Supplementary material:
Computational design of treatment strategies for proactive therapy on atopic dermatitis using optimal control theory

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We conducted sensitivity analysis to confirm that the optimal strategies calculated for the nominal parameter set (Tables 1 and 2) are robust to the choice of the model parameters and the weighting coefficients for the objective function. The robustness was evaluated by whether

- the duration of the optimal induction phase ($T_i$) corresponds to the clinically accepted range of 2-3 weeks,
- the duration of the optimal treatment period in each of the maintenance phase ($T_i^c$) corresponds to 2-3 days (weekend therapy), and
- the lower potency of corticosteroid can achieve the maintenance compared to that required for the induction phase ($C > C^i$).

1 Sensitivity to risk factors ($\kappa_P, \alpha_I$)

We calculated the optimal treatment strategies for $N = 1600$ combinations of ($\kappa_P, \alpha_I$) within the ranges $0.83 \leq \kappa_P \leq 1$ and $0.03 \leq \alpha_I \leq 0.06$ (Fig. S1). Among the 1600 combinations, 683 combinations successfully achieved the remission, and their calculated optimal treatment strategies for both the induction and maintenance phases are robust to the changes in the values of ($\kappa_P, \alpha_I$) (Fig. S2).

Fig. S 1: Characterisation of the calculated optimal treatment strategies for the induction phase for different combinations of ($\kappa_P, \alpha_I$). The black circle represents the nominal parameter pair ($\kappa_P, \alpha_I$) = (0.85, 0.05).

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Fig. S 2: Sensitivity of the calculated optimal treatment strategies with respect to the changes in \((k_p, \alpha_I)\), weights for the objective function terms \((k_i)\), and model parameters. The values shown are mean \pm std.

2 Sensitivity to weights of objective functions \((k_1^r, k_2^r, k_3^r, k_4^r, k_1^m, k_2^m, k_3^m, k_4^m)\)

To see the sensitivity of the optimal treatment strategies to the weights for the objective function terms, we varied eight weights simultaneously by \(\pm 50\%\) from their nominal values \((N = 400)\): four for the induction phase \((k_1^r, k_2^r, k_3^r, k_4^r)\) and four for the maintenance phase \((k_1^m, k_2^m, k_3^m, k_4^m)\). We assumed \(k_2^r = k_2^m\) since the efficacy of the corticosteroid treatment is the same in both remission and maintenance phases. Our analysis (Fig. S2) confirmed that the calculated optimal treatment strategies were robust to the changes of the weighting parameters.

3 Sensitivity to model parameters \((\gamma_B, \delta_P, \kappa_B, \gamma_R, \gamma_G, \delta_B, \beta_1, \beta_2, \beta_3)\)

To see the sensitivity of the optimal treatment strategies to the model parameters, we varied them simultaneously by \(\pm 50\%\) from their nominal values \((N = 529)\). Our analysis (Fig. S2) confirmed that the calculated optimal treatment strategies were robust to the changes in the model parameters.