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In populo

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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”¹ – 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”¹) is generally taken to refer to science performed outside of living organisms, *in vivo* (literally, “in live beings”¹) 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”¹) typically refers to live cells (or organs²) isolated from an organism,³ and is sometimes used interchangeably with *in vitro*.⁴ The Latinate (that is, not proper Latin) *in silico* refers to experiments done only on computer, such as modeling or simulation studies;^{5,6} the similar, Latinate, and little-used *in papyro* indicates that the study has been performed on paper, as with a meta-analysis.⁷ 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

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reasons, ranging from random error, to dynamic population-level phenomena such as herd immunity.⁸

Examples in which *in vivo* and *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 *in vivo*; nonetheless, use of the ring vaccination strategy *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 *in vivo* during Phase I/II trials¹⁰⁻¹² but failed to prevent HIV acquisition in two large *in populo* Phase III trials.^{13,14}

When does an *in vivo* study graduate to *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,^{10,11} while the two Phase III trials included 5403 and 2546 subjects, respectively.^{13,14} Less clear is the 2003 study,¹² which included 370 subjects: *in vivo*, or *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.

In populo provides a useful counterpoint to *in vivo* and *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 *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.

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Table 1

Use of selected Latin and Latinate terms in the medical literature

Term	Meaning	First use, PubMed 15	Total uses, PubMed 15
<i>In vitro</i>	In glass	1911 ¹⁶	962,506
<i>In vivo</i>	In live beings	1918 ¹⁷	482,751
<i>Ex vivo</i>	Out of live beings	1964 ²	27,253
<i>In silico</i>	In computer simulation	1991 ¹⁸	6,715
<i>In papyro</i>	On paper	None indexed	0
<i>In populo</i>	In the population	2009	1 [‡]

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