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Letter to the Editor

Persistent Worms, Cumulative Injury: A Digital Twin Approach to Onchocerciasis

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Dear Editor-in-Chief

Onchocerciasis, also known as river blindness, is a distinct infection, in which disease unfolds not through rapid progression but through prolonged biological coexistence (1). Following transmission by blackfly vectors, larvae mature into adult worms that reside in subcutaneous nodules and persist for many years. During this time, female worms continuously release microfilariae that migrate through the skin and ocular tissues. It is the host inflammatory response to these microfilariae, particularly when they die, that drives progressive tissue injury (1). Unlike acute infections, onchocerciasis imposes a gradual but relentless burden (1,2).

Skin inflammation, depigmentation, pruritus, and nodular disease accumulate slowly, while ocular involvement can progress from subtle visual disturbance to irreversible blindness (1,2). Neurological manifestations, including epilepsy in endemic regions, further extend the disease beyond its traditional dermatological and ophthalmological framing (2). Importantly, the severity and pattern of disease vary markedly between individuals, even within the same transmission setting (2).

Current management strategies focus on population-level control rather than individual disease modelling. Repeated mass drug administration with ivermectin suppresses microfilarial loads and reduces transmission, yet it does not eliminate adult worms, nor does it fully

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prevent long-term tissue damage in all individuals. Clinical monitoring is episodic, and tools to anticipate who will develop severe disability are limited. This reflects a broader challenge: onchocerciasis is a time-dependent disease, yet it is managed using static assessments.

Digital twin technology (Fig. 1) provides a framework suited to capturing slow, cumulative disease processes (3). A digital twin is an adaptive virtual model that evolves alongside its physical counterpart, updating predictions as new data are acquired. In healthcare, such models offer the capacity to simulate disease trajectories, evaluate intervention strategies, and personalise risk assessment (4). Applied to onchocerciasis, a digital twin enables the integration of parasite persistence, treatment cycles, immune responses, and tissue injury into a single longitudinal model (5). At the core of an onchocerciasis digital twin is a parasite longevity and reproduction layer. This layer represents adult worm survival, microfilarial production rates, and the temporal relationship between parasite burden and tissue exposure. Because adult worms persist for many years, this layer introduces a long memory into the system, where early infection events shape disease expression far into the future. A treatment and parasite suppression layer captures the effects of repeated ivermectin administration. Rather than treating treatment as a binary event, the digital twin models cumulative drug exposure, adherence patterns, and inter-treatment intervals. This allows simulation of how different treatment schedules influence microfilarial dynamics and long-term morbidity, highlighting why some individuals continue to accumulate damage despite participation in control programmes. An immune-mediated injury layer represents host inflammatory responses to microfilarial death. This layer is central to understanding disease progression, as immune activation drives skin pathology, ocular damage, and neuroinflammation (2). The digital twin tracks inflammatory trajectories over time, enabling distinction between individuals who mount self-limiting responses and those who develop chronic immune-mediated injury (5). A tissue damage and disability layer translate biological processes into functional outcomes. This includes progressive visual impairment, skin disease severity, and neurological sequelae that affect quality of life and socioeconomic participation (2). By modelling disability as an evolving process rather than a fixed endpoint, the digital twin can forecast long-term burden and identify windows for intervention before irreversible harm occurs. Contextual modifiers form an additional layer, incorporating factors such as age at infection, intensity of exposure, nutritional status, and co-infections. These variables influence immune competence and tissue resilience, shaping how disease manifests across individuals. Inclusion of contextual data allows the digital twin to represent heterogeneity within endemic populations more accurately than population averages.

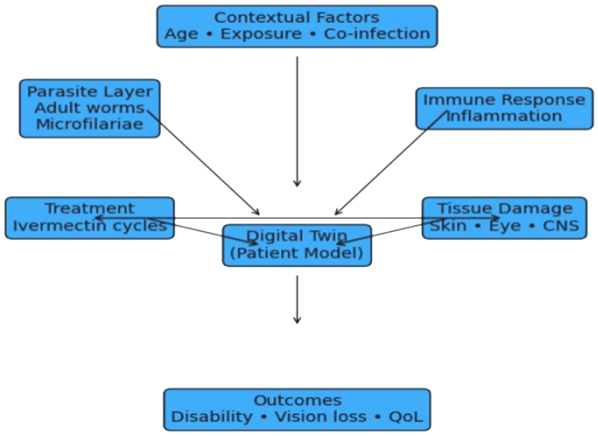

Fig. 1: Digital twin model of onchocerciasis. A patient-specific digital twin integrates parasite burden, treatment dynamics, host immune responses, and tissue pathology within a continuously updated framework. Contextual factors modulate disease progression, enabling prediction of clinical outcomes and supporting personalized interventions

The translational value of an onchocerciasis digital twin lies in its capacity to support morbidity-focused precision strategies. Rather than

evaluating success solely by reductions in transmission, the model enables prediction of individual disability trajectories and optimization of treatment timing to minimize cumulative harm (3,5). In silico experimentation can explore alternative strategies, such as intensified treatment for high-risk individuals or adjunct approaches targeting inflammation and tissue repair. At a population level, aggregated digital twins could inform elimination programmes by identifying subgroups likely to sustain residual morbidity despite reduced transmission. This has important implications for post-elimination surveillance, where the focus shifts from infection control to long-term health outcomes. A digital twin framework supports this transition by linking past exposure and treatment history to future disability risk. However, limited access to longitudinal clinical data and variability in outcome assessment across endemic settings remains a challenge (6). Validation of predictive models will require sustained follow-up and integration with existing control programmes (7). Ethical considerations are also critical, particularly in ensuring that digital tools enhance equity rather than exacerbate disparities (8). Nevertheless, advances in digital health platforms and community-based data collection make the implementation of such models increasingly realistic.

Conflict of interests

The authors declare no conflict of interests.

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