Antimalarial drug resistance in *P. falciparum* malaria in Tanzania: Current status and challenges

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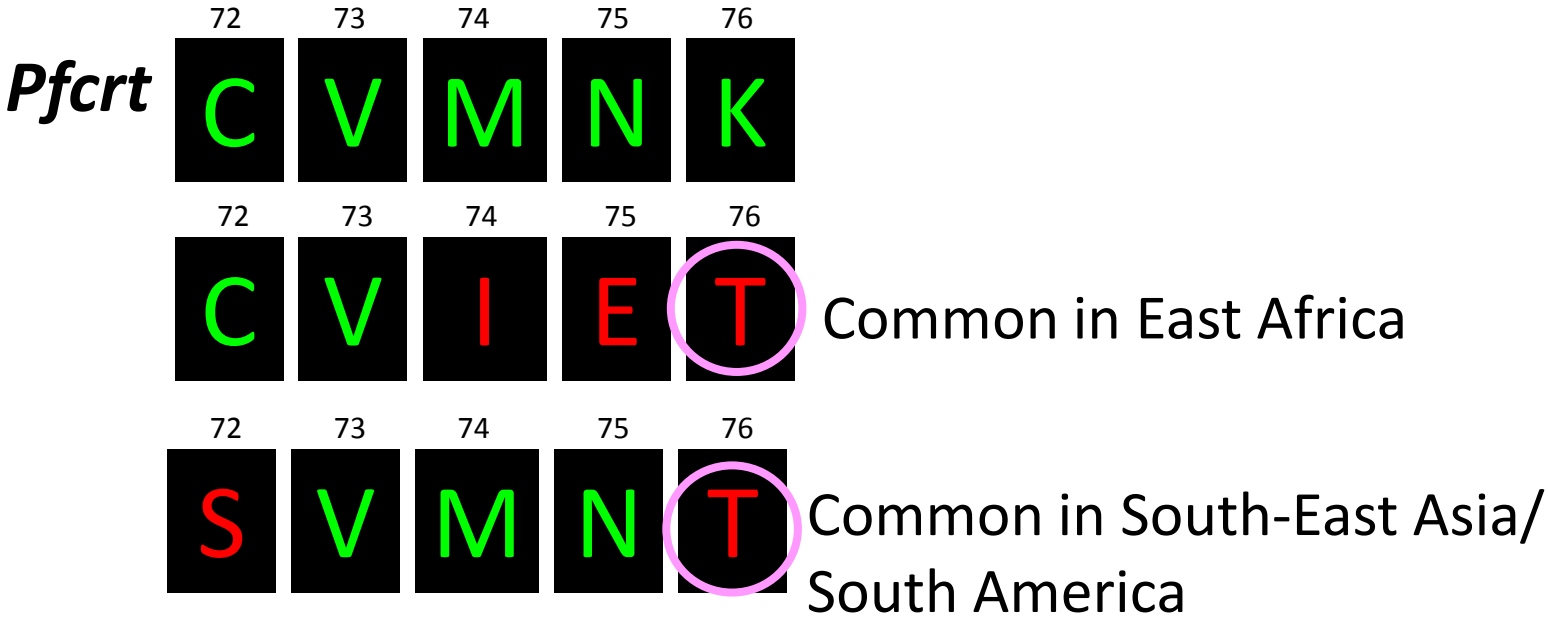
Commonly used antimalarials

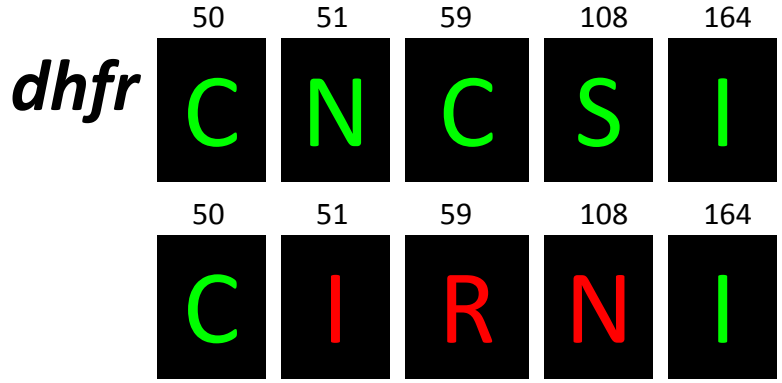
- Chloroquine (CQ) – up to 2001
- Sulphadoxine-pyrimethamine (SP) up to 2006
- Artemisinin-based combinations (ACTs) – currently

CQ resistance



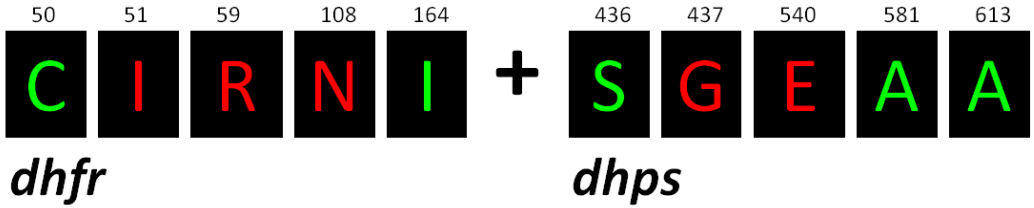
Pfcrt 76T – strong predictor of CQ resistance

SP resistance

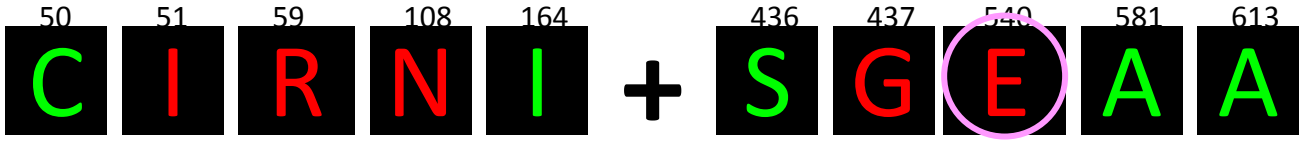


*Dhfr **triple** mutation*
High Pyrimethamine resistance

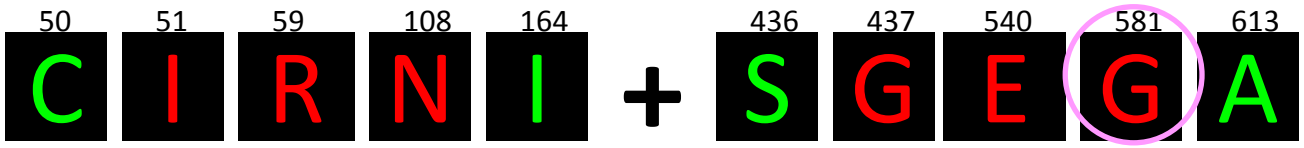
*Dhps **double** mutation*
High sulphadoxine resistance



Quintuple - High SP resistance



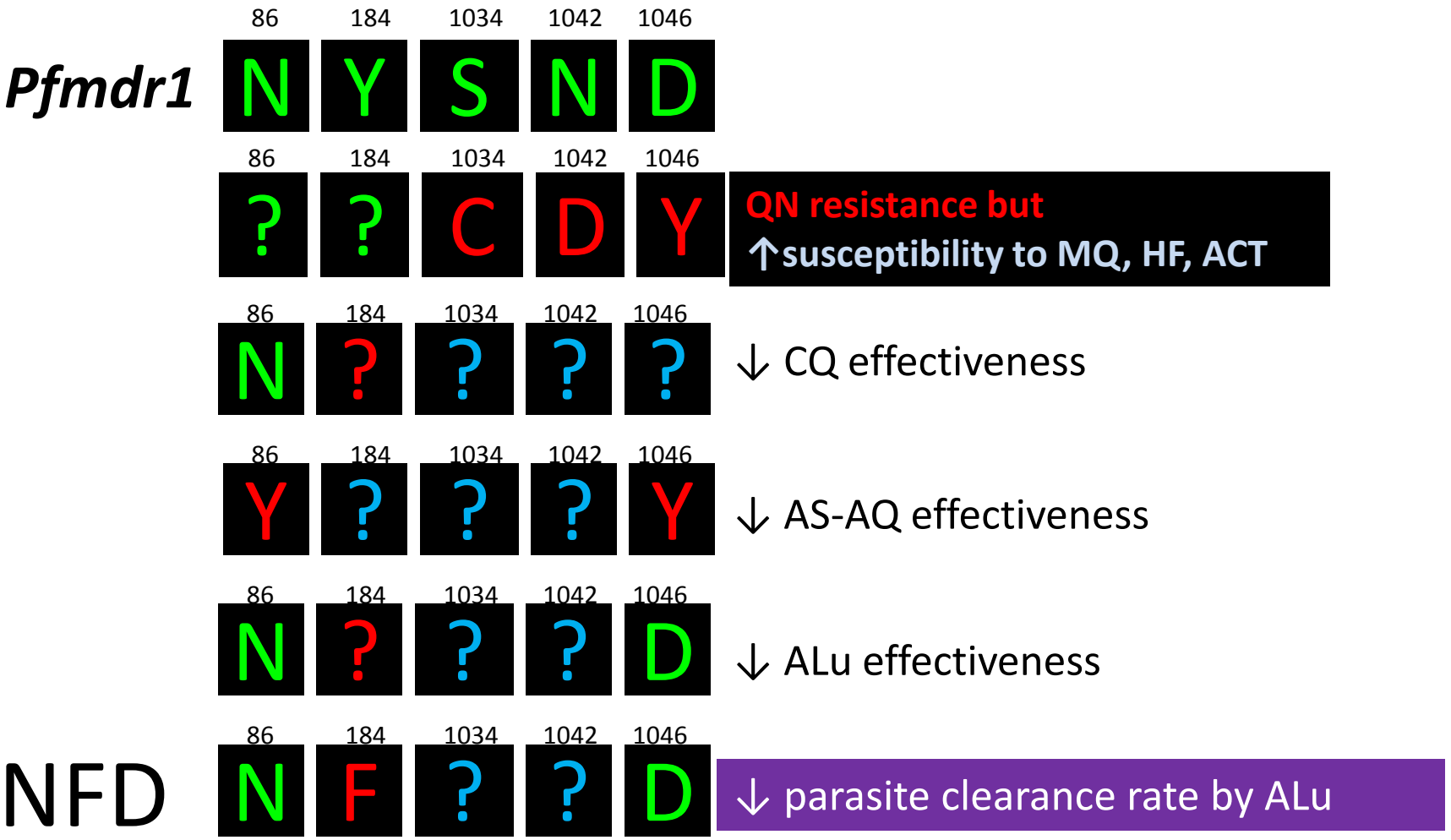
540E – a strong predictor of treatment failure



581G mutation, SP super-resistance

ACT resistance

- Pfmdr1 Mutations



Replacement of CQ in 2001

- Was complete
- CQ use was banned
  - It remained for prophylaxis and treatment of malaria in sickle cell

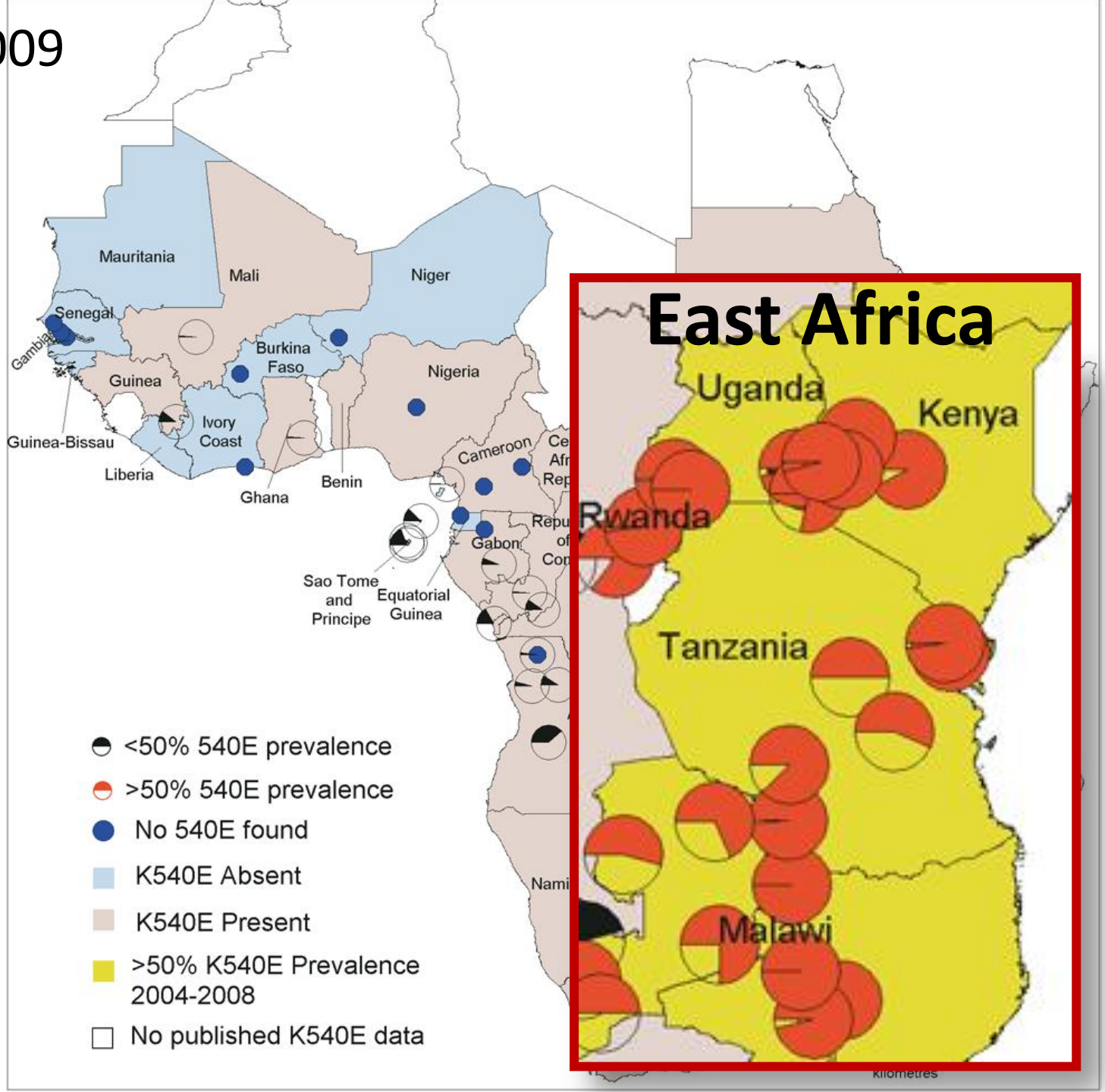
- SP was first line
- However SP was already in use before
  - SP policy = transient,
  - Replace by ACTs in December 2006

- SP continued in IPTp and IPTi programmes

- IPTp and IPTi, very effective in reduction of malaria, reduction of maternal and infant mortality

- In 2010 WHO (2010) recommended application of IPT where dhps 540E is < 50%

Roper *et al*.,2009



Country	**Author/year**	**Mutation (K540E)**
Tanzania (Morogoro)	(2006) Malisa *et al.,* 2011	70%
Tanzania (Mbeya)	(2005) Schonfeld *et al*., 2007	77.4%
Tanzania (Korogwe)	(2006) Gesase *et al*., 2009	94.3%
Rwanda	(2005) Karema *et al*., 2010	84%→97%
Kenya	(2006-2007) Bonizzoni *et al*., 2009	74%→99%
Uganda	(2002-2004) Lynch *et al.,* 2008	98%→100%
Mali	(2006) Dicko *et al*., 2010	1.6%
Senegal	(2009-2010) Wurtz *et al.,* 2012	0%

Where are we currently?

CQ resistance surveillance in Tanzania 2010 - 2011

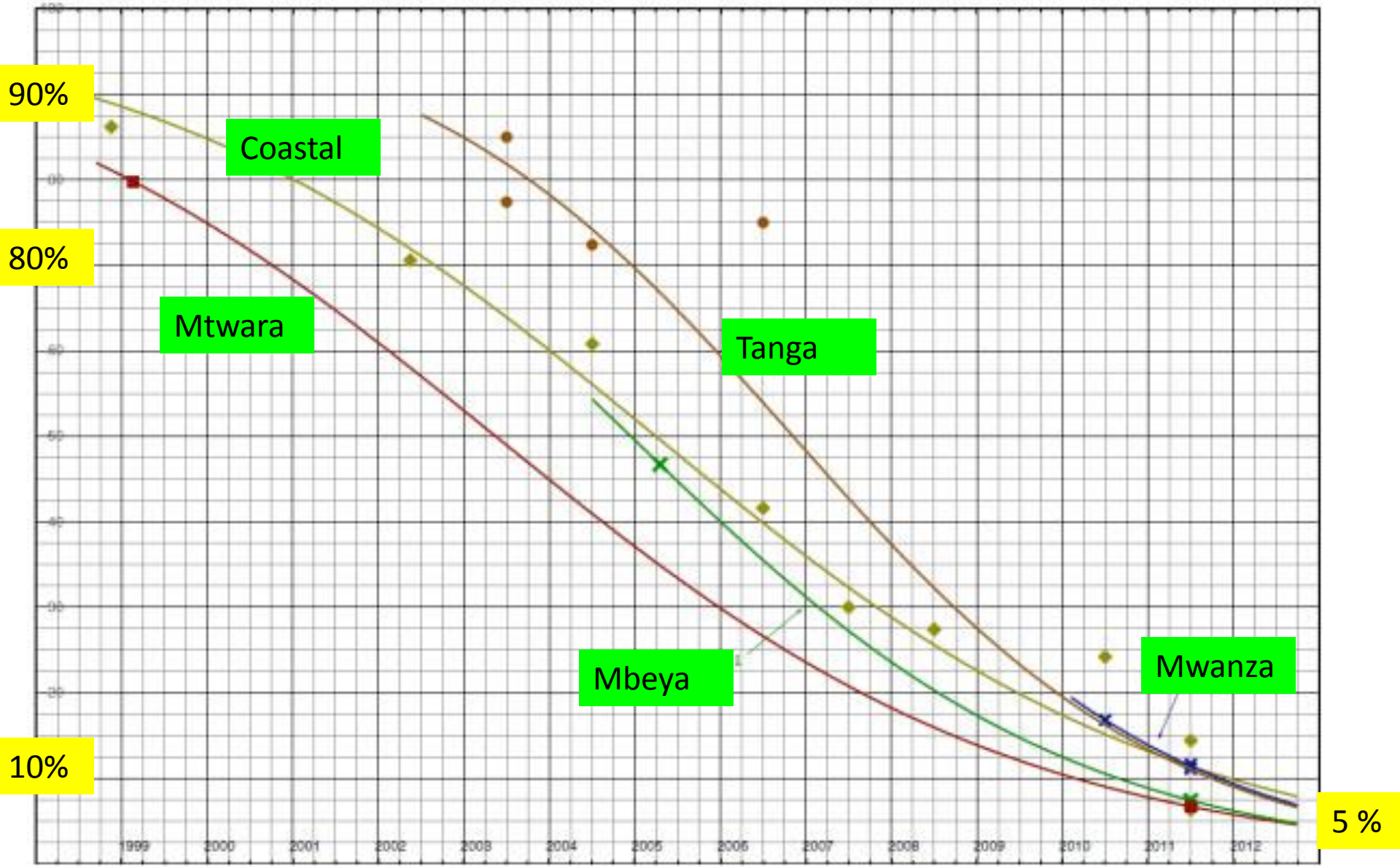
Table 1: Distribution of *Pfcrt* K76T resistance marker in 6 regions of Tanzania

	Frequency of K76T				Prevalence of K76
Region	**K76 (%)**	**76T (%)**	**Mixed**	**n**	**%**
Tanga	108 (94.7)	6 (5.3)	2	116	93.2
Coastal	130 (93.5)	9 (6.5)	0	139	93.5
Mtwara	66 (97.1)	2 (2.9)	3	71	93.2
Kagera	82 (92.1)	7 (7.9)	8	97	85.7
Mwanza	150 (93.2)	11(6.8)	10	171	88.4
Mbeya	136 (95.1)	7 (4.9)	4	147	92.7
Overall	672 (94.3)	42 (5.7)	27	741	91

($\chi 2=7.88$, p=0.163)

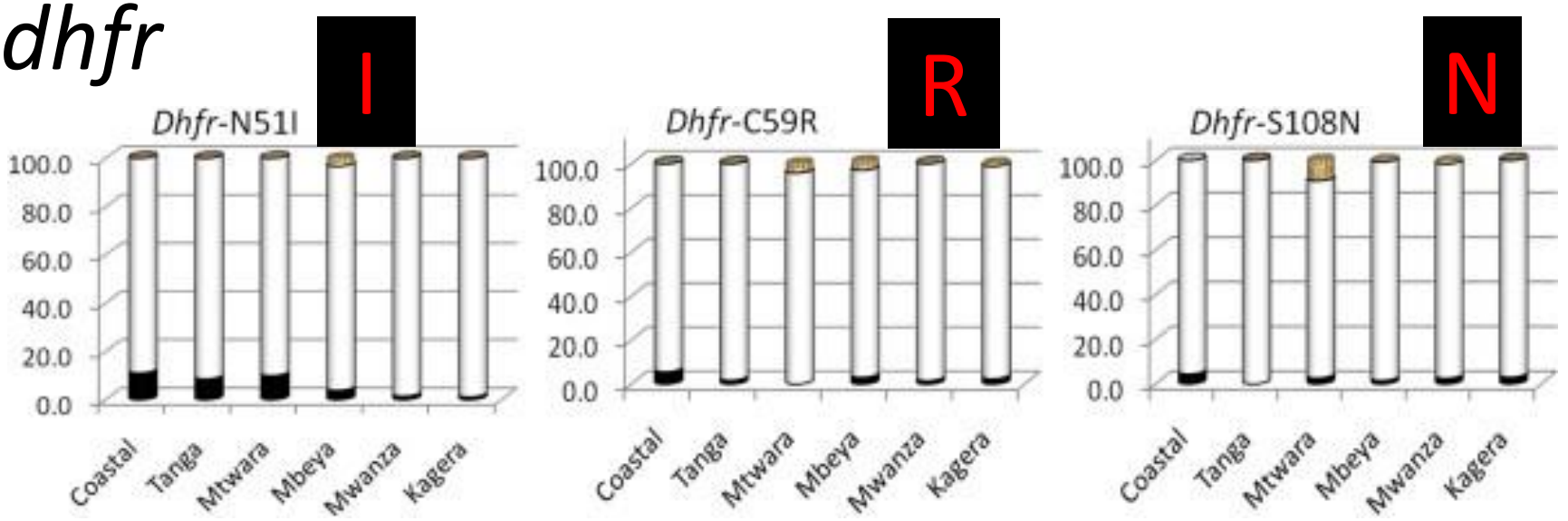
Mohamed et al, 2013

CQ resistance trends

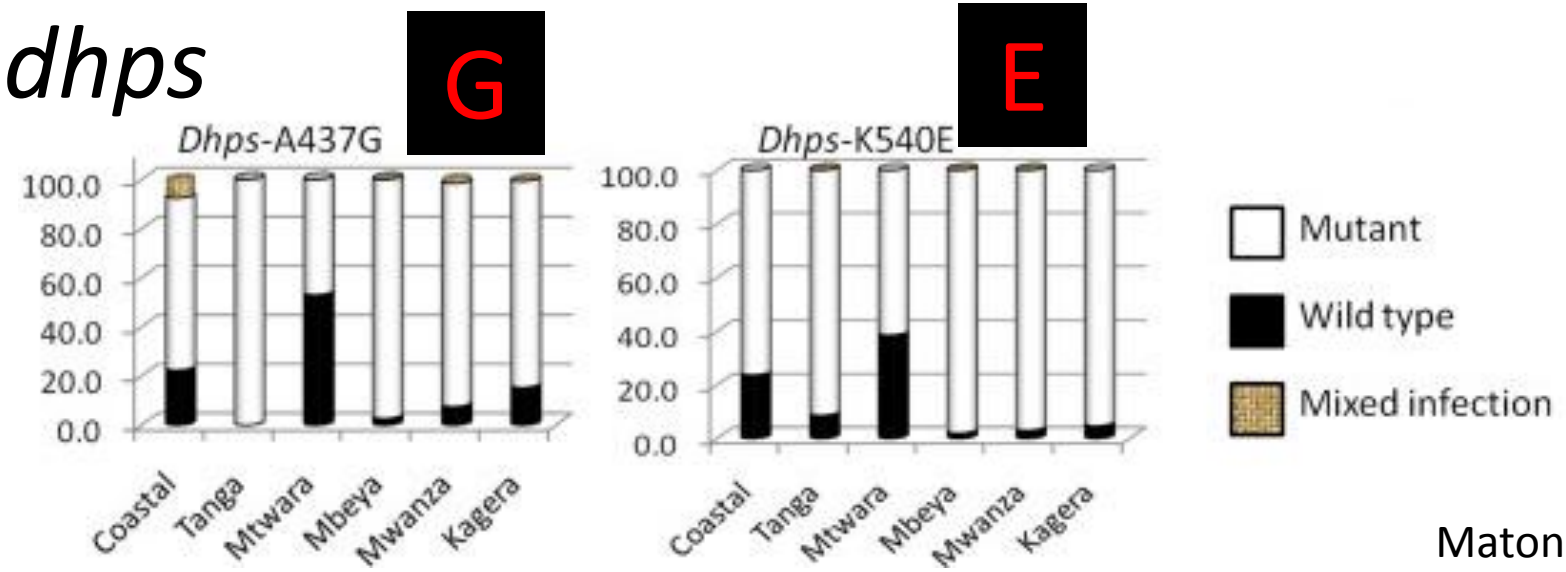


SP- resistance

dhfr



dhps

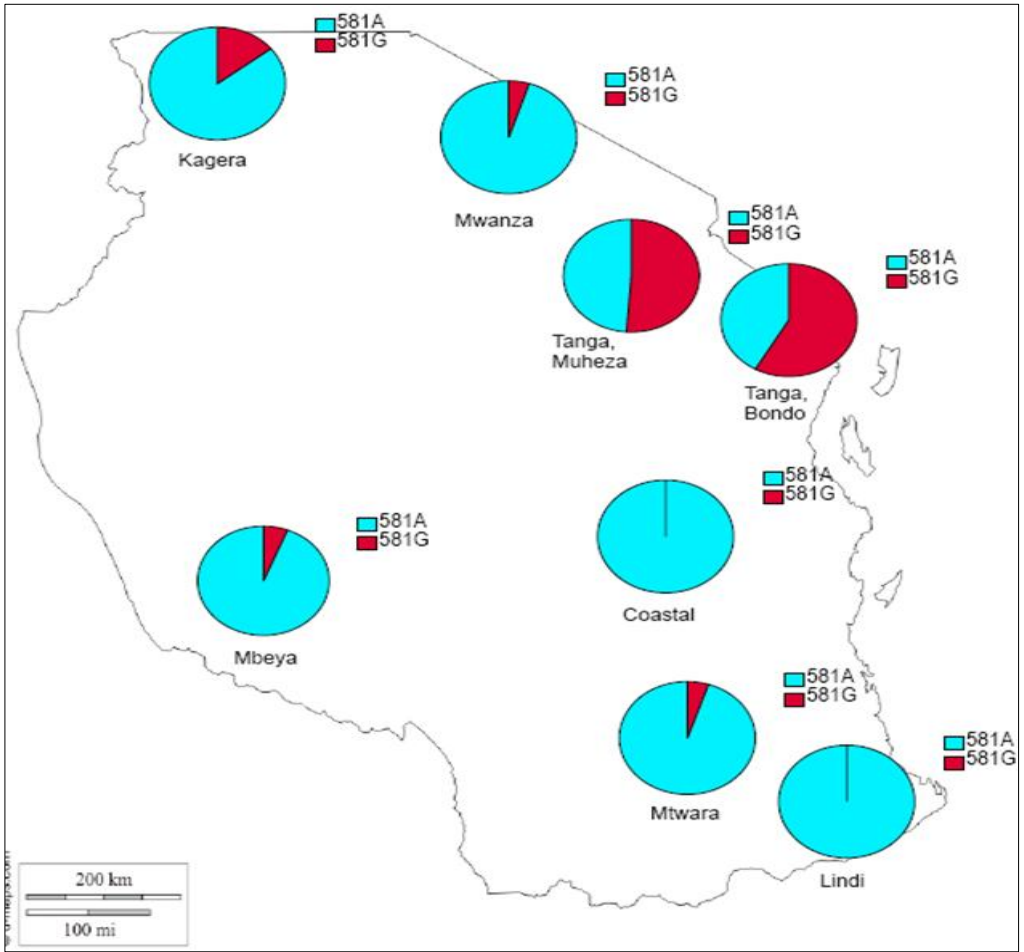


Matondo et al, 2014

Pfdhps 581G

- Super resistance to Sp
- IPTP failure (Minja DT et al 2013)

<u>Dhps 581G</u>
Tanga – 55%
Kagera – 20%

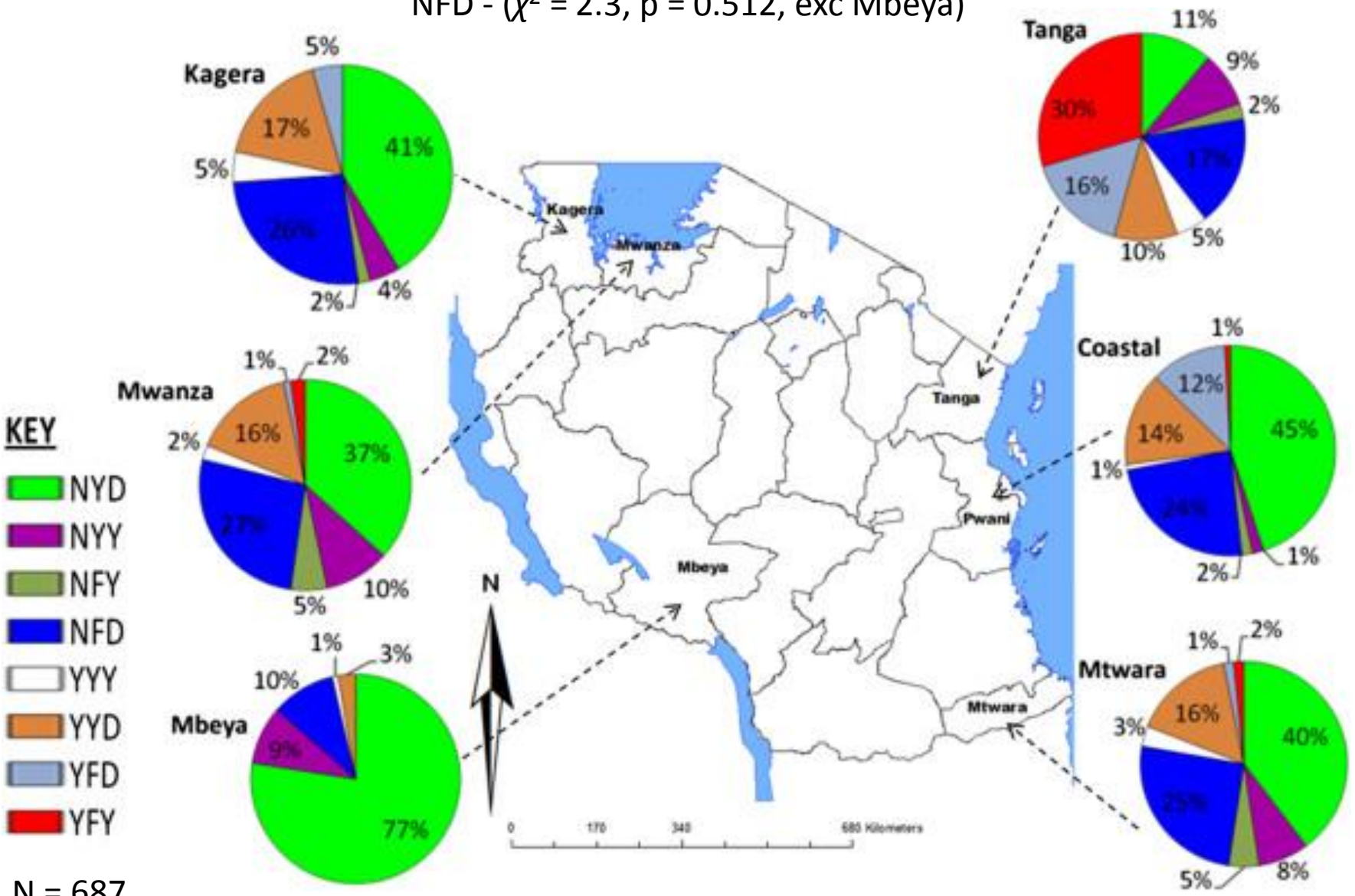


Kavishe et al, in preparation

ACT resistance

- NFD polymorphisms in Tanzania

NFD - (χ^2 = 2.3, p = 0.512, exc Mbeya)



N = 687

Kavishe RA et al 2014

Conclusions

- CQ resistance down to app 5%
  - Well implemented ban
  - Possible return of CQ in treatment,
  - Increase restriction on CQ importation and use for few more years? A decade?

- ACT resistance, though not confirmed in East Africa, rise in ALu associated polymorphisms = alarm for intensified pharmacovigilance studies
  - K13 propeller – a matter of time to enter African shores

- High SP resistance an alarm for SP-IPT programmes

- WHO (2012)
  - IPTp should continue even if quintuple mutations are >90%
- The emergence and spread of dhps 581 – threat
- WHO 2013 recommendations:
  - Need more data on dhps 581 for informed decisions

- Current observations in Tanzania
  - Urgent need to find alternative to SP for IPTp in E. Africa
  - In west Africa – situation is different
  - However, resistance levels also growing

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