In populo

Daniel Westreich1, Brian W. Pence2, and Abigail Norris Turner1
1Department of Epidemiology, UNC Gillings School of Global Public Health, Chapel Hill, North Carolina, USA
2Department of Community and Family Medicine, Global Health Institute, and Center for Health Policy, Duke University, Durham, North Carolina, USA
3Division of Infectious Diseases, Department of Internal Medicine, College of Medicine, The Ohio State University, Columbus, Ohio, USA

Abstract

While the Latin phrase in vitro and in vivo are well understood in the medical literature, neither term accurately describes the science performed at the level of the population by epidemiologists and others. In particular, results in a single organism can differ broadly from results in a population, for reasons from random error to herd immunity. We suggest that in populo, meaning literally “in the people”, can fill this gap in the literature, and urge its wide adoption.

We write this brief note to propose the adoption of a new term – in populo, meaning “in the people” or “in the public” – to describe population-based health sciences research, and to parallel the widely used terms in vitro and in vivo.

While in vitro (meaning literally “in glass”) is generally taken to refer to science performed outside of living organisms, in vivo (literally, “in live beings”) refers to experiments done in whole organisms. To these two mainstays, additional terms have been added over the years. Ex vivo (literally, “out of live beings”) typically refers to live cells (or organs) isolated from an organism, and is sometimes used interchangeably with in vitro. The Latinate (that is, not proper Latin) in silico refers to experiments done only on computer, such as modeling or simulation studies; the similar, Latinate, and little-used in papyro indicates that the study has been performed on paper, as with a meta-analysis. Table 1 summarizes the extent of the use of these terms in the medical literature.

None of these terms, however, correctly describes the population-level work of many public health scientists. While clinical trials are often considered in vivo research, we propose that population-based health research is not well-served by a term which does not distinguish between a 5,000-subject observational study and a pharmacokinetics study with n=1.

Importantly, the inferences drawn from individual-level observations may not hold at the level of the population. A given therapy may improve the clinical outcome in a given patient (an in vivo finding), while in a clinical trial with low probability of confounding, that same therapy may not significantly improve clinical outcomes across the full patient population (an in populo finding). Individual effects may differ widely from population effects for a number of

Author contributions.
D.W. wrote first draft. All authors edited text, contributed ideas, and reviewed final draft.

Conflicts of interest.
We have no conflicts of interest for this work.
reasons, ranging from random error, to dynamic population-level phenomena such as herd immunity.\(^8\)

Examples in which \textit{in vivo} and \textit{in populo} effects differ are abundant in the medical and public health literature. For example, while the smallpox vaccine is highly effective, it is not 100\% efficacious \textit{in vivo}; nonetheless, use of the ring vaccination strategy \textit{in populo} led to the eradication of that disease in the general human population.\(^9\) Many other vaccines benefit from herd immunity in similar ways. In contrast, the rgp120 candidate HIV vaccine produced a promising antibody response \textit{in vivo} during Phase I/II trials\(^10\text{-}12\) but failed to prevent HIV acquisition in two large \textit{in populo} Phase III trials.\(^13\text{-}14\)

When does an \textit{in vivo} study graduate to \textit{in populo} status? At the extremes of sample size, there are fairly clear lines: rgp120 trials published from 1994 and 2000 included 57 and 33 subjects,\(^10\text{-}11\) while the two Phase III trials included 5403 and 2546 subjects, respectively.\(^13\text{-}14\) Less clear is the 2003 study,\(^12\) which included 370 subjects: \textit{in vivo}, or \textit{in populo}? We would argue that more important than sample size is that these studies are clearly measuring qualitatively different kinds of effects. While the Phase II trial studied vaccine immunogenicity, the Phase III trials studied vaccine efficacy for prevention of HIV infection. This distinction between biological and clinical outcomes seems key, although usage in the medical literature will doubtless refine these ideas further.

\textit{In populo} provides a useful counterpoint to \textit{in vivo} and \textit{in vitro}, reminding us that scientific and analytical issues differ widely between the study of a single individual and the study of a thousand. Thus we believe that \textit{in populo} can find a useful place in the medical and public health literature, and urge its adoption by the public health and medical research community.

**Acknowledgments**

We thank Dr. Emily Baragwanath of UNC-Chapel Hill Department of Classics for her help with Latin definitions, and Dr. Michael Hudgens of UNC-Chapel Hill Department of Biostatistics for his help with information about HIV vaccines.

**Funding.**

D.W.\ receives support from NIH/NIAID 5 T32 AI 07001-31 Training in Sexually Transmitted Diseases and AIDS; this funding source had no role in the preparation of this work or the decision to submit.

**REFERENCES**


Table 1

Use of selected Latin and Latinate terms in the medical literature

<table>
<thead>
<tr>
<th>Term</th>
<th>Meaning</th>
<th>First use, PubMed</th>
<th>Total uses, PubMed</th>
</tr>
</thead>
<tbody>
<tr>
<td>In vitro</td>
<td>In glass</td>
<td>1911</td>
<td>962,506</td>
</tr>
<tr>
<td>In vivo</td>
<td>In live beings</td>
<td>1918</td>
<td>482,751</td>
</tr>
<tr>
<td>Ex vivo</td>
<td>Out of live beings</td>
<td>1964</td>
<td>27,253</td>
</tr>
<tr>
<td>In silico</td>
<td>In computer simulation</td>
<td>1991</td>
<td>6,715</td>
</tr>
<tr>
<td>In papyro</td>
<td>On paper</td>
<td>None indexed</td>
<td>0</td>
</tr>
<tr>
<td>In populo</td>
<td>In the population</td>
<td>2009</td>
<td>†‡</td>
</tr>
</tbody>
</table>

†‡ This essay, excepting five citations with an author last name Populo.