



Technology Assessment of Next Generation Sequencing in Personalized Oncology

Zorginstituut Nederland

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Rationale

- Large variability of sequencing/NGS tests in the Netherlands
- Increased use of immunotherapy, while this is effective for only a small part of the patients

Consequences:

↑ Toxicities

↓ QoL

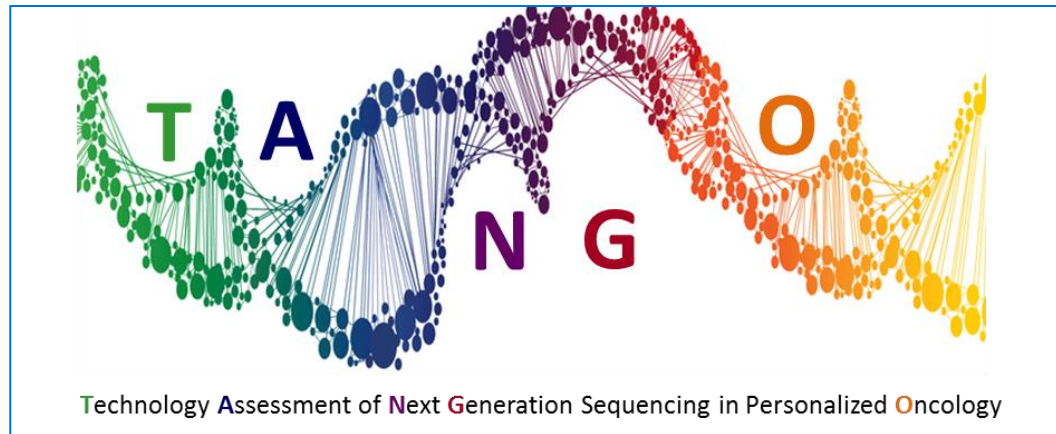
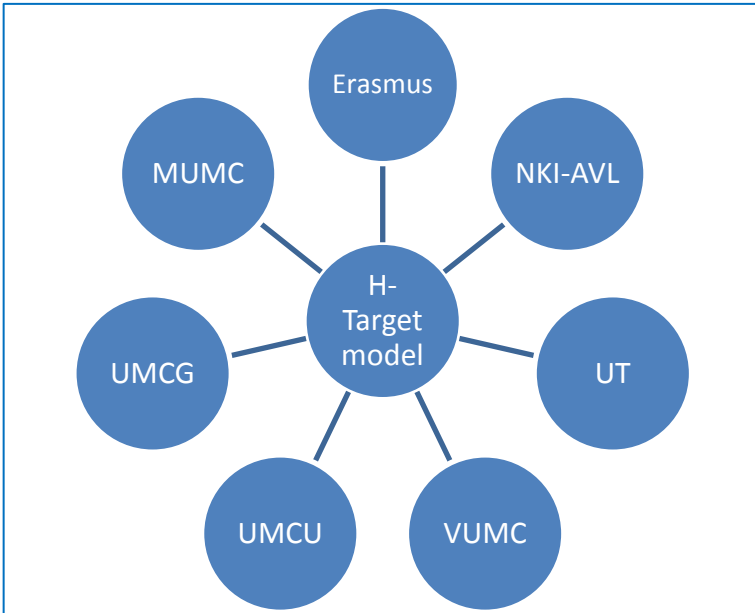
↑ Health care costs



ZonMW GGG ronde Personalized Medicine

RQ: *How can we optimize the use of NGS in the Netherlands?*

HTA-network meets CPCT



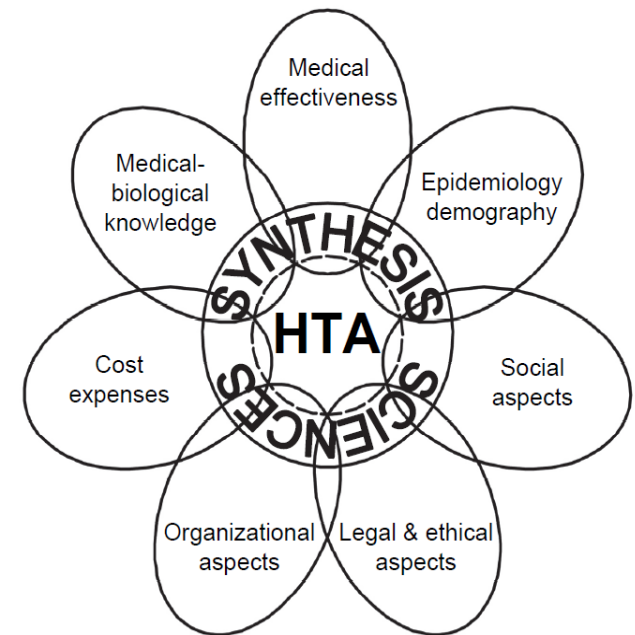
TANGO

Technology Assessment

HTA: broad evaluation of new or existing health technologies

- Clinical effectiveness
- Financial (cost-effectiveness)
- Patient related
- Ethical/legal
- Organizational

- Information for policy making
- Decision making for groups of patients

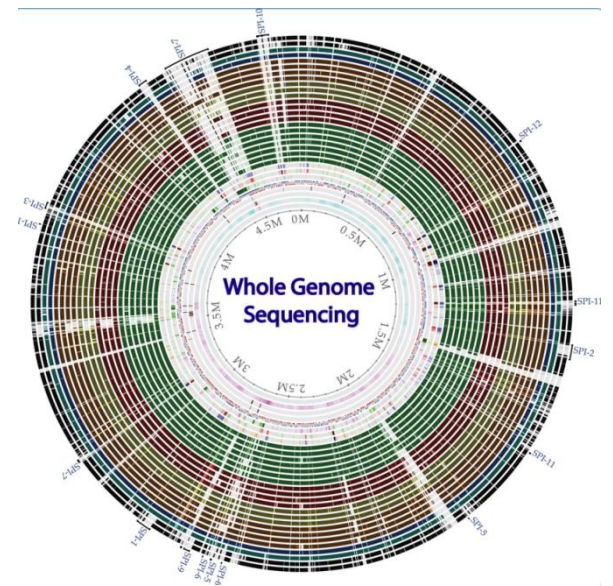


TANGO

Next Generation Sequencing in Oncology

- Tests for all relevant mutations in 1 experiment
- To prescribe the most optimal therapy
- This could improve survival with less toxicity

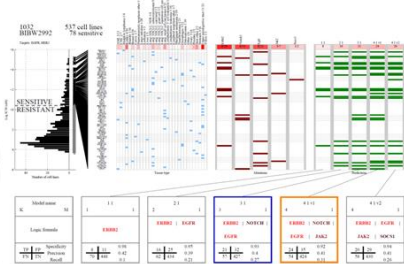
- Assist in controlling healthcare costs :
→ Offering (often expensive) treatment to only those likely to benefit.



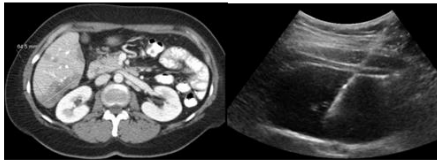
Center for Personalized Cancer Treatment (CPCT)



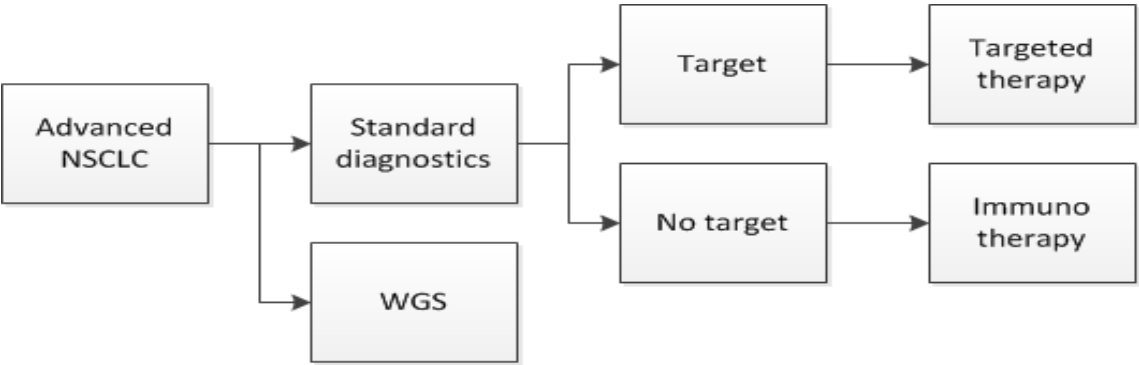
Treat patient with selected drug(s) until disease progression



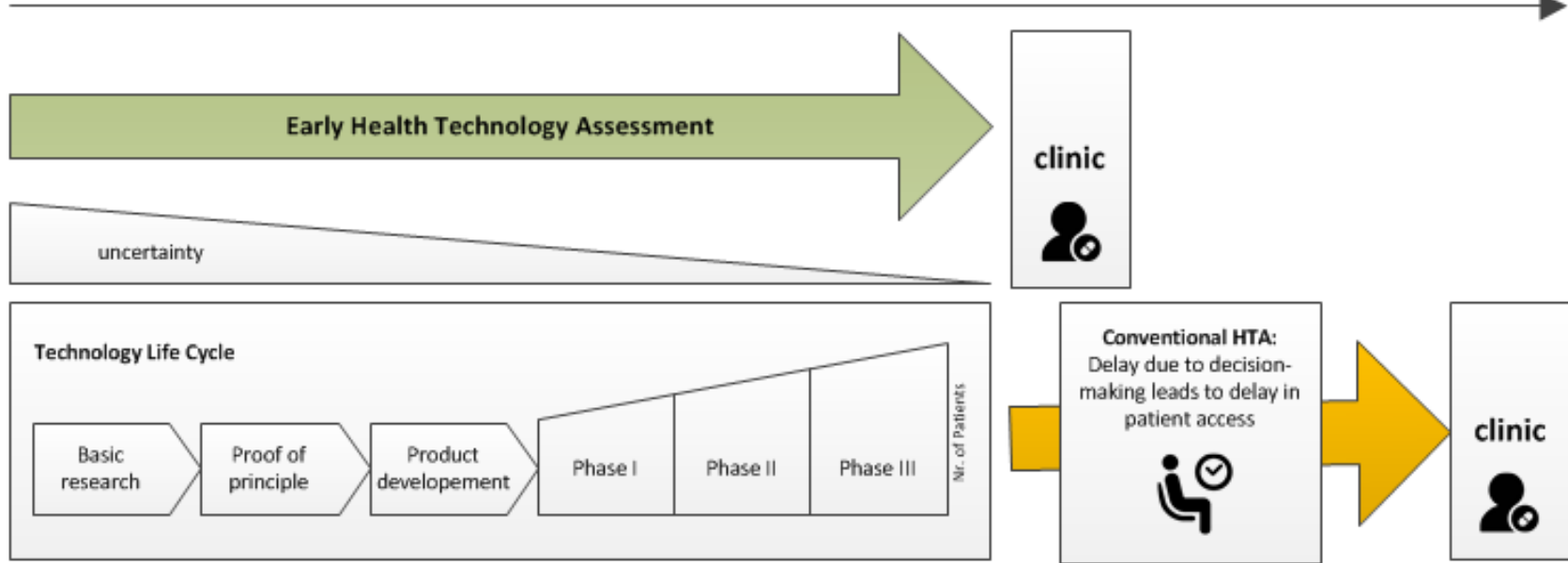
Bioinformatics and Systems Biology to identify pathways



Obtain patient biopsy



Early HTA



- little data available
- technology still dynamic
- adoption limited

“it is always too early, when it is suddenly too late”

-> anticipation!



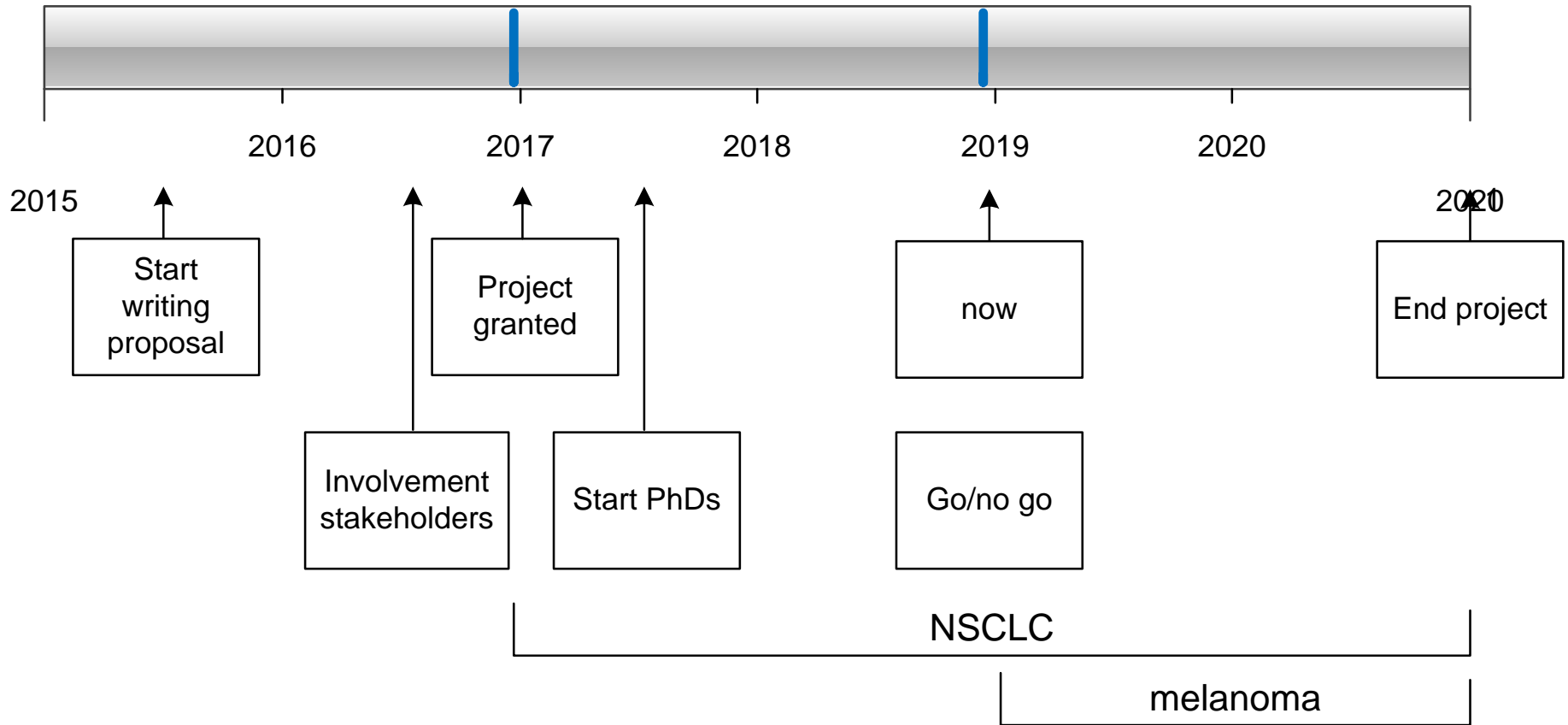
Purpose TANGO

A) to expand molecular profiling of tumors in order to improve immune- and targeted treatment selection and outcomes in patients with advanced NSCLC (and melanoma)

B) to project long-term cost-effectiveness, budget impact, and relevant patient & organizational issues related to the introduction of WGS compared to standard diagnostics.

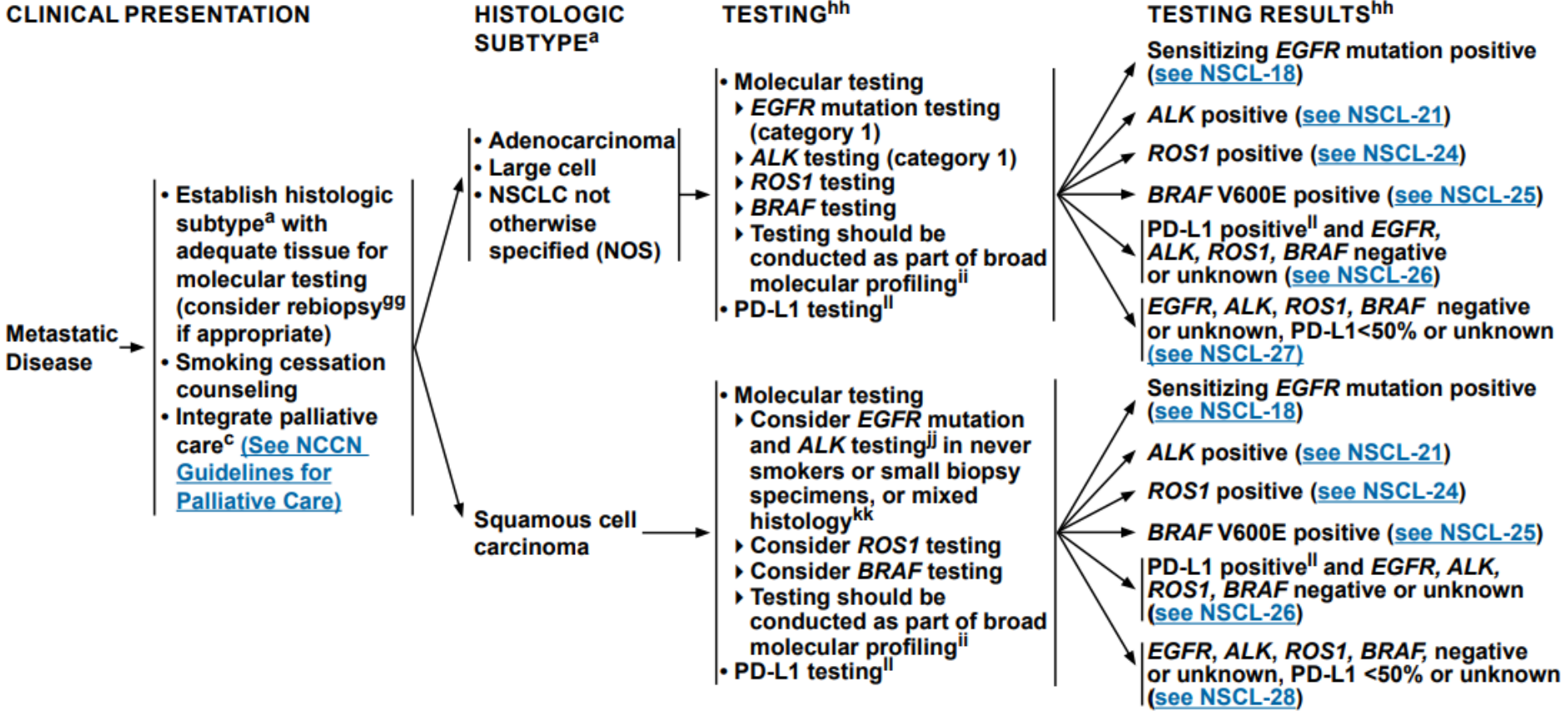


Timeline

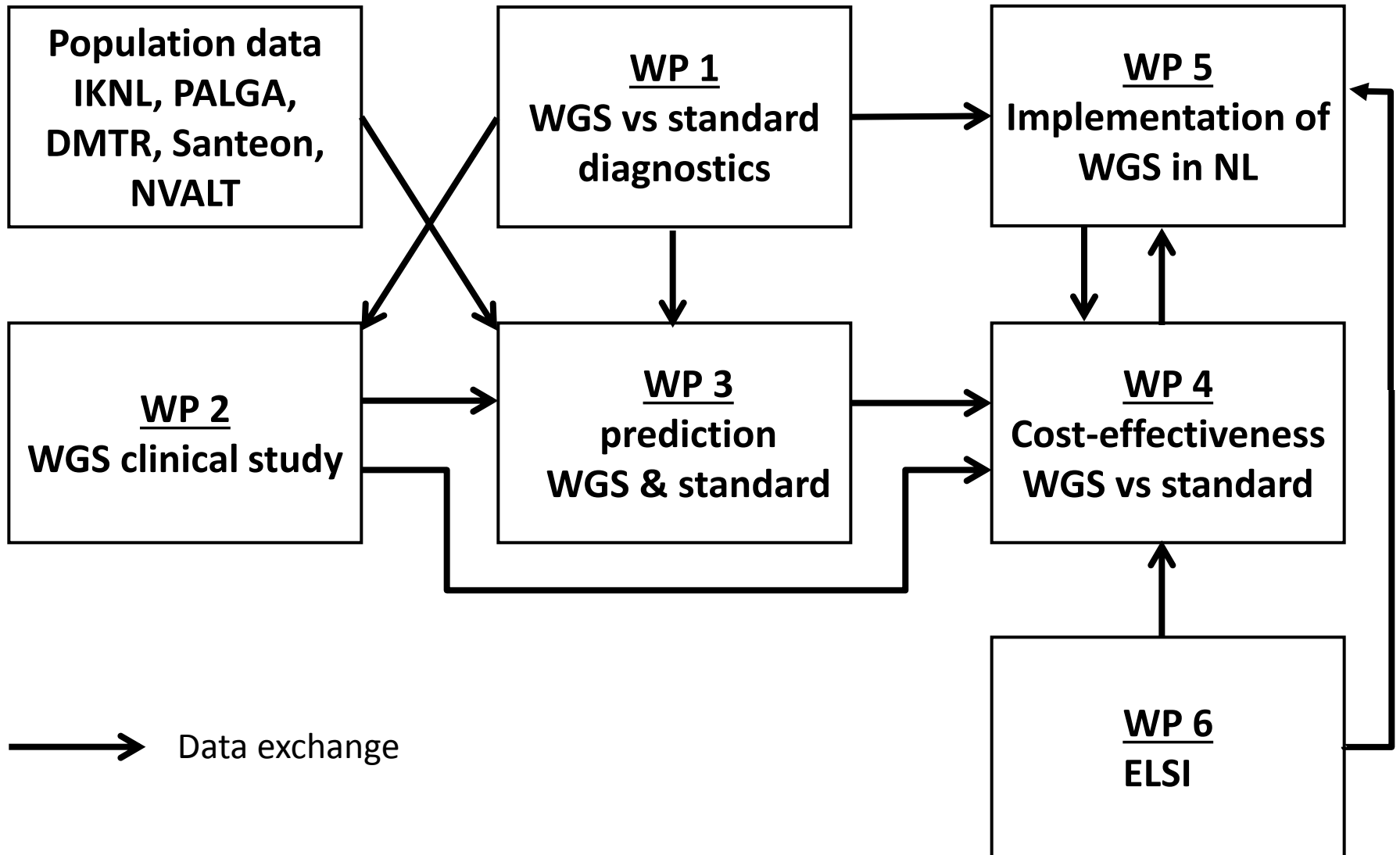




Clinical pathway NSCLC

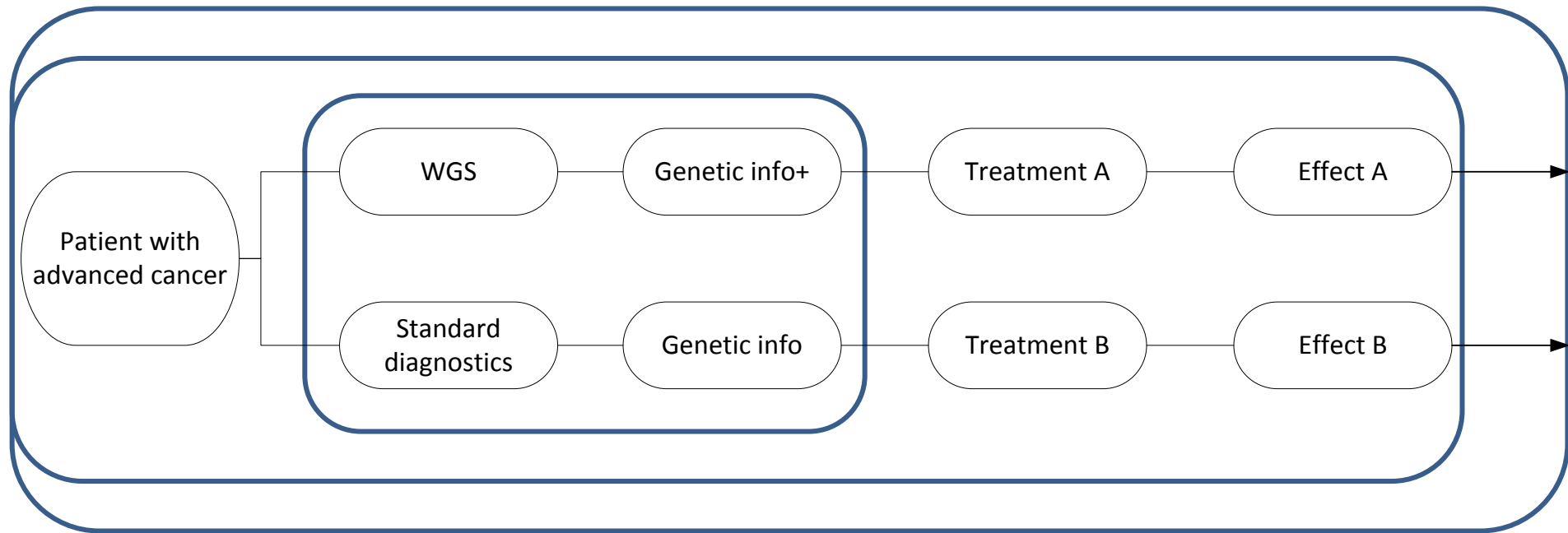


Workpackages





Patient pathway (micro level)



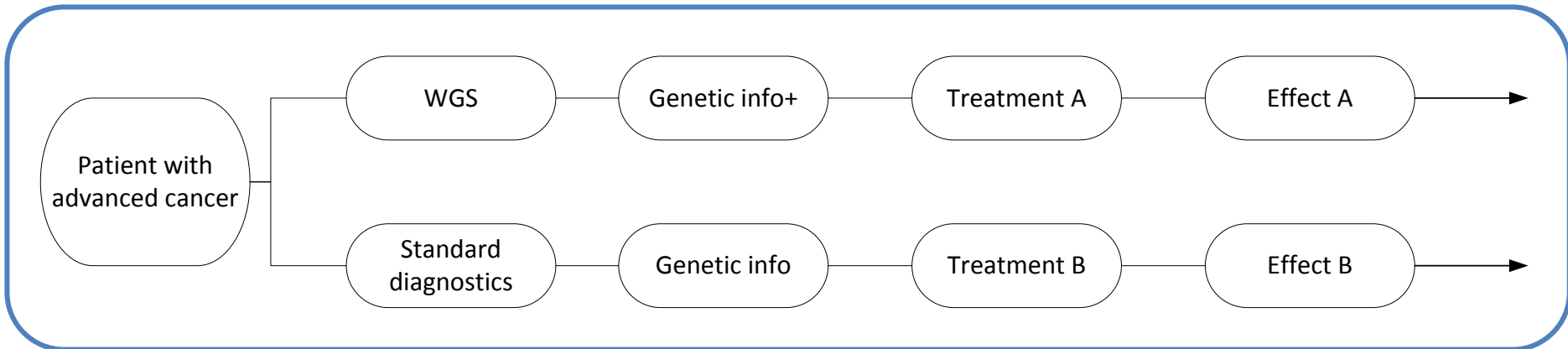
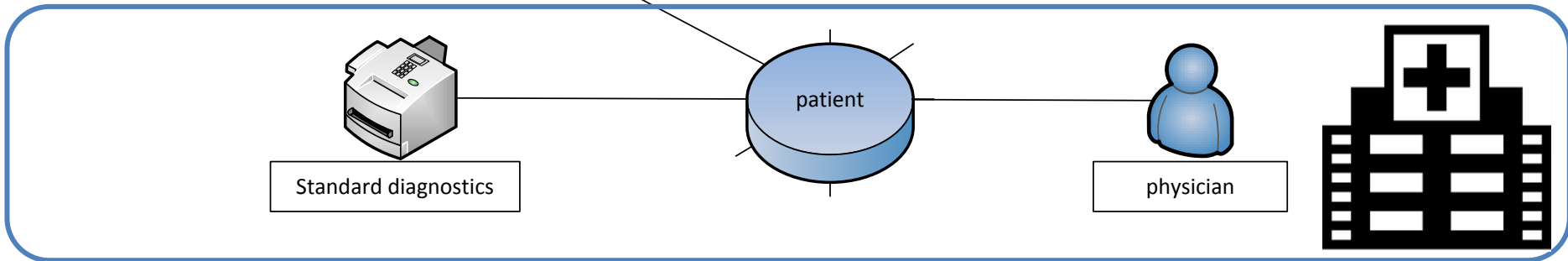
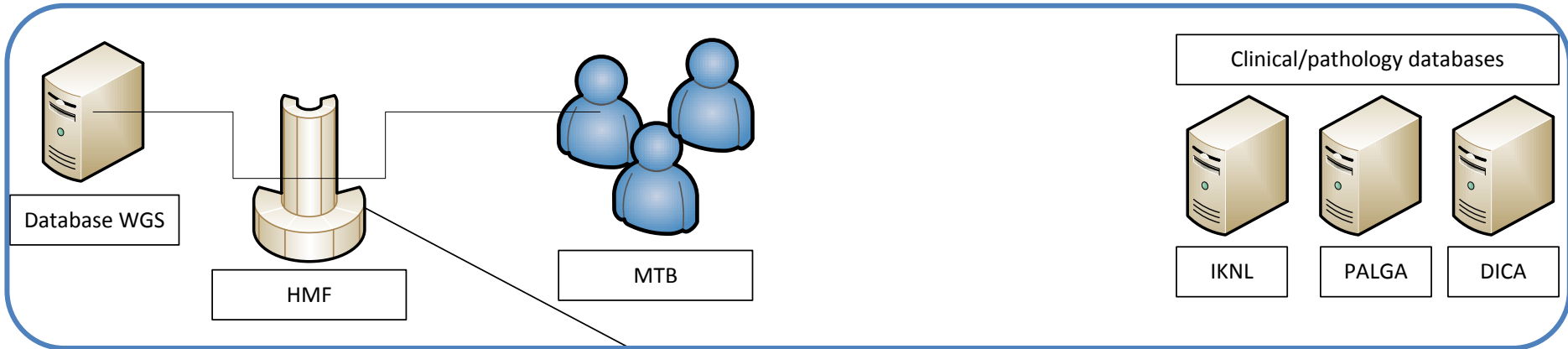
WP1 diagnostic pathway

WP2 diagnostics + treatment + survival

WP3,4 diagnostics + treatment longer FU, costs, QoL

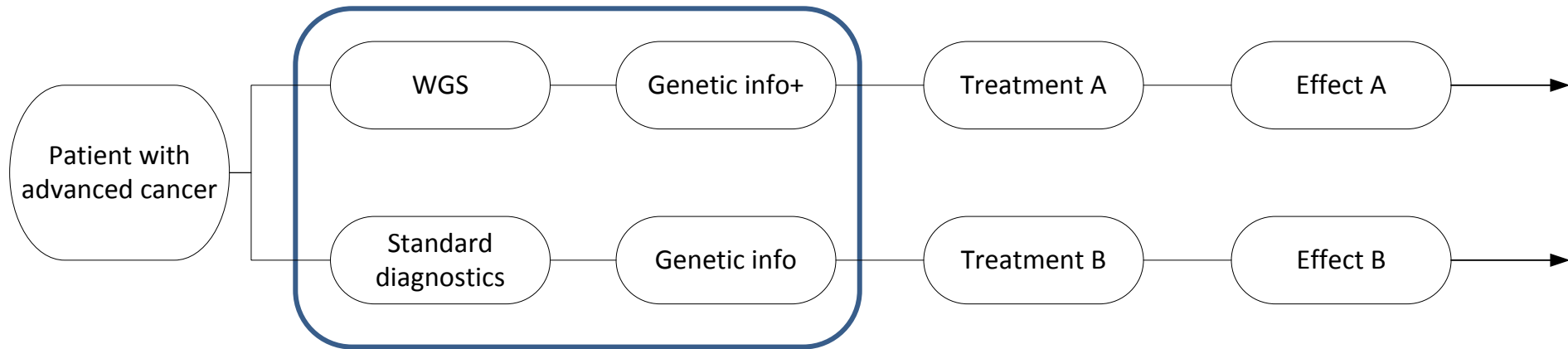
System level

WP4,5,6





Patient pathway (micro level)



WP1 diagnostic pathway

WP2 diagnostics + treatment + survival

WP3,4 diagnostics + treatment longer FU, costs, QoL



Standard diagnostics vs WGS

- Analysis standard diagnostics results vs WGS
 - number of targets
 - type of targets
 - costs
- Organization Molecular Tumor boards (in collaboration with PATH project)

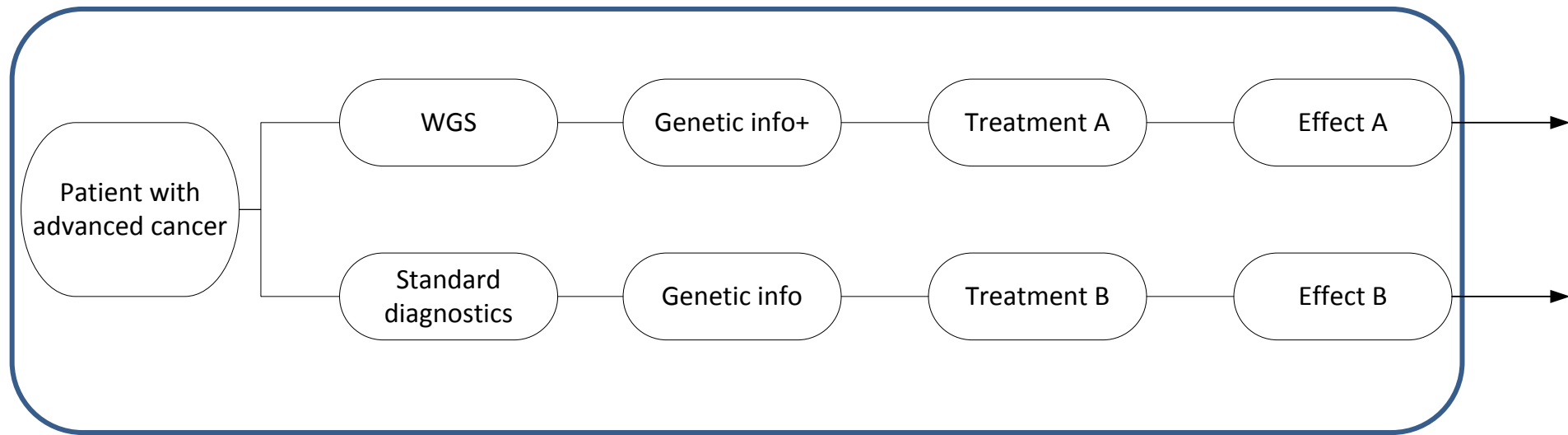


Costs of diagnostics

- Costs WGS (HMF)
 - Costs current diagnostics (PATH)
 - Costs current diagnostics with total diagnostic pathways (ZA codes)
 - UMCU
 - NKI-AVL
 - Rijnstate
 - Linkage IKNL and PALGA data nationwide (NZa)
- } based on microcosting
} method (activity based)



Patient pathway (micro level)



WP1 diagnostic pathway

WP2 diagnostics + treatment + survival

WP3,4 diagnostics + treatment longer FU, costs, QoL



Status CPCT-02

	2016												2017												2018											
	04	05	06	07	08	09	10	11	12	01	02	03	04	05	06	07	08	09	10	11	12	01	02	03	04	05	06	07	08	09	10	11	12			
Included/month	3	6	5	2	6	7	7	8	9	9	6	15	9	6	16	10	7	8	18	18	12	21	20	22	18	24	28	15	7	9	5	0	0			
Included/year	53												134												169											
Sequenced/month	3	2	3	2	3	5	5	8	4	6	4	12	5	5	8	7	1	7	9	11	9	12	13	11	15	17	22	5	4	5	2	0	0			
Sequenced/year	35												84												106											
Sequenced + Immuno/month	3	1	2	1	1	0	0	2	2	1	0	7	1	2	2	5	1	3	2	3	5	4	5	3	6	4	9	3	1	1	0	0	0			
Sequenced + Immuno/year	12												32												36											
Included													356																							
Sequenced													225																							
Sequenced + Immuno													80																							



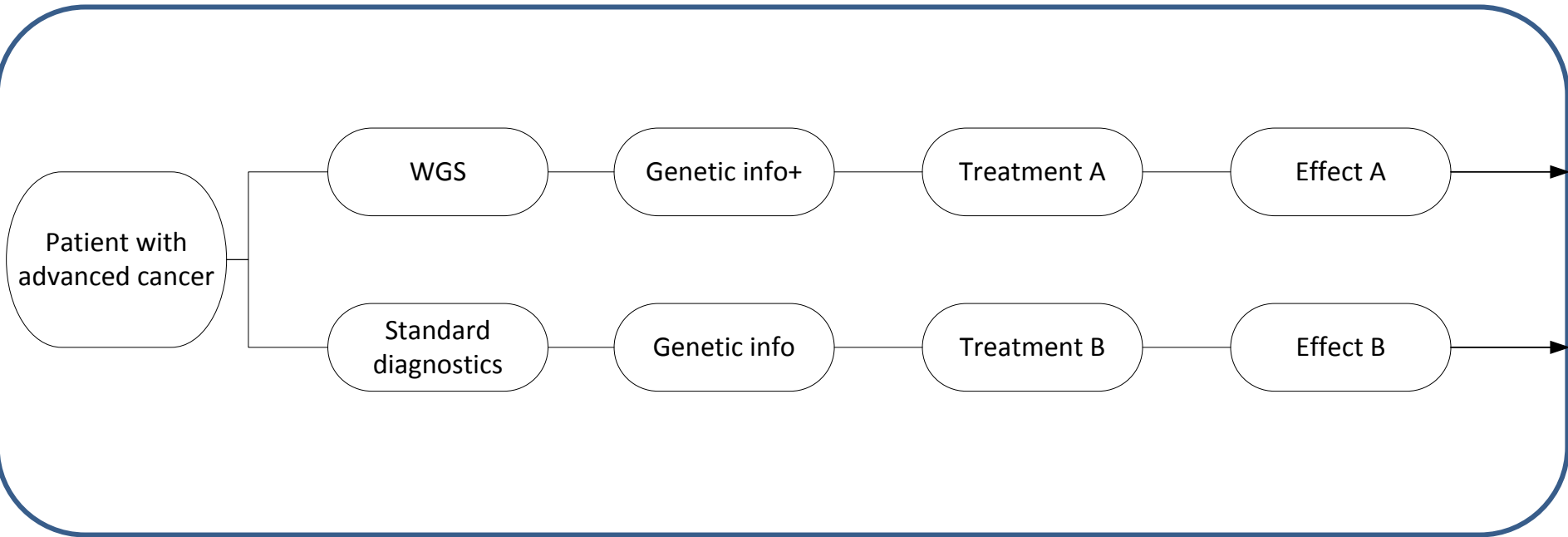
Statistical plan (WP1+2)

Confirmation findings biomarker by:

- Literature
- Larger sample
- Longer FU
- Clinical validation
- > e.g. Simon 2-stage design?



Patient pathway (micro level)



WP1 diagnostic pathway

WP2 diagnostics + treatment + survival

WP3,4 diagnostics + treatment longer FU, costs, QoL



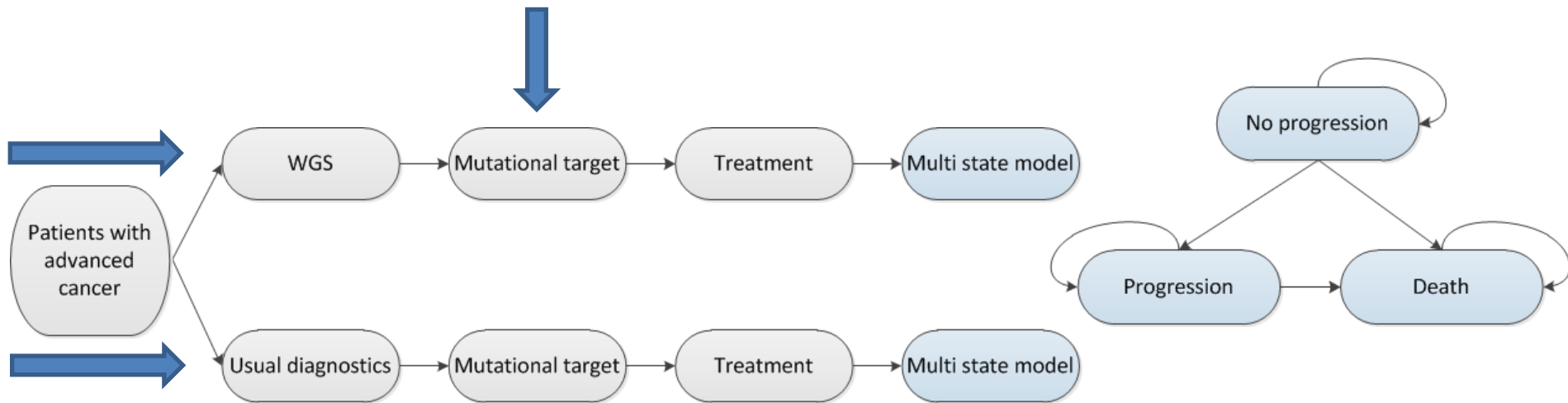
Long term survival from various databases

	CPCT-02 amendment questionnaires	DMTR	SANTEON	NVALT	IKNL
QoL	X				
utility	X				
Productivity	X				
Informal care	X				
Patient characteristics	X	X	X	X	X
Tumour characteristics		X	X	X	X
Treatment type					
Targeted therapy	X	X		X	X
Immunotherapy	X	X		X	X
Chemotherapy	X	X	X	X	X
other	X	X			X
Medicine type					
Targeted therapy		X		X	
Immunotherapy		X		X	
Chemotherapy		X	X		
other		X			
OS		X	X	X	X
PFS		X		X	
Toxicity		X	X	X	
Performance score		X	X	X	X
Mutation type		X		X	
Risk factors		X		X	



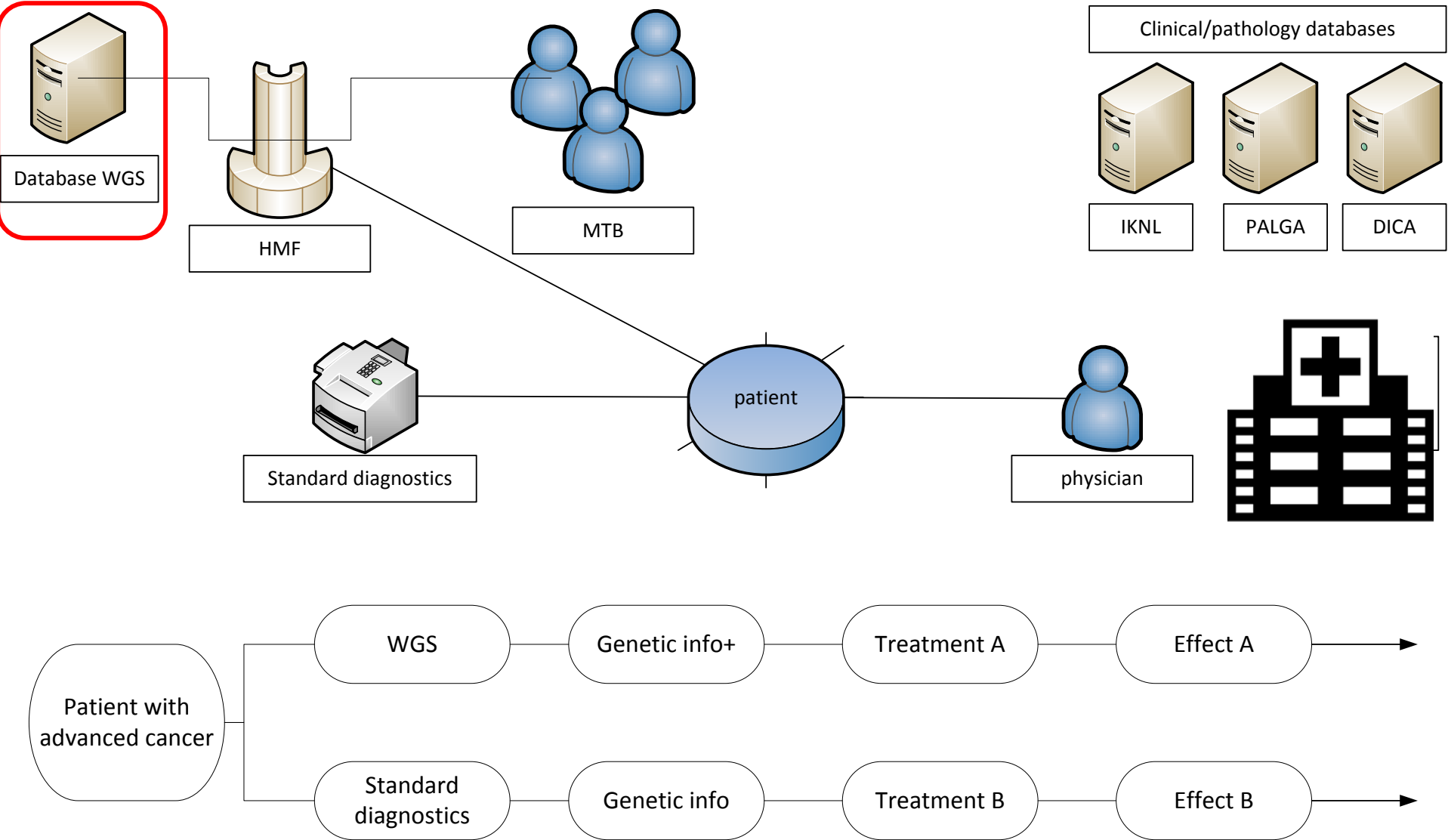
Cost-effectiveness model: H-Target model

Hybrid: decision tree (grey) + multi state model (blue)

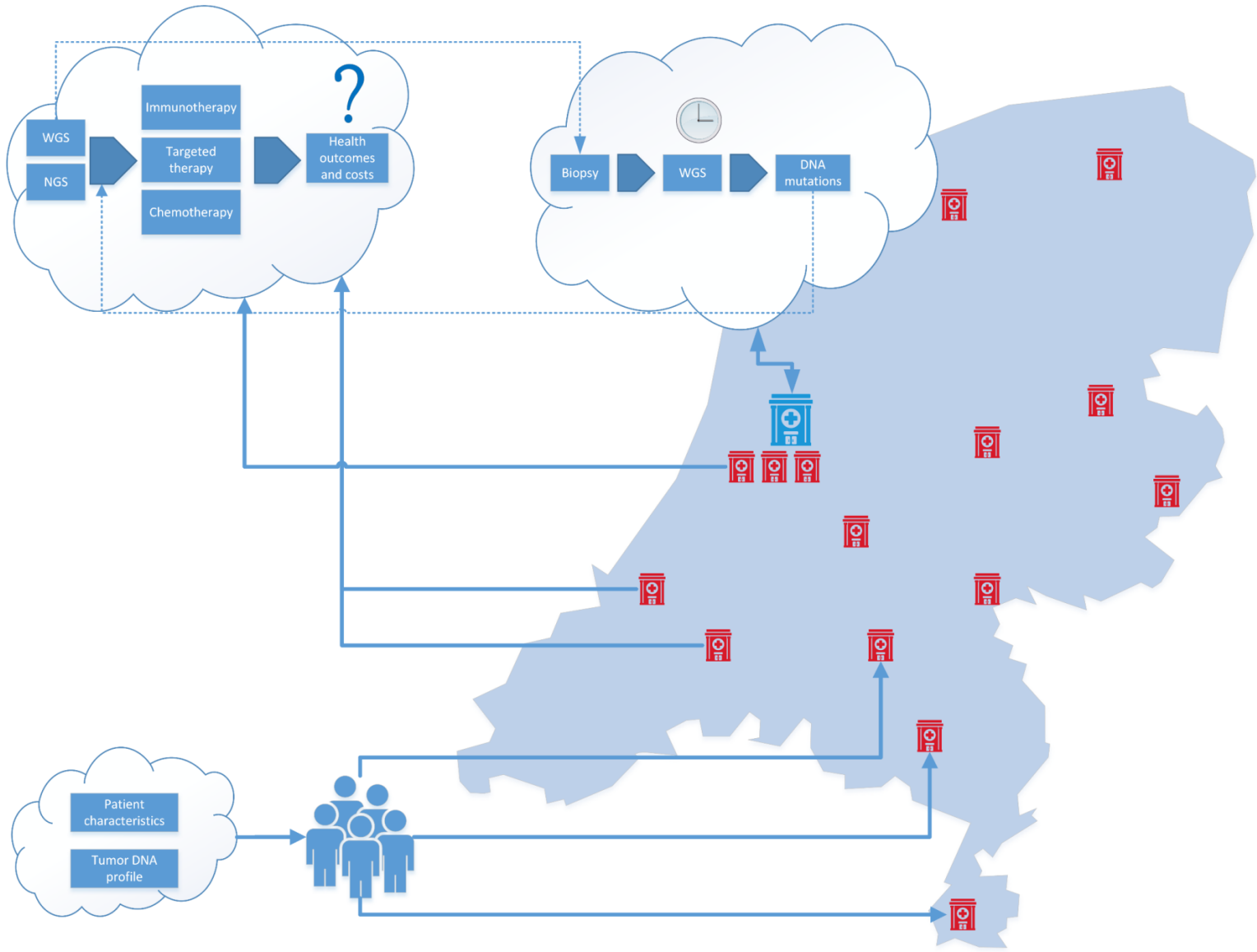




Cost-effectiveness: “future value”

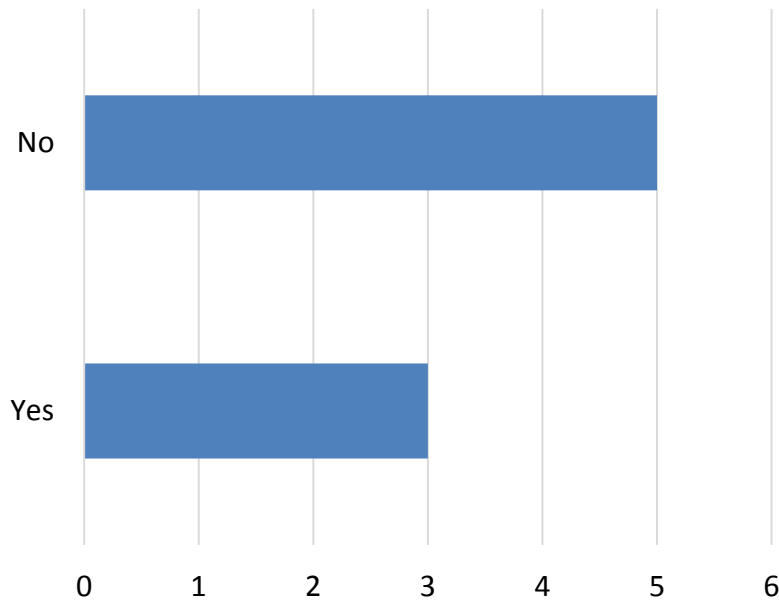


WP5: System dynamic model

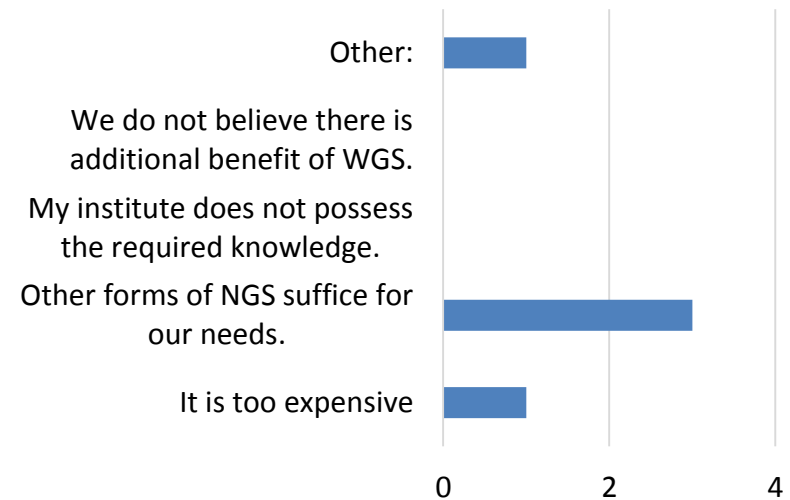


International survey on the future of WGS

According to your expectations, will your institution use WGS in the future?



What is / are the reason(s) that your institute will not be conducting or using WGS?



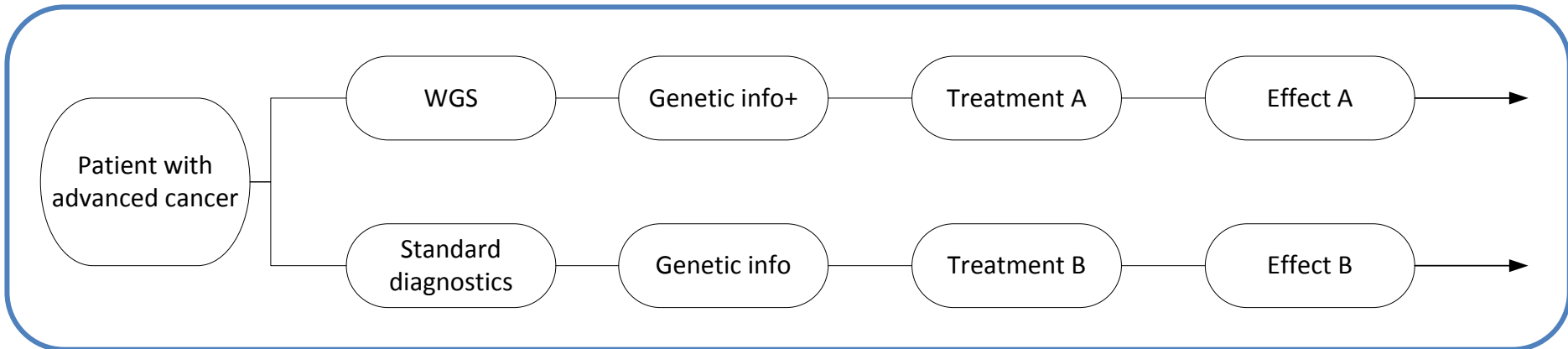
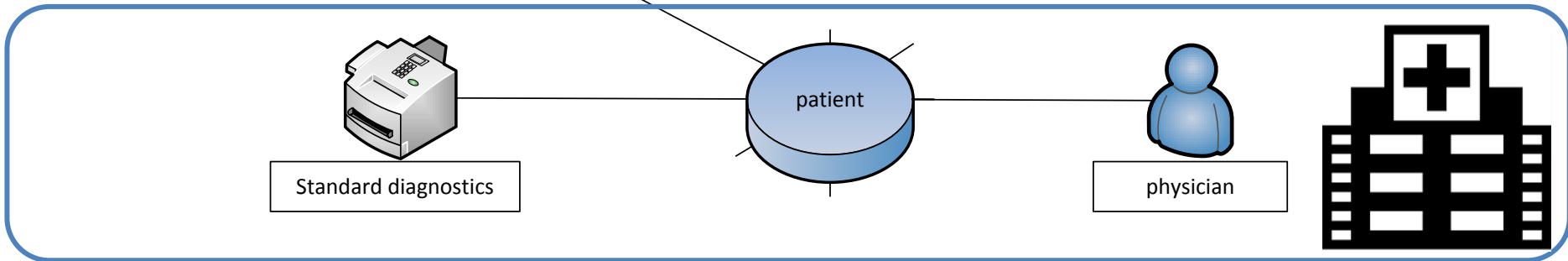
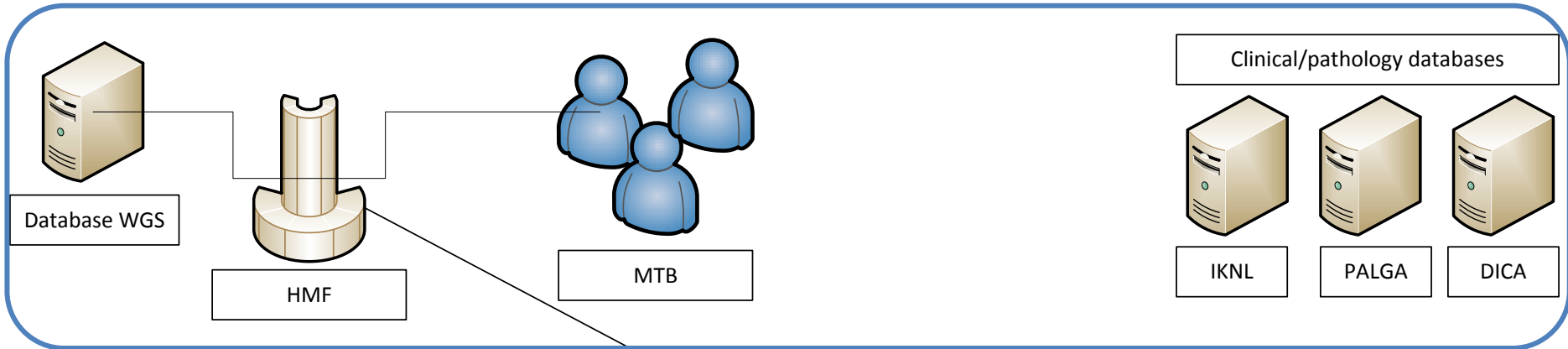


Scenario drafting (WP4&5)

- The turnaround time of WGS will in the next 5 years become equal to standard diagnostics
 - > How likely is this scenario?
- The costs for WGS will be twice as high as standard diagnostics
 - > How likely is this scenario?
- WGS will be in routine practice as a diagnostic tool for advanced NSCLC
 - > How likely is this scenario?

System level: WP6

WP4,5,6





Ethical & legal implications

- Focus on duty to recontact
- First legal framework, afterwards ethical focusgroups
- First conclusion legal: no grounds for the existence of a “relative” duty
 - > recommendation to prepare guideline



Planning

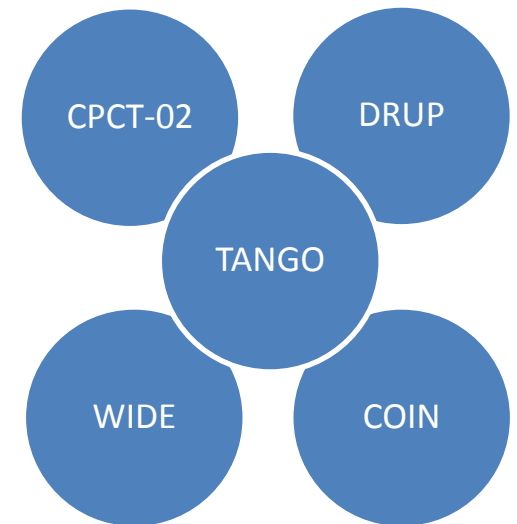
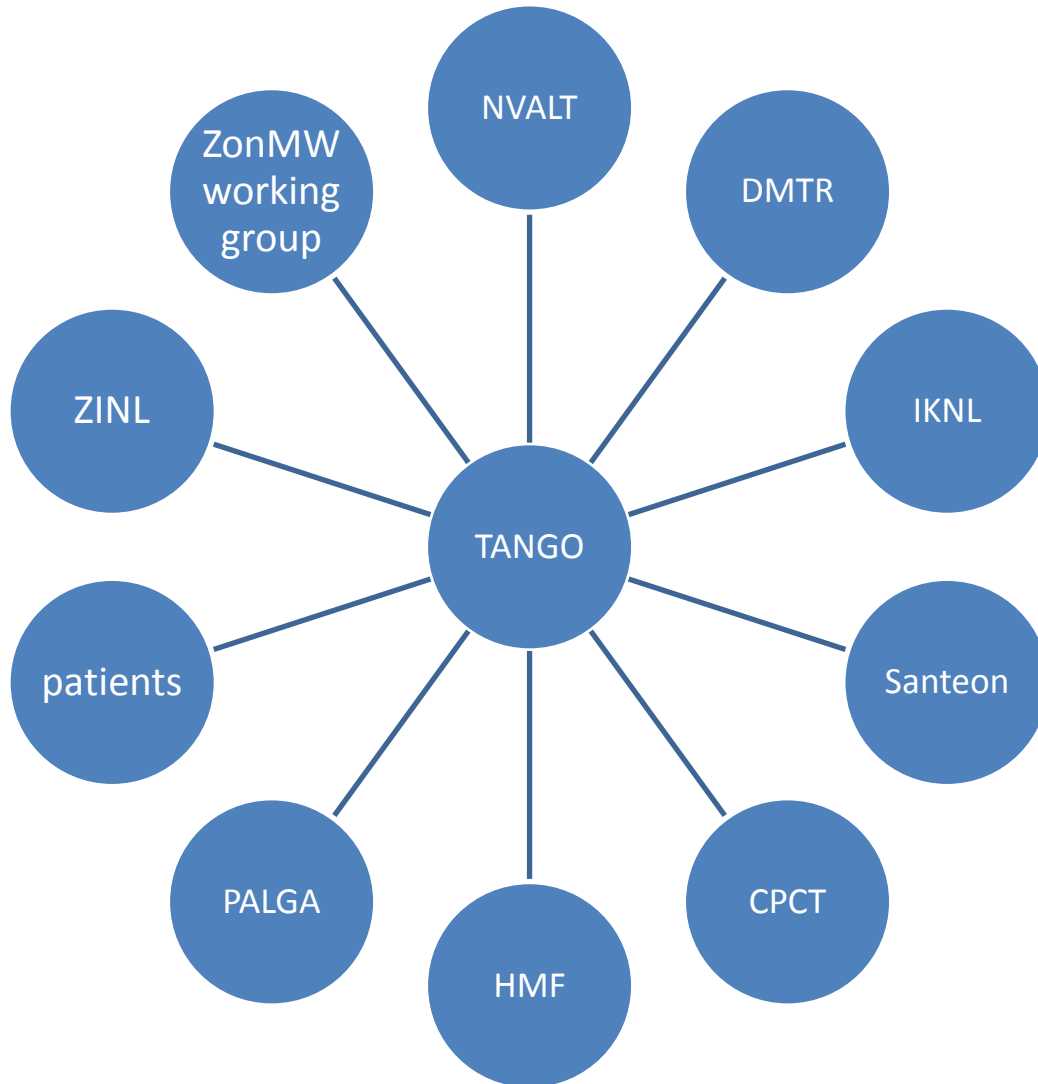
WP1	-finish costs standard diagnostics
	-analyze data for comparison SD & WGS
WP2	-analyze data for comparison SD & WGS
	-finish statistical plan
WP3	-analyze survival data from databases
	-tumor growth models
WP4	-analyze cost-effectiveness tumor-overarching
	-wider public benefits, scenario drafting
WP5	-analyze system dynamic model
	-scenario drafting
WP6	-finish legal papers
	-start patient and professional focus groups



Overall milestones

- Presentations
 - CPCT-HMF symposium 2018
- Congress:
 - Health-RI 2017
 - SMDM: concept model TANGO HTA 2018
 - Mini symposium TANGO 2018

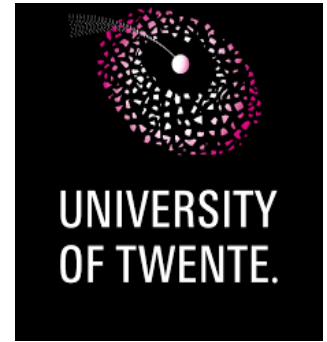
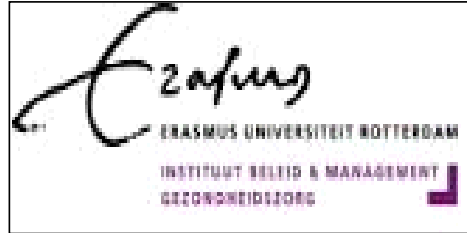
Collaborations/networks



Acknowledgements



Collaborating hospitals & institutions



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