric reactivity with the hydroxyl radical. The trade-off of computational efficiency versus accuracy was a major consideration given the large number of compounds to screen. The method achieved a logarithmic root-mean-square deviation of 3.0 for the GWP100 estimate compared with available literature values, and this accuracy was adequate for screening purposes. Applying a screen of GWPIp < 200 resulted in 52,565 compounds, that is, the vast majority of these molecules have short atmospheric lifetimes and low GWP. Further screens for compression cycle were not considered further. The selection of a fluid for conducting, except that fluids with a low volumetric capacity in the ideal vapour were ions, radicals and molecules enriched in specific atomic isotopes. Kazakov et al.15, and a constraint of 300 K < Tcrit < 550 K was applied. The number of candidates was further reduced to 1,234 by eliminating unstable or highly reactive functional groups.

The list of 1,234 compounds was examined by McLinden et al.13 and compared against the optimum thermodynamic parameters for a refrigerant that were revealed by the analysis of Domanski et al.7. The main thermodynamic criterion was critical temperature. Only 62 fluids had Tcrit < 400 K. (The higher upper limit on Tcrit in the database screening was selected before the results of Domanski et al.7 were obtained and also to encompass high-temperature applications.) The 62 fluids were examined with regards to thermodynamic parameters and a more detailed consideration of toxicity and chemical stability. Only 13 of these fluids were considered as viable candidates.

Given this small number of viable candidates, a second screening of the PubChem database was carried out (McLinden et al.11). In this screening, the maximum size of the molecule was increased to 18 atoms (with the intent of enabling a future search for fluids suitable for high-temperature applications); the result was 184,000 compounds. The most significant changes in the second screening, however, were the elimination of the screens on toxicity and flammability, and a relaxing of the GWP screen to GWPIp < 1,000. These were carried out to avoid prematurely excluding promising candidates and in the recognition that a flammable fluid or one with a moderate value of GWP might be acceptable in some applications or as a component of a blend. The calculation of critical temperature was carried out as the first filter using the method of Kazakov et al.14; 1,728 low-GWP compounds had Tcrit < 550 K and 138 candidates had Tcrit < 420 K.

Cycle simulations (as described below) were carried out on these 138 fluids. A literature search on the toxicity and chemical stability of the candidates was conducted, except that fluids with a low volumetric capacity in the ideal vapour compression cycle were not considered further. The selection of a fluid for inclusion in the ‘final’ list (that is, Table 1) was based on (1) Qrev > 0.33 O-Qrev,14,10,24 (that is, Qrev = 2.2 MJ m-3); (2) COP > 3; (3) low toxicity (or, at least, no acute effects); and (4) acceptable chemical stability. These additional fluids were also included in Table 1 to present a ‘complete’ list of options for unitary AC applications: Carbon dioxide is the only low-toxicity, nonflammable, high-pressure fluid that was identified; it would operate in a transcritical cycle and was not simulated here. Ethane and R-41 (fluoromethane) would also operate near their critical temperature in an AC application; they would be unlikely single-component refrigerants, but they might be useful as blend components. R-134 (1,1,2,2-tetrafluoroethane) is a HCFC with GWPIp = 1.120 (ref. 32); it is nonflammable and, despite its relatively high value of GWP, it might be useful as a blend component. We included R-1123 and R-1225(ye) (Table 1 and Fig. 2) because these fluids are (or were at one time) the subjects of active research. Other refrigerants that might be useful as a blend component are R-113 and R-123.

Critical properties. The two form an equilibrium mixture, which is stable and acceptable in some applications or as a component of a blend. The calculation of critical properties of thermal conductivity and viscosity. These were calculated with the methods implemented in the NIST REFPROP database, where available. For the remaining fluids, we used a dilute-gas model based on the Lennard–Jones (1–1) fluid, with the L–J parameters estimated with the method of Chung37, combined with the ECS model of Huber et al.38 for the dense-gas contribution. We used the model of Chae et al.39 for estimating the surface tension.

Cyclus simulations. The basic vapour-compression refrigeration cycle and two modifications of this cycle were considered; these are shown in Fig. 1. In the basic vapour-compression refrigeration process, the refrigerant absorbs heat from the cold space (for example, indoor air), cools, and the refrigerant vapour then flows through an expansion device, which lowers the pressure in an adiabatic (constant enthalpy) process. The expansion process can be as simple as a liquid capillary tube, but it is usually a thermostatically or electronically controlled valve in most AC equipment. In the expansion process, a portion of the liquid flashes to vapour, cooling the refrigerant to the saturation temperature corresponding to the pressure in the evaporator. The remaining liquid vaporizes in the evaporator (which is typically also a finned, air-to-refrigerant heat exchanger), extracting heat from the cool space and then flows to the compressor, completing the cycle.

The LL/SL-HX (Fig. 1b) adds an additional internal heat exchanger to the basic cycle. The hot refrigerant leaving the condenser is cooled by rejecting heat to the cold refrigerant vapour exiting the evaporator. This reduces the quantity of refrigerant that flashes to vapour upon exiting the expansion device; this increases the refrigeration effect in the evaporator, which increases the COP. Simultaneously, however, it heats the vapour entering the compressor, which increases the compression work—an effect which decreases the COP. As a result, this internal heat exchanger can improve or decrease the COP of the cycle, depending on the properties of the fluid; those with a high latent heat of condensation or a high boiling point temperature (corresponding to small molecules, such as ammonia) suffer a COP penalty, while relatively complex molecules (such as those with three carbons) usually benefit40.

The final cycle considered here is the two-stage flash economizer cycle, shown in Fig. 1c. Here there are two expansion devices, with a liquid–vapour separator between them. After the first expansion device, the refrigerant that has flashed to vapour is sent directly to the compressor, rather than flowing through the evaporator. As a result of this flash refrigeration, the mixture of refrigerant in the evaporator is vapour at the state point at which the refrigerant flashed to vapour, and this mixture is at a pressure and temperature intermediate between that in the condensed phase and that on the saturation line. This flash reduces the pressure and temperature differences, which decreases compression work to raise it back to the condenser temperature. The economizer cycle yields a higher COP than the basic cycle for all fluids, but this comes at the expense of additional components and a more complex compressor.

The ‘optimized’ cycle model used to simulate the results presented in Table 1 was derived from the CYCLE11 model of Domanski and McLinden28 with the addition of an optimization of the refrigerant circuitry in the evaporator and condenser to maximize the COP. The model represents the heat duties, Q, of the evaporator and condenser (in a cross-flow configuration) through the overall heat transfer coefficient, U, heat transfer area, A, and mean effective temperature difference, AT, where the heat duties and the overall heat transfer coefficients are given by: $\dot{Q} = U A T$. To account for the mean effective temperature differences, AT, are determined from the temperature profiles of the heat sink and heat source and the refrigerant-side temperature profiles in the evaporator and condenser. The solution scheme divides the heat exchangers into as many as 128 segments and includes sections in the condenser for vapour-liquid and liquid-slip situations; we used this model in the evaporator for two-phase evaporation and vapour superheating. The ‘optimized’ model is not a detailed simulation model. Rather it accounts for the effects of
refrigerant thermophysical properties on heat transfer coefficients and refrigerant pressure drops in the heat exchangers in relation to those of a reference refrigerant in a reference system (either simulated with a much more detailed model or experimentally measured), and it assumes heat transfer resistances on the air sides of the heat exchangers to be constant, as presented by Brown et al.27-41.

The refrigerant flows through multiple tubes in the evaporator and condenser, and the COP of the cycle by districting one or more refrigerant circuits in each heat exchanger. An increase in the number of tubes per refrigerant circuit in effect lowers the refrigerant mass flux per tube leading to a lower refrigerant-side heat transfer coefficient more or less proportionally with mass flux while at the same time lowering the refrigerant-side pressure drop per tube. This is ultimately with mass flux, decouples the number of tubes per refrigerant circuit has the opposite effects on the refrigerant-side heat transfer coefficient and pressure drop. These effects result in an optimum refrigerant-side refrigerant flow path that maximizes COP by striking a balance between the positive influence on COP of higher refrigerant mass flux through increasing heat transfer coefficient and the negative influence on COP of higher refrigerant mass flux through increasing pressure drop.

Uncertainties. The screening of candidate molecules in this study was based primarily on values of GWP100, the thermodynamic properties and the simulated cycle performance in an AC application (which, in turn, depended on the thermodynamic properties). The GWP100 for 17 of the 27 fluids presented in Table 1 are available in the literature, and for the other 10 (and a large majority of the fluids discussed in this paper) fluids in Supplementary Table 1) it was estimated by the method of Kazakov et al.10 Based on 95 fluids with literature values of GWP100, Kazakov et al.10 determined that the logarithmic root-mean-square deviation of the estimated GWP100 corresponded to a factor of 3.0. Although this is a large uncertainty, it is adequate for screening purposes, especially considering that a refrigerant-side refrigerant flow path that maximizes COP by striking a balance of lower refrigerant-side heat transfer coefficient more or less proportionally with refrigerant circuit in effect lowers the refrigerant mass flux per tube leading to a lower refrigerant-side heat transfer coefficient, and the properties; the MAD approximates a standard uncertainty. The cycle performance in an AC application (which, in turn, depended on the thermodynamic properties) was for the basic cycle and we assumed similar uncertainties for the LL/SL-HX 8.

Likewise, the maximum value of the allowance that was selected in view of the uncertainty in the cycle performance.

for inclusion in Table 1, for example, was 33% that of the R-410A baseline—an uncertainty, it is adequate for screening purposes, especially considering that a refrigerant-side refrigerant flow path that maximizes COP by striking a balance between the positive influence on COP of higher refrigerant mass flux through increasing heat transfer coefficient and the negative influence on COP of higher refrigerant mass flux through increasing pressure drop.

Values of $T_{crit}$, $P_{crit}$ and ideal-gas heat capacity ($C_p$). Uncertainties arise from the estimates of $T_{crit}$, $P_{crit}$ and $C_p$. The standard uncertainties of the group contribution estimates based on normal boiling point (a method used for six fluids) were estimated by Brown et al.20 to be 1.0, 10, 12 and 6.5% for $T_{crit}$, $P_{crit}$ and $C_p$, respectively. To estimate the uncertainties in cycle performance, we simulated three of the fluids (R1132(E), R1141 and R1225ye(Z)) with varying estimates of the input parameters. A variation in $T_{crit}$ of ±2% resulted in uncertainties in COP of ±4%, ±8% and uncertainties in $Q_{out}$ of 13.1% ±17.4%. A variation in $P_{crit}$ of ±10% resulted in virtually no change in COP and uncertainties in $Q_{out}$ of +10.0% / −10.0%. A variation in $C_p$ of ±15% resulted in virtually no change in both COP and $Q_{out}$. Finally, varying $C_v$ by ±15% resulted in uncertainties in COP of −2.1% / ±1.9% and uncertainties in $Q_{out}$ of −3.6% / ±3.6%. These simulations were done for the basic cycle and we assumed similar uncertainties for the LLC/LL-HX and economizer cycles.

The sensitivity study described above for R1132(E), R1141 and R1225ye(Z) will apply for all the fluids. Additional fluids were estimated by the method of Carande et al.14, who provide ‘median average deviations’ (MAD) for the estimated thermophysical properties as given in Table 1 or Supplementary Table 1. These data were calculated with NIST REFPROP, Version 9.1 (Standard Reference Data Program, National Institute of Standards and Technology, 2013). The new optimalized cycle model (Figs 3 and 4 Table 1) will be documented in a forthcoming paper: a preliminary version is available upon request. For both models, the thermophysical properties were calculated with the NIST REFPROP database32, see http://www.nist.gov/srd/nist23.cfm. For the 22 fluids, the standard property formulations in REFPROP were used. For the remaining fluids, ad hoc fluid data files were generated with the ECS method, as outlined in the main text and detailed in ref. 24 (for the fluids with limited experimental data) with the estimation methods36,39 described in the main text.

The GWP100 values and some of the property estimates were based on quantum mechanical calculations: specifically, the vibrational frequencies, infrared intensities, radiative efficiency, ideal-gas heat capacities and enthalpies of formation were computed at the PM6 level of theory with Gaussian 09 Rev B01 (ref. 43). The thermophysical properties estimated by the method of Kazakov et al.14 made use of MOPAC version 6 (ref. 44), CODESSA version 2.7.9 (ref. 45) and LIBSVBM version 3 (ref. 46). The critical properties estimated by the method of Carande et al.13 made use of Indigo10, PaDEL version 2.21 (ref. 48), RDKit (development version)10 and the R Statistical Environment10. The chemical structural analysis needed for additional corrections to the results of AOPWIN were performed with OpenBabel version 2.3.1 (ref. 52). As described in the main text, limited toxicity estimations were performed with the T.E.S.T. tool of the US Environmental Protection Agency15.
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Author contributions
P.A.D. and M.M. formulated the project, with M.M. serving as principal investigator. A.F.K. carried out the database screenings and associated estimation of properties. M.M. evaluated the stability and toxicity of the candidate molecules. J.S.B. and R.B. developed the cycle simulation model and performed the cycle simulations. P.A.D., R.B. and J.S.B. evaluated the cycle simulation results. M.M., P.A.D. and J.S.B. wrote the paper; and all authors contributed to revising the paper.

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