pKa

Acid–base ionization and its impact on drug behavior

NEZU
Biotech GmbH

Dear Client,

first and foremost, thanks for downloading this free resource. All graphics in this report are predictions made by our AI systems. They show the profile of this ADMET endpoint for thousands of marketed drugs. We divided it by indication, and as you can see, it changes a lot from one category to another. Therefore, try to find the closest indication to the compounds you are currently developing.

Acidic pKa and basic pKa describe how readily a molecule gains or loses a proton as the surrounding pH changes. In practical terms, they help predict whether a potential drug will be electrically neutral, negatively charged, or positively charged in the stomach, intestine, blood, tissues, and intracellular compartments. A suitable ionization profile balances aqueous solubility with passive membrane permeability and supports access to its biological target.

The most established measurement is an aqueous potentiometric titration. Researchers dissolve the compound in water or a defined buffer and add standardized acid or base while monitoring pH with an electrode. The resulting titration curve shows how protonation changes with pH. Mathematical fitting gives the pKa, which is the pH at which the relevant ionizable group is approximately 50% protonated and 50% deprotonated. Ultraviolet-visible spectrophotometric methods can instead measure pH-dependent changes in absorbance. Capillary electrophoresis can derive pKa from changes in molecular mobility. pKa is reported on a dimensionless logarithmic scale. Poor aqueous solubility, impurities, temperature, ionic strength, overlapping ionization sites, and the use of organic cosolvents can alter the measured value.

For an acidic group, a lower pKa means stronger acidity and easier proton loss. At a pH above its acidic pKa, the group is predominantly deprotonated and negatively charged. **A higher acidic pKa means weaker acidity and a larger neutral fraction at the same pH.**

For a basic group, reported pKa usually refers to the dissociation of its protonated conjugate acid. A higher basic pKa means stronger basicity and greater protonation. At a pH below its basic pKa, the group is predominantly positively charged. **A lower or negative basic pKa indicates a weak base that remains largely neutral under ordinary physiological conditions.**

Ionization generally increases aqueous solubility but reduces passive diffusion through lipid membranes. Neutral species usually cross membranes more readily, while charged species can show stronger transporter interactions, altered protein binding, ion trapping, renal elimination, and target binding. **No pKa is universally favorable.** Interpretation must include physiological pH, molecular structure, route

of administration, and target location, together with aqueous solubility, lipophilicity, passive permeability, plasma protein binding, transporter activity, metabolic clearance, and renal excretion.

We generated these insights using advanced AI systems designed to analyze complex biotech data and highlight potential trends. While we strive for accuracy, AI models can occasionally make mistakes or miss context, so please treat these predictions as informative guidelines rather than absolute facts.

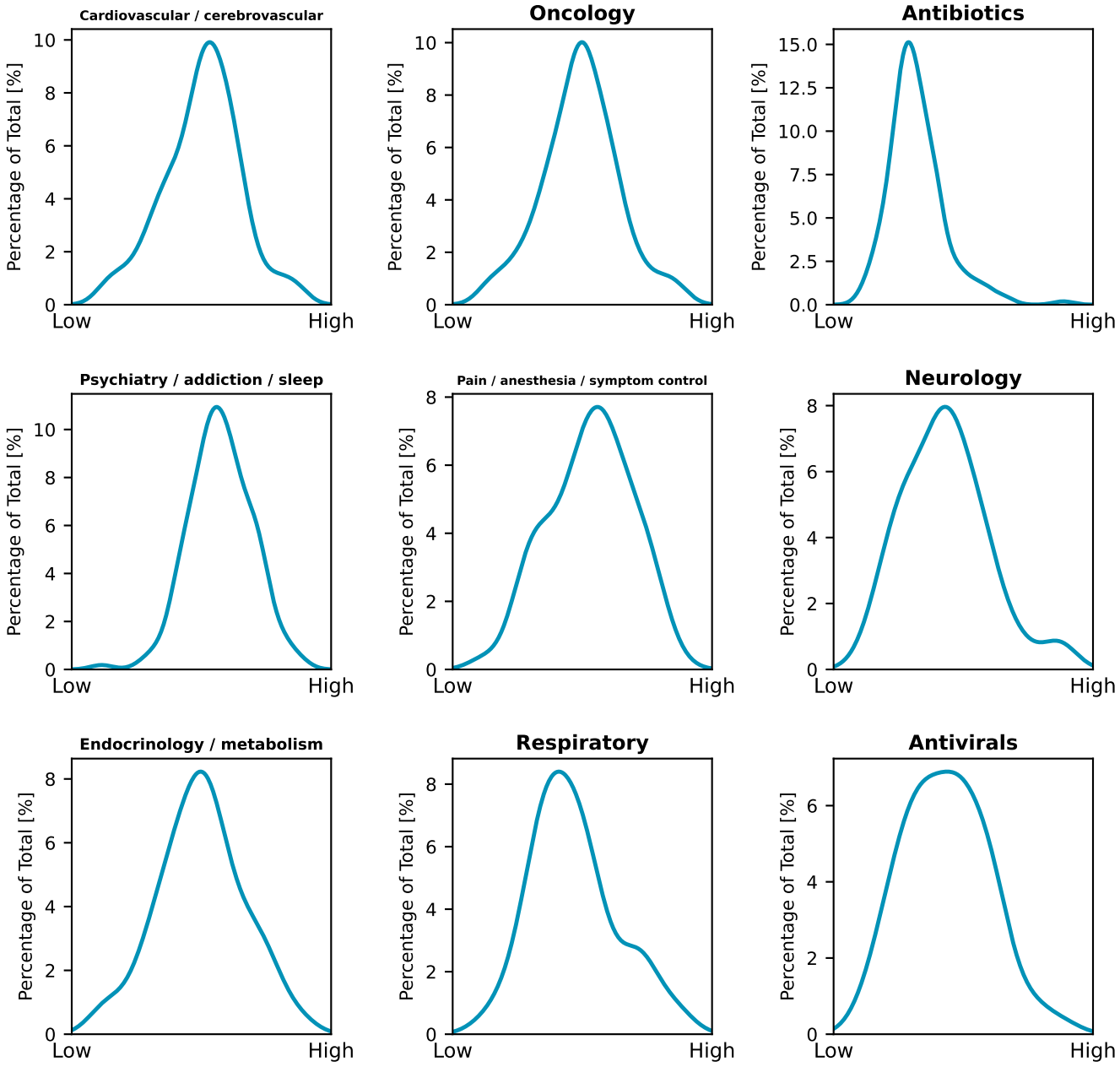
This report is provided for general informational and educational purposes only, not for medical diagnosis, treatment decisions, or financial advice. Because individual circumstances and data can vary, we cannot be held responsible for any decisions made or losses incurred based on these predictions.

Now that we got this out of the way, we genuinely hope these results are useful for your research.

Sincerely,

Your friends at Nezu Biotech GmbH.

pKa Acidic


Cardiovascular / cerebrovascular
Oncology
Antibiotics
Psychiatry / addiction / sleep
Pain / anesthesia / symptom control
Neurology
Endocrinology / metabolism
Respiratory
Antivirals
Percentage of Total [%]
Low
High
Derived from thousands of marketed drugs

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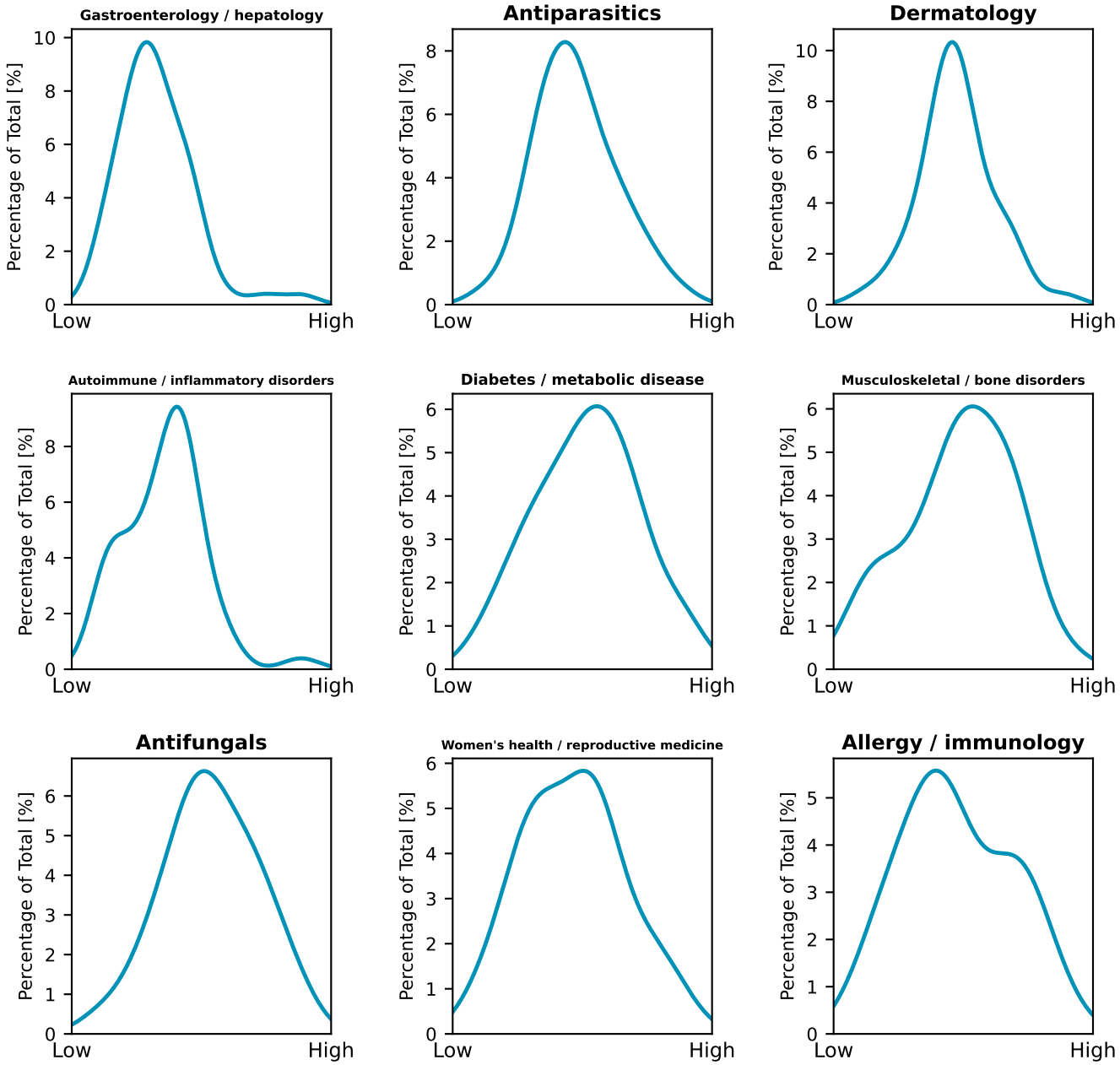
Gastroenterology / hepatology
Antiparasitics
Dermatology
Autoimmune / inflammatory disorders
Diabetes / metabolic disease
Musculoskeletal / bone disorders
Antifungals
Women's health / reproductive medicine
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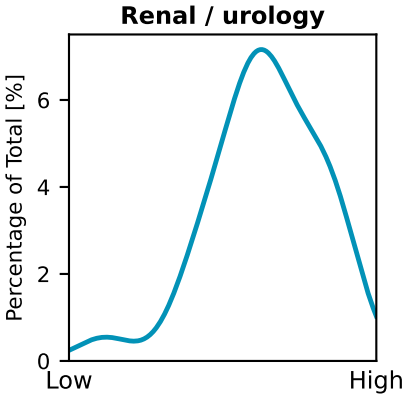

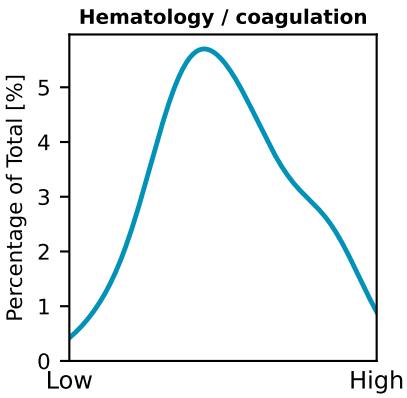

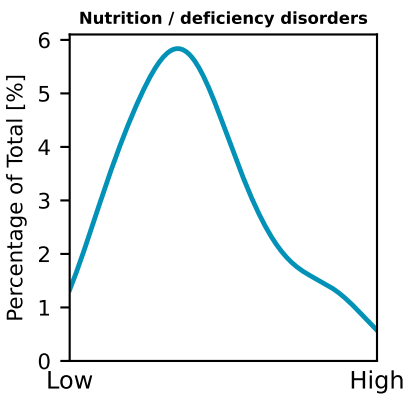

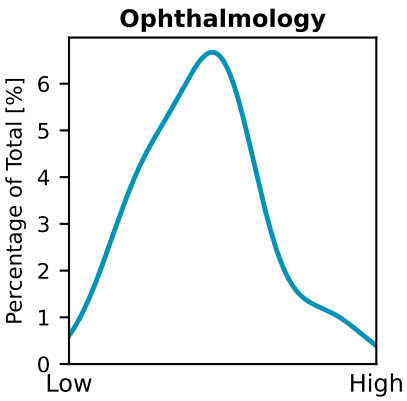

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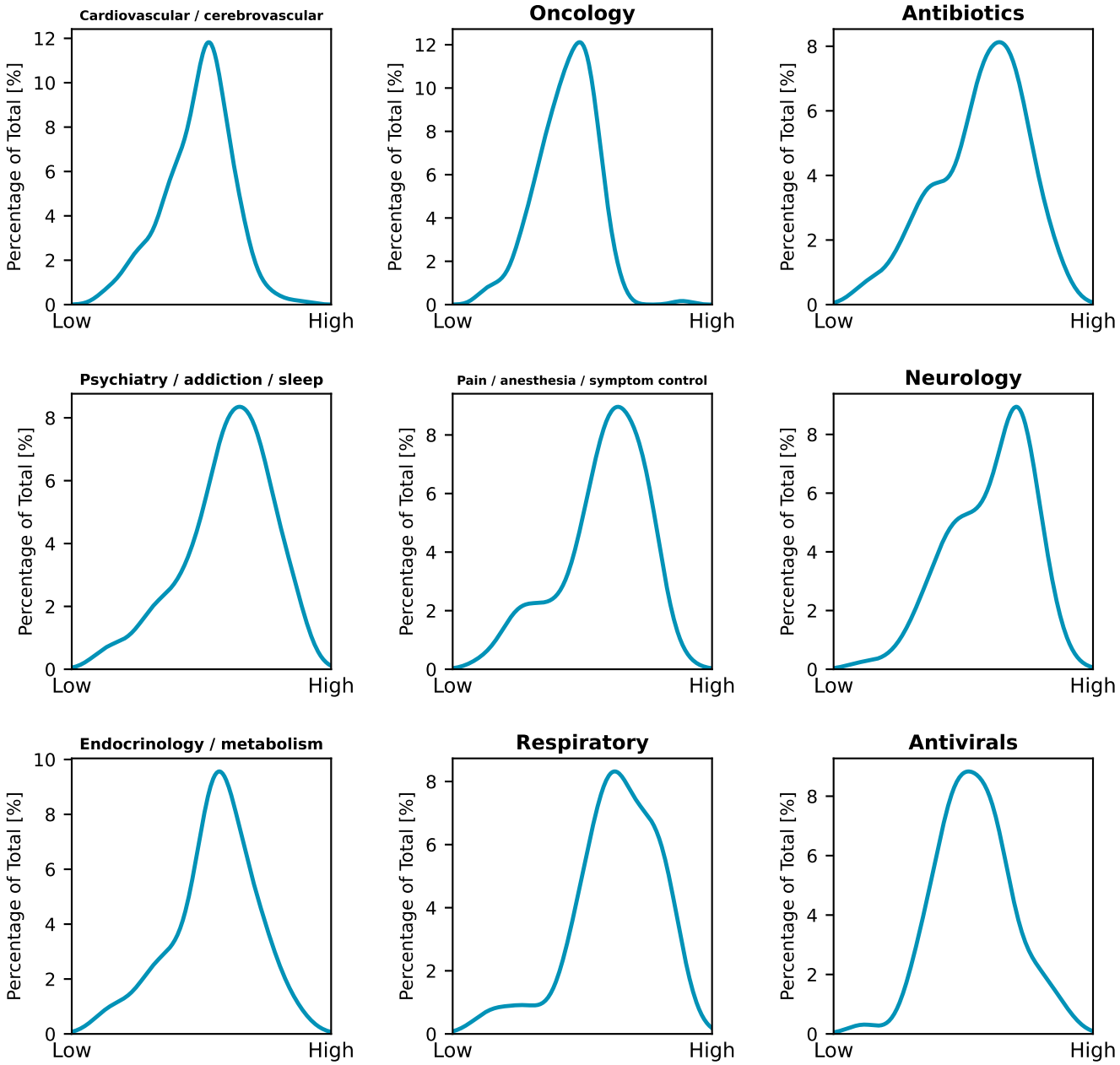
pKa Basic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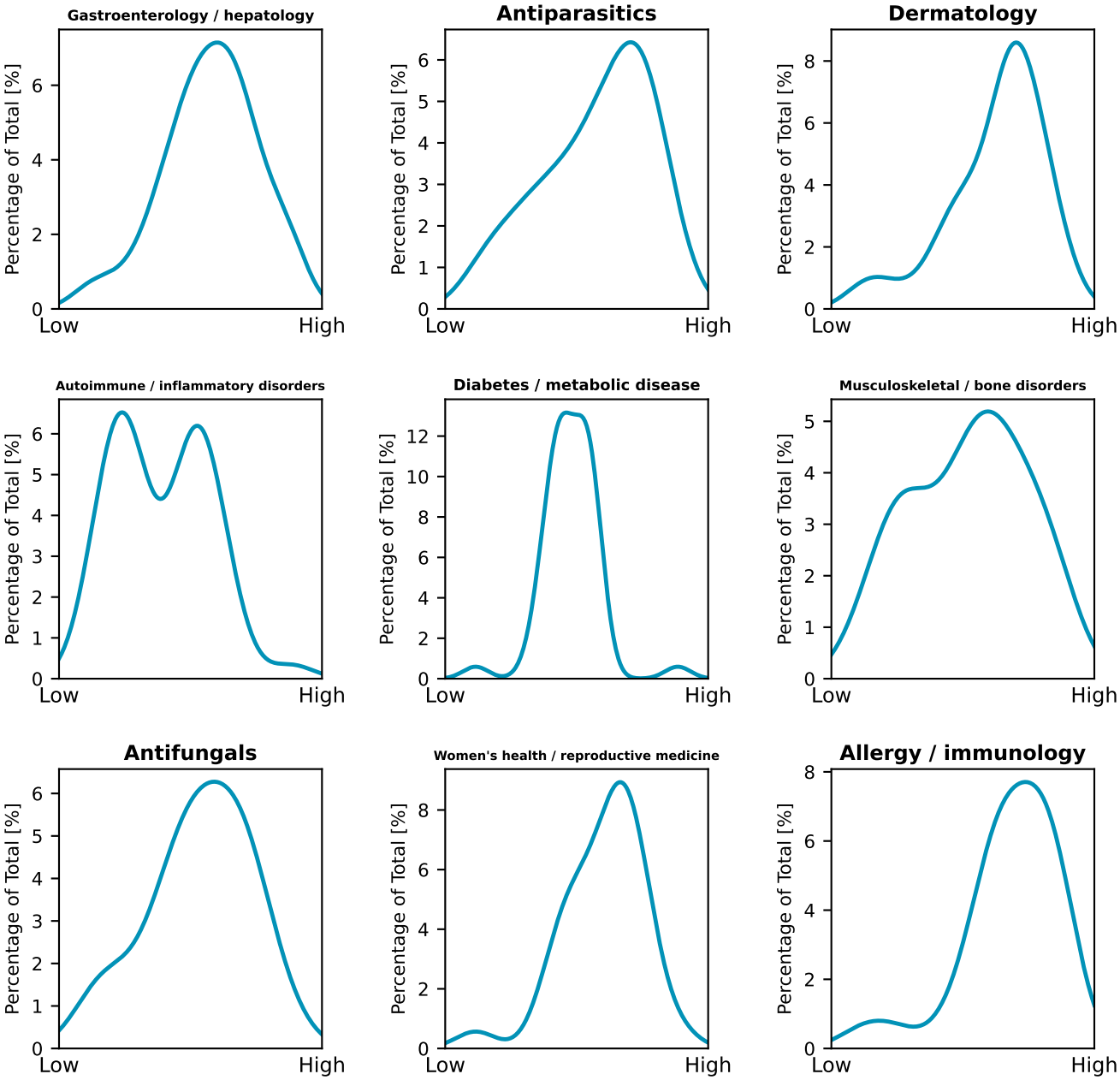
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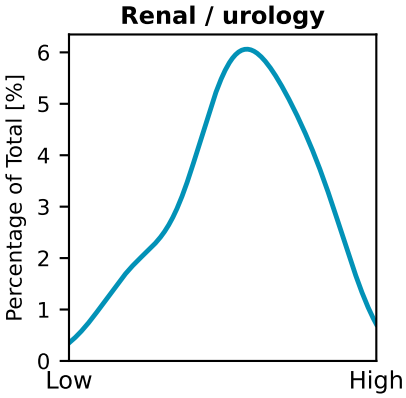

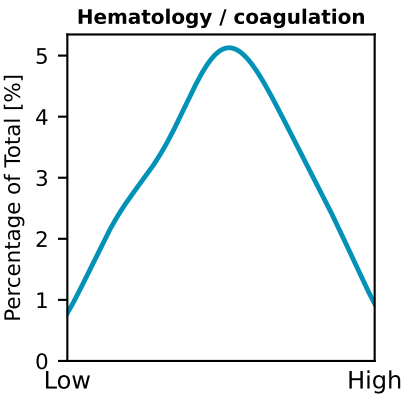

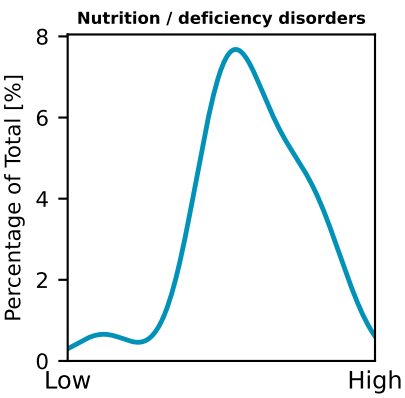

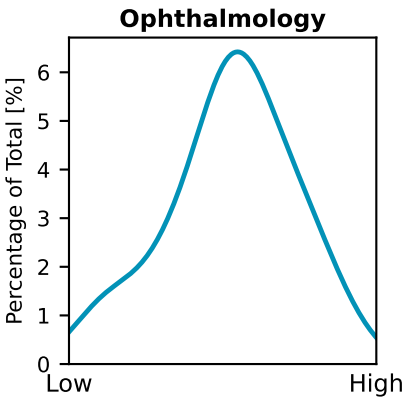

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